Medical-treatment Recommendation and the Integration of Process Models into Knowledge-based Systems

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Keywords: Ontologies, Rule-based Reasoning, Cardiac Rehabilitation Processes, Clinical Decision Support Systems.

Abstract: Decision making based on evidence other than human reasoning is becoming increasingly important in healthcare. Valuable evidence is in the form of treatment processes used by healthcare institutions and this paper presents a new framework for representing and modeling knowledge from these processes. Specifically, it presents the integration of data from literature, business processes and decision trees through workflows that cover the full cycle of health care, from diagnosis to prognosis and treatment. With respect to patient status, as single instants cannot convey sufficient information, time series are analyzed and classified to improve decision-making ability. The elicitation of new knowledge takes into account international standards, ontologies, information models, nomenclatures and multiple types of indicators. The integration of formal process-modeling in knowledge-based systems is exemplified by a real-world recommendation scenario. After evaluation with a medical-rehabilitation data set, results show a strong correspondence between treatment recommended by the proposed system and clinical practice.

1 INTRODUCTION

In *medical rehabilitation*, to evolve from the current situation to a more individualized one and to solve interoperability problems, the involvement of all stakeholders in the development of models for *rehabilitation processes* is needed. Clinicians use guidelines, workflows and experience in the form of past cases.

Here, we focus the attention on the integration of *past cases* and *workflows* as a valuable source of implicit knowledge not previously recognized by clinicians. Because workflows are often informally described (e.g., in diagrammatic languages, such as the *business process modeling notation* or the *unified modeling language activity diagram*), they cannot be automatically included into a computational reasoning system, but need to go through some sort of nontrivial formalization process. For this, a variety of languages can be used, viz. procedural languages (e.g., the *business process execution language*) or highly-formal languages (e.g., *Petri nets*). Existing knowledge, including case libraries when a *case-based reasoning* (CBR) system is used, constitutes the input source for workflows, and the output data of these workflows are then delivered back to knowledge containers as well as case libraries.

Effective management of processes is critical to the development as well as sustainment of rehabilitation capabilities. In the context of this paper, a *process* defines a description and ordering of work activities across time and space that is designed to yield specific results or services while ensuring the rehabilitation's overall objectives. It provides a conceptual basis for the integration and coordination of distributed resources, tasks and individuals (Cichocki et al., 1998).

Process models produced by healthcare experts are represented as formal rules, providing a framework that allows their semantic enrichment. Whilst some progress in this direction has been made in recent research (Jafarpour et al., 2011; Peek et al., 2011 and Smith et al., 2012], the integration of data from *literature*, *business processes* and *decision trees* through workflows that cover the full cycle of health care, from diagnosis to prognosis and treatment, has not been presented before.

The rest of the paper is organized as follows. Section 2 introduces a real-world scenario with 200

Subirats L., Ceccaroni L., María Maroto J., de Pablo C. and Miralles F..
Medical-treatment Recommendation and the Integration of Process Models into Knowledge-based Systems.
DOI: 10.5220/0004822004910498
In *Proceedings of the 6th International Conference on Agents and Artificial Intelligence* (ICAART-2014), pages 491-498
ISBN: 978-989-758-015-4

cases, which illustrates the complexity of the domain at hand. Section 3 describes the methods and the architecture of a reasoning system that provides recommendation about personalized rehabilitation therapy and prognosis. Section 4 presents the results of the application of the recommendation system to the real-world scenario. Finally, conclusions and future work are drawn in Section 5.

2 SCENARIO

This study is based on the anonymized data of 200 patients who performed cardiac rehabilitation at the Hospital Universitario Ramón y Cajal that is summarized in Table 1. The map of processes performed in cardiac rehabilitation programs at the Hospital Universitario Ramón y Cajal is described in Calvo et al., (2013). We will consider, as representative examples, the *Walking* and the *Relaxation sessions* activities. Each activity is part of a hierarchy; the *Walking* activity, for example, is a subprocess of *Motor rehabilitation*, which is a subprocess of *Cardiac rehabilitation*.

Let us consider a 50-year-old man from Spain (the patient), who suffered an acute myocardial infarction. (This refers to the condition when blood supply to the heart is stopped. When the heart does not get enough oxygen, heart muscles die or get permanently damaged.) Now, two weeks after his hospital discharge, he starts a cardiac rehabilitation program. His initial evaluation shows he has some risks factors, such as smoking and hypertension, and some problems with his functional capacity, measured in *metabolic equivalent of task* (MET). His left ventricular ejection force is normal, and he does not have problems with anxiety, depression, dyslipidemia, sedentary lifestyle, diabetes, alcohol, abdominal perimeter or body mass index. His therapist wants to plan a personalized rehabilitation process for him. The aim of the *clinical decision support system* (CDSS), apart from providing him a summary of his main indicators, is to provide her:

- **Personalization of the Treatment.** It provides a recommendation about the personalization of a treatment, such as the intensity of the *Walking* activity, if the *Relaxation* activity should be performed.
- **Prognosis.** The state of risk factors such as hypertension and other indicators after rehabilitation treatment can be predicted.

Therefore, his therapist, based on her knowledge and experience, decides to prescribe the patient a *Cardiac rehabilitation* process including the *Walking* activity and the *Relaxation* activity. His therapist documents her decision in the rehabilitation platform which the CDSS is integrated to. The next week, our patient starts the first rehabilitation session of the *Walking* activity. The aim of the CDSS in this stage of the rehabilitation process is to **personalize the session** providing the therapist support about when to stop it. Figures that summarize the map of processes performed in the cardiac rehabilitation scenario, the methodology and the main structure of the ontology can be found at https://code.google.com/p/cardiacrehabilitation/wiki/Summary.

3 METHODOLOGY

The proposed rule-based framework is composed of five components.

(1) **An *ontology***, written in the *ontology web language* (OWL) with rules implemented in the *semantic web rule language* (SWRL). SWRL was chosen because it is a *de facto* standard to extend OWL and can be easily integrated in Protégé (the editor used to define the ontology). Rules are extracted from several sources with different levels of interpretation: literature (requiring more interpretation), business processes and decision trees (requiring less interpretation):

Business Processes are modeled using *business process modeling notation* 2.0 (BPMN). BPMN was chosen for being a standard for business process modeling. These rules are used to personalize a session.

Literature rules can be extracted from Velasco *et al.* (2009). These rules are used to provide prognosis and to personalize a rehabilitation treatment.

Decision Trees are obtained using Weka, a data mining and machine learning software. Weka was chosen for being a Java-based open source tool. The J48 classifier is applied to the Hospital Universitario Ramón y Cajal data set to obtain personalization of *psychotherapy* and *psychotropic therapy* and predict risk of *hypertension*, *emotional functions* and *exercise tolerance functions.* Due to the limited number of patients, only solutions which a certain level of recall and precision set by the professional are taken into account. These rules are used to provide prognosis and to personalize a rehabilitation treatment.

(2) **A *reasoner***, Pellet, which infers properties

and relationships from rules. Pellet was chosen because it is an open-source Java OWL DL reasoner with SWRL-support.

(3) **A *querying system***, SPARQL Protocol and RDF Query Language (SPARQL), to perform the queries.

(4) **A *Java framework***, Jena, to link with data applications.

(5) **A Java-based *content management system*** (CMS), Liferay, to provide an interface to interact with users. The CMS includes the *medical health record* (MHR) were data from patients is stored. SPARQL, Jena and Liferay were chosen because they are open-source Java-based systems.

This section includes a description of the ontology's structure and examples of rules and queries.

3.1 Ontology

Data obtained from the MHR of the hospital are expressed as *virtual medical record* (vMR) classes. The vMR is an information model developed within HL7, which is designed to solve interoperability problems in the electronic exchange of clinical information and to reduce development costs and time responses in CDSSs that use it. The vMR is used by the CDSS and stored in an ontology.

Evaluated Person (subclass of *Person)* contains patient's static information such as birth time and sex. *Problem* is used to represent diseases, following the ICD-10, such as myocardial infarction, chronic rheumatic heart diseases, heart failure, atherosclerosis, other peripheral vascular diseases and congenital malformations of the circulatory system. *Observation Base* (subclass of *Observation*) is coded following the ICF and is used to represent indicators, such as risk factors (e.g., tobacco, hypertension, alcoholism, body mass index, sedentarism, abdominal perimeter, arrhythmia, creatinine, glucose), range of emotion, walking activity, functional capacity, left ventricular ejection fraction, state-trait anxiety inventory, Beck depression inventory, and work situation. Data are available in three instants of time: before disease, before rehabilitation, and after rehabilitation. *Goal* is used to represent the indicators whose value we want to predict. Finally, *General Knowledge* is used to represent the recommended therapeutic plan and includes: (1) *medical and surgical procedures*, such as surgical revascularization, valve prosthesis, corrected congenital pathology, defibrillator implantation, pacemaker implantation or arrhythmias correction, (2) *processes*, such as intense aerobic exercise, motor rehabilitation, psychological rehabilitation, and (3) *specific activities*, such as walking or psychotherapy.

These standard annotations of processes and result indicators from biomedical ontologies and terminologies (ICF, SNOMED CT, ICD-10 and ICD-11) are used in a semantic, rule-based framework.

3.2 Rules

Rules are extracted from literature, a fragment of BPMN 2.0 and decision trees from classification algorithms; needing different degrees of human interpretation during the formalization process. In

Table 1: Summary of some attributes of the cardiac data set (SD = standard deviation).

Attribute: options (separated by /)	**Values**	**# Missing values**
Gender: man / woman	163 / 37	0
Age	[11, 78], Mean: 53, SD: 14.3	0
Left ventricular ejection fraction (LVEF)	[0, 89], Mean: 35, SD: 29.4	35
METs before rehabilitation	[2, 12], Mean: 7, SD: 2.3	57
Beck index before rehabilitation	[0, 34], Mean: 8, SD: 6.2	35
Psychotherapy: yes / no	15 / 157	15
Psychotropic therapy: yes / no	6 / 166	28
Exercise tolerance after rehabilitation: no / mild / moderate / severe / complete deficiency	19 / 58 / 51 / 20 / 4	48
Emotional functions after rehabilitation: no / mild / moderate / severe / complete deficiency	93 / 48 / 18 / 4 / 1	36
Hypertension risk after rehabilitation: low / medium / high	94 / 39 / 43	24

this section, rules to execute therapies, define activities, execute activities and evaluate patients are specified using SWRL. All rules are available at [http://code.google.com/p/cardiacrehabilitation]; in the following paragraphs a representative set of examples is described in details.

Rules from Rehabilitation Processes Written in BPMN 2.0. In Fig. 1 it is modeled the *Walking* activity as an example. The tasks carried out (by different actors) in the *Walking* activity are: routine personalization; time personalization; pulsometer placement and heart rate measurement; warm up; walk; cardiac frequency observation; cool down; basal heart rate measurement; patient's activity evaluation. The core tasks of the *Walking* activity consist of the three typical phases of a walking physical exercise in an open environment outside of a healthcare institution: *Warm up*, *Walk* and *Cool down*, each of which has a predefined duration, which can be respected or not by the patient. In the *Walking* activity, three indicators are monitored and their values are stored in a MHR. (1) *Treatment-result* indicators, which are periodically quantified. METs are extracted from an exercise testing is a treatment-result indicator. (2) *Process* indicators are execution, security or end-session. In this activity heart rate is a process indicator. (3) *Session* indicators to indicate the end of the session. In the walking activity maximum heart rate, Borg score, walked distance and walked time are session indicators. As described in Section 1, decision support is provided to the *Walking* activity in prognosis and session's personalization. The walking activity ends when one of the following conditions is reached in the *patient's evaluation* if a certain level of *maximal oxygen consumption* (VO_2 max); the maximum heart rate below a predefined limit and the walked distance above a predefined limit.

The *Relaxation* activity is included in *Psychological rehabilitation*, which is a subprocess of *Cardiac rehabilitation*. It is modeled in a similar way as the *Walking* activity in Fig. 1. The tasks performed in the *Relaxation* activity are: place the patient, relaxation tasks and patient assessment. The core tasks of the *Relaxation* activity consist of inhaling, exhaling, muscle contraction and muscle extensions. In the *Relaxation* activity, several **indicators** are monitored and their values are stored in a MHR. Treatment result-indicators are *occupational status* and *Beck depression inventory* (BDI); process indicators are *depth of inhalation, depth of exhalation* and *muscle activity*; and activity result-indicators are *therapist visualization*, *measuring tape*, *Borg scale* and *anxiety assessment*.

As an example, let us consider rule (1), below, which ends an activity if a process indicator is greater than or equal to 2 (moderate deficiency).

ActivityEnd (?ae),
ProcessIndicator (?pi),
Patient (?p),
greaterThanOrEqual (?pi, 2),
hasIndicator (?p, ?pi)
→ *hasNextTask (?p, ?ae)* (1)

This codification means that, if a patient *p* has a process indicator *pi* which is greater than or equal to 2, the activity is stopped and the next task is *ae*. Similar rules are applied to several process indicators of rehabilitation activities. Process indicators are used to stop activities because of severe alterations in body functions (such as a too high heart rate) or in environmental factors (such as a too high temperature or humidity).

Rules from Cardiac Rehabilitation Literature. The risk of having another infarction after cardiac rehabilitation is translated to rules using semantic annotations. Problems appear when there are partial matches in rules. To solve them, priorities among attributes are established according to the proximity to the root of the generated decision tree after applying a classifier. These priorities are: disease, tolerance to exercise, contraction force of ventricular muscles and heart rhythm. A sample rule is (2), which predicts that a person will have medium risk of suffering a myocardial infarction, if a patient has thallium stress test abnormal, a severe deficiency in the treatment indicator of contraction force of ventricular muscles and has suffered an angina pectoris.

Patient (?p),
Thallium stress test abnormal (?th),
hasIndicator (?p, ?th),
Contraction force of ventricular muscles (?cfvm),
Deficiency (?severe),
hasDeficiency (?cfvm,?severe),
TreatmentIndicator (?ti),
hasType (?cfvm,?ti),
hasIndicator (?p, ?cfvm),
Angina Pectoris (?ap),
hasDisease (?p, ?ap),
Risk (?mediumRisk)
→ *hasRisk (?p, ?mediumRisk)* (2)

Rules from Decision Trees. The J48 classifier from Weka is applied on data sets about *psychotherapy*, *psychotropic therapy*, risk of *hypertension* and prognosis of *emotional functions* and *exercise tolerance functions*; and rules are obtained from the resulting decision trees. An example is the rule (4), which predicts that if a patient does not suffer from arrhythmia, has as treatment indicators a severe deficiency in emotional functions and dyslipidemia less than or equal to 3 (severe deficiency) and follows a psychotropic therapy; the prognosis of the treatment indicator of emotional functions after cardiac rehabilitation is no deficiency.

Patient (?p), Arrythmia (?a), hasnotDisease (?p, ?a), Dislipidemia (?di), TreatmentIndicator (?ti), hasType (?di,?ti), lessThanOrEqual (3, ?di), hasIndicator (?p, ?di), hasTherapy (?p, ?psychotropic), EmotionalFunctions (?ef), Deficiency (?severe), hasDeficiency (?ef, ?severe), hasType (?ef, ?ti), EmotionalFunctions (?efa), Deficiency (?no), hasDeficiency (?efa, ?no), CardiacRehabilitation (?cr), after (?efa, ?cr), hasType (?efa,?ti)
→ *hasIndicator (?p, ?ef)* (4)

This rule is part of the implementation of the decision tree in Fig. 2.

3.3 Querying

The proposed framework allows querying using *SPARQL*. The following example shows how the definition of the *Walking* activity is used by the therapeutic plan. First, the system evaluates which session indicators the patient should improve through the following query:

Count(?i) where Patient (?p),
SessionIndicator (?i), Deficiency (?mild),
hasDeficiency (?i, ?mild),
has Indicator (?p, ?i) (5)

Then, activities which cover this objective are shown. If Apollo wants to improve his *exercise tolerance functions,* the query would be:

Select (?a) where Activity (?a),
Exercise Tolerance Functions (?i),
has Objective (?a, ?i) (6)

Finally, it is checked if the activity is not contraindicated to the patient. In the *Walking* activity, the corresponding query would be:

Count (?contraindication) where Patient (?p),
Moderate, severe or complete neuromusculoskeletal and movement-related functions (?mscn),
has Contraindication (?p, ?mscn) (7)

4 RESULTS

Results are based on the application of the cardiac rehabilitation scenario described in Section 1. Fig. 3 shows the interface of the CDSS provided to the therapist. The interface shows an initial diagnosis which includes causes of the functional limitation, past procedures and functioning indicators. Functional diversity levels of indicators are represented as red/4 (complete), orange/3 (severe), yellow/2 (moderate), green/1 (mild) and blue/0 (no functional diversity) (Subirats et al., 2013). The

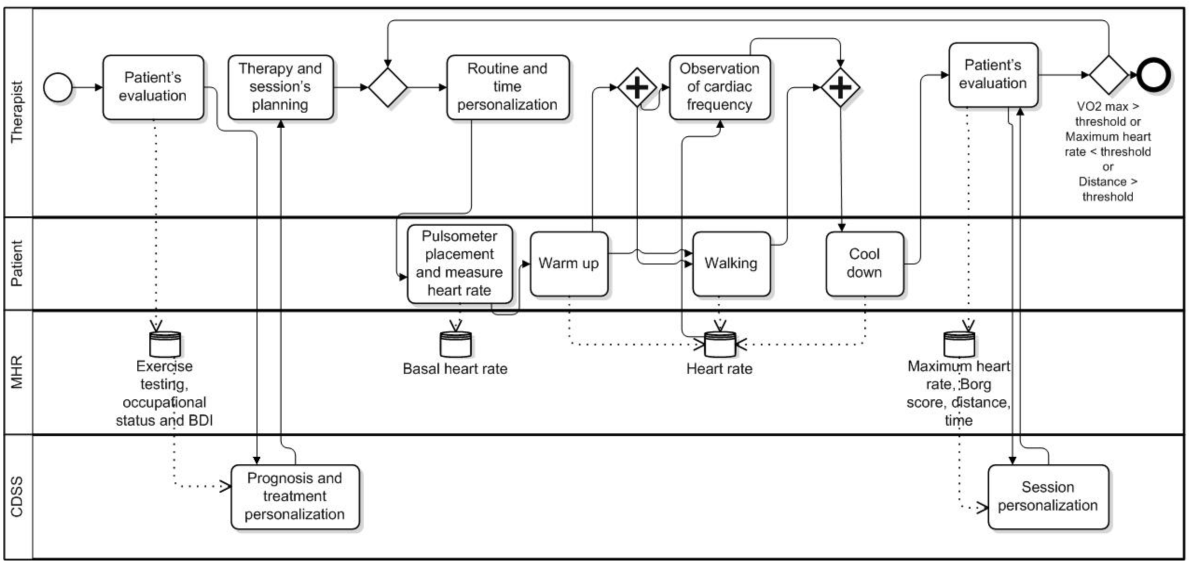

Figure 1: Cardiac rehabilitation processes.

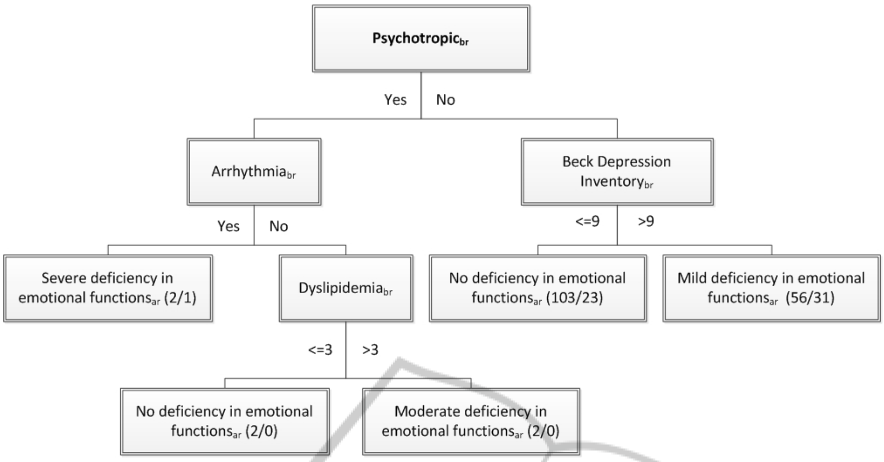

Figure 2: Decision tree of emotional functions prognosis (br = before rehabilitation; ar = after rehabilitation); in brackets, total/misclassified instances reaching the leaf.

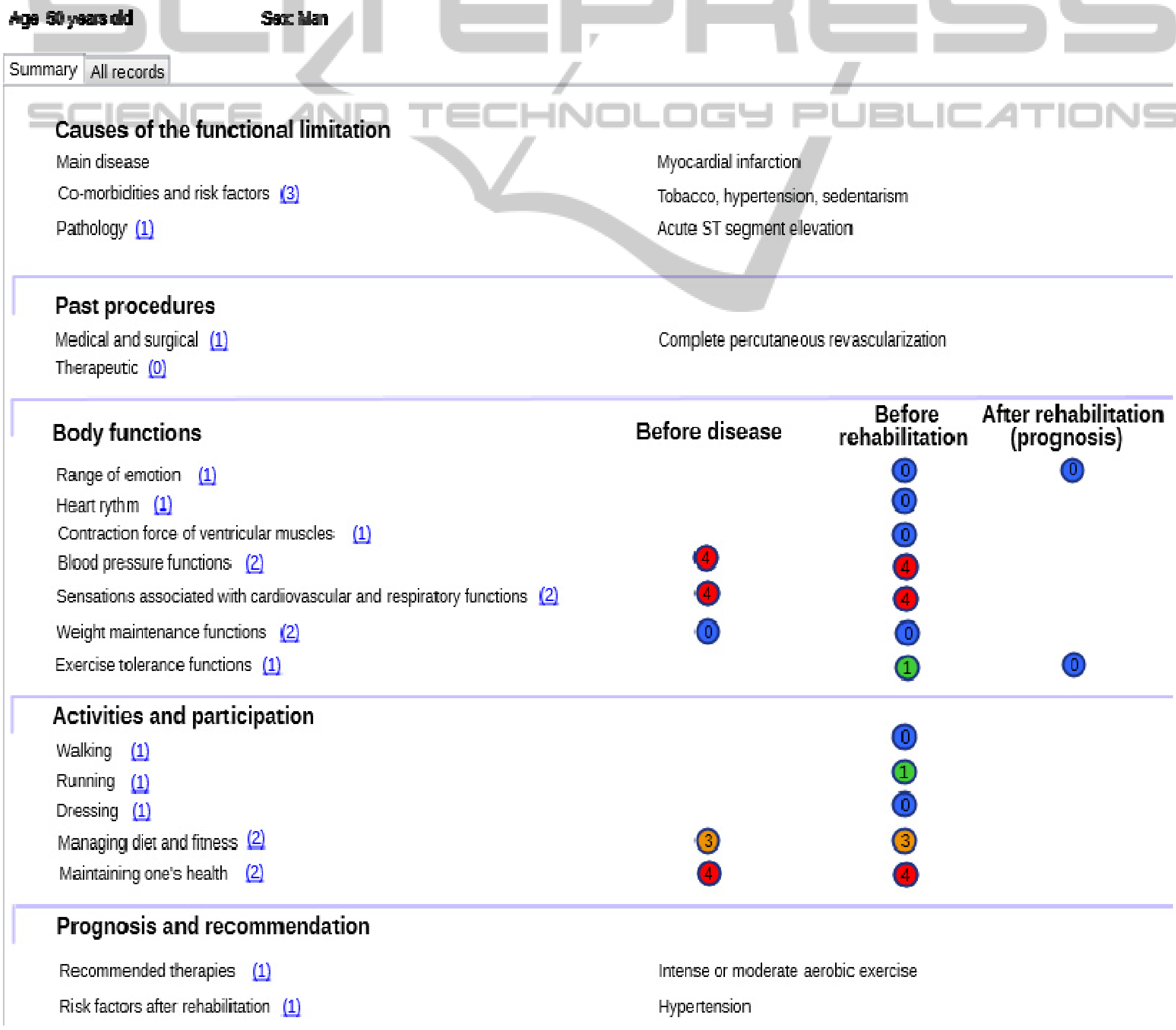

Figure 3: CDSS's interface of patient's prognosis and personalization.

Table 2: Evaluation of the CDSS.

Decision support	**Treatment or treatment indicator: possible solutions** (separated by /)	**Accuracy**	**Precision**	**Recall**
Personalization of the treatment	Psychotherapy: yes / **no**	0.8	0.2 / 0.9	0.6 / 0.8
	Psychotropic therapy: yes / **no**	0.9	0.2 / 0.9	0.3 / 0.9
Prognosis	Exercise tolerance functions after rehabilitation: no / **mild** / moderate / severe / complete deficiency	0.5	0.2 / 0.6 / 0.5 / 0 / 0	0.1 / 0.8 / 0.6 / 0 / 0
	Emotional functions: **no** / mild / moderate / severe / complete deficiency	0.6	0.7 / 0.5 / 0.3 / 0 / 0	0.8 / 0.4 / 0.2 / 0.1 / 0
	Hypertension risk after rehabilitation: **low** / medium / **high**	0.7	0.8 / 0.8 / 0.6	1.0 / 0.4 / 0.8
	Infarction risk: **low** / **medium** / **high**	0.9	0.9 / 0.9 /1.0	0.9 / 0.9 / 1.0

prognosis of the treatment indicators *range of emotion* and *exercise tolerance functions* are provided, and in the prognosis section it appears the recommended therapy (that in this case *is intense or moderate aerobic exercise* and *hypertension* risk factor after rehabilitation).

Rules are evaluated through the correct execution of the cardiac rehabilitation process in order to verify completeness of the rule set. However, the knowledge of the system can increase/change over time due to (1) more patients (rules from decision trees can change), (2) an update of processes; and (3) an update of literature. As all rules in this model are static, in the future, a Java library which generates decision trees using Weka, converts them automatically to SWRL rules, and integrates them in the ontology will be created.

Table 2 shows the evaluation of the personalization of therapies, prognosis and risk. In order to evaluate the performance of prediction of treatment indicators' behavior, *accuracy*, *recall* (or sensitivity) and *precision* (or positive predictive value) are considered and defined as follows:

$$accuracy = \frac{TP+TN}{TP+FP+FN+TN},\ precision = \frac{TP}{TP+FP},$$
$$recall = \frac{TP}{TP+FN}.$$

where TP are *true positives*, FN are *false negatives*, FP are *false positives* and TN are *true negatives*. Considering that low values of recall can cause potential harm in the clinical domain, hypothesis which higher values of recall are generally considered better, while maintaining precision above a specific threshold set by an expert (Huang et al., 2006). In the personalization of the treatment, the CDSS has recall values of 0.8 and 0.9 when recommending *not to prescribe psychotherapy* and *not to prescribe psychotropic therapy*, respectively. In the prognosis of *exercise tolerance functions after rehabilitation*, recall values for *mild* and *moderate deficiency* are 0.8 and 0.6, respectively. In the prognosis of *emotional functions*, recall values for *mild* and *no deficiency* are 0.4 and 0.8, respectively. In the prognosis of *hypertension risk after rehabilitation*, the recall value for *high risk* is 1.0. In the prognosis of *infarction risk*, recall values for *low, medium* and *high risk* are 0.9, 0.9 and 1.0, respectively; however, in this case, the CDSS was tested only on 19 patients. Some very low recall and precision values are due to classes with a very low number of cases (see Table 1). This is the case, for example, of *severe* and *complete deficiency* in *emotional functions*.

Paths of the decision trees which correspond to predictions with a recall less than 0.8 or a precision less than 0.6 are not encoded as rules. In these cases, consequently, no support is provided to therapists. Paths of the decision trees which are encoded as rules correspond to bold values in the *Treatment or treatment indicator: possible solutions* column of Table 2.

In Van et al. (2011), a study that predicts risk factors with decision trees with data from 3931 patients, the accuracy of the prediction of *emotional functions* (which is the ICF encoding of the Hospital Anxiety and Depression Score) is 0.5, while the accuracy of the prediction of *hypertension* is 0.5. Although the accuracy of the prediction of emotional functions and hypertension is a little bit higher in the proposed approach than in the study of Van *et al.* (2011), this approach is not able to predict minor classes. On the other hand, the study of Chang *et al.* (2011), predicts the risk factors of hypertension and hyperlipidemia with a combined accuracy of 0.9.

5 CONCLUSIONS

This paper introduced a framework, based on rules from three sources (business processes, literature and decision trees) and including biomedical annotations, to provide formal semantics to cardiac rehabilitation processes represented in BPMN 2.0. This semantics, together with rules obtained from literature and data mining, can be used to introduce automatic reasoning in decision support. The rule-based framework uses existing ontologies and formal process notation to enhance interoperability and reasoning in rehabilitation and, specifically, to allow working with different types of indicators, and to merge medical ontologies and terminologies such as ICF, SNOMED CT, ICD-10 and ICD-11.

Different issues appeared when implementing rules obtained from sources needing different degrees of human interpretation. Difficulties due to the high number of rules coming from BPMN 2.0 processes were solved generalizing them. And only rules from decision trees which have recall and precision above a threshold of 0.8 and 0.6, respectively, were encoded.

The proposed CDSS, which uses data from 200 patients carrying out cardiac rehabilitation at a hospital, has high values of recall in the personalization of therapies, and in the prognosis of activities and risk factors.

Future work includes making the framework more dynamic and able to automatically reorganize itself when new or updated data or processes are available. In addition, more cases will be analyzed to cover classes which are less represented in the knowledge base.

ACKNOWLEDGEMENTS

The research described in this paper is partly supported by a Spanish research project called Rehabilita (Disruptive technologies for the rehabilitation of the future) (CEN-2009-1043). This work is also partly supported by the Catalonia Competitiveness Agency (ACC1Ó).

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