Towards a Clinical Practice Guideline implementation for asthma treatment

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Abstract. There is a tremendous amount of effort involved in the definition of Clinical Practice Guidelines (CPG) by physicians. Because the quality of medical assistance is highly impacted by the use of CPG, and establishing their use is difficult, we consider necessary to develop an effective solution that implements CPG through Decision Support Systems (DSS). Among the many existing representation models for CPG, we have selected and applied GLIF. In addition, we have created ontologies for the domains of asthma severity and Fuzzy Multicriteria Decision Aid approach (PROAFTN method). The results have been integrated into our DSS called Arnasa in order to provide support via Web to asthmatic patients.

1 Introduction

Several CPG have been developed in the last years in order to reduce the unjustified disparities in clinical practice, and therefore improve the quality of medical care while decreasing costs [5]. Because of the importance of using CPG, medical institutions should promote their implementation and deployment through computer systems, so that physicians are provided with decision support.

Given that Telemedicine is considered a strategic priority in developed countries [23], several studies [12] show that Clinical Decision Support Systems (CDSS) may improve the fulfilment of CPG by physicians, as well as results on patients [9] [26], as long as they are developed to provide specific decision support within the action context. The development of CDSS has been proposed as a strategy to promote the implementation of CPG [5]. However, the implementation of CPG through CDSS faces the difficulty of translating the CPG narrative format to an electronic format that is suitable as a Computer Interpretable Guideline (CIG). Moreover, we should not forget about the integration to existing medical records.

A possible solution to this problem is to develop a unique and standard representation model that allows sharing the guidelines among different medical institutions, offers consistency while interpreting the guidelines, reduces costs, and puts together the needed efforts for creating and improving the model quality and its tools.

On the other hand, the use of CIG in the medical environment offers decision aid, reduces ambiguities, assures the quality of medical care, and improves patients' education. Because of the appeal of this research direction, different representation models have been defined [29]. Some of them use ontologies [7] for specifying and reusing medical knowledge, and make use of frames for the representation [13].

For these models to be effective, they have to be integrated to existing medical records so that they procure individual information for each patient, use a standard medical vocabulary, and are expressive enough.

In the decision nodes of the CPG, recommendations are offered to the user. They are calculated by means of Multicriteria Decision Aid (MCDA) methods [21].

We have planned the following goals for this present work:

1. Development of an ontology for representing the knowledge in the asthma domain.
2. Development of an ontology for representing the knowledge in the MCDA domain, which will be used by the CPG whenever they need to make assignments.
3. Representation of the asthma CPG and the Fuzzy Multicriteria Assignment Method PROAFTN through the GLIF model ontology, and integrating both representations with the previously developed domain ontologies.
4. Evaluation of tools for representing and executing processes.

Obtaining an effective solution to the real problem of asthma through the implementation of a CPG would improve the way this disease is treated and hence patients' quality of life.

On the other hand, if we consider the management of asthma treatment to be similar to managing a process, the results of the present work could be reused for managing other domain's processes without major additional efforts. Software development is a domain with a special interest for us, particularly the support to project management and the development process. It would make significantly easier to build complex solutions in Telemedicine. We follow similar methods in both lines.

The present paper describes the work performed in order to implement the asthma CPG. This implementation includes the integration of an ontology for the asthma domain, and the MCDA method using the algorithm PROAFTN for multicriteria assignations. In the next section, we will introduce the work carried out in this area. In section 3, we will introduce the methods and resources employed; in section 4, the obtained results, and in the last one, the main conclusion gained from these results.

2 Background

After nine years of multidisciplinary work with medical staff from *Osakidetza – Basque Health Service* for research and development of DSS focused on the treatment of paediatrics chronic diseases [19][24], it is important to point out the importance of building safe and Web-accessible DSS that allow managing data and knowledge about CPG or processes.

Several representation models have been defined in the last couple of years [29]. These models offer the possibility to translate a CPG into CIG. An abstract of the latest models is shown on Table 1.

Table 1. Different representation models of CPG

		Beginning year	Ending year
ArdenSyntax	[10]	1990	->
Asbru	[15]	1996	->
EON	[27]	1996	2003
GASTON	[2]	1998	->
GEM	[22]	1999	->
GLARE	[25]	1997	->
GLIF	[17]	1998	->
GUIDE	[20]	1998	2000
PRESTIGE	[9]	1996	1999
PRODIGY	[11]	1995	->
PROforma	[6]	1998	->
Siegfried	[14]	1996	->

A recent study about the Asbru, EON, GLIF, GUIDE, PRODIGY, and PROforma models was coordinated by Stanford University [18] to extract similarities and differences that would lead to standardise them in the future.

The decision aid following the guideline can be realized through justified recommendations based on a classification method, which can connect the problem data to a set of categories or alternatives.

There are different analysis than can be obtained for an alternative: 1) identify the best alternative, 2) order the alternatives from the best to the worst, 3) classify the alternatives in predetermined homogeneous sets, and 4) identify the distinctive attributes to describe them. We will focus on the first, applying the PROAFTN method due to its classificatory capacity in the applying medical domain [1].

We will mention the asthma DSS developed by the Iowa University (USA)[26], because it follows a similar work line. It is a DSS implemented using CGI technology to evaluate the asthma severity, and offers recommendations based on the information entered by the user.

3 Materials and methods

Once we have examined all the existing methodologies [29], we chose GLIF as the model to implement the asthma CPG. There were several reasons for this decision. One of them is that its ontology (v. 3.5) is available, and includes examples and documentation. GLIF has been developed in agreement by several institutions. It supports multiple medical vocabularies and adds complementary specifications (Arden Syntax, HL7), which make it easy to incorporate to medical environments. This formalism can work as the foundation for a standard one taking the best from other modelling methodologies [3].

To provide a solution for the diagnostics problem, different methods were used: statistics, pattern recognition, Artificial Intelligence, and neuronal networks. The multicriteria decision aid (MCDA) approach is another approximation that uses the preference relational system described by Roy [21] and Vincke [28], for the comparison between the individuals to classify and the prototypes or reference objects from categories. Among the advantages that this approach offers, it is important to point out that it prevents distance measures reclassification. It allows using both qualitative and quantitative criteria, which helps when data is expressed in different units. Moreover, it uses both inductive (from clinical data) and deductive (from available knowledge) learning. It differs from other classifiers that use knowledge based on actual cases, meaning they only use deductive learning. But the main advantage of MCDA, compared to traditional methods based in a single global criterion, is the use of both concordance and non-discordance principles (non-totally compensatory) to determine the preference relations.

The recent application of the PROAFTN method to the diagnosis of acute leukaemia has obtained superior results compared to other methods like decision trees, production rules, K-NN, logistic regression, and multi-layer perceptrons [1].

In classification problems the PROAFTN method is capable of resolving multicriteria assignation issues. To begin with, we need a set of categories denoted by $? =\{C^1,\ldots, C^k\}$, a prototype set $B^h=\{b^h{}_1, b^h{}_{2},\ldots,b^h{}_{L_h}\}$ for each category and a set of attributes $F =\{g_1,\ldots g_n\}$, where each g_j is defined by an interval $[S^1{}_j(b^h{}_i), S^2{}_j(b^h{}_i)]$, being $S^2{}_j(b^h{}_i)$? $S^1{}_j(b^h{}_i)$, for j=1,..,n, h=1,..,k and i=1,.., L_h. With this information we can calculate the indifference indexes using (**1**), where $W^h{}_j$ is the positive coefficient that shows the relative importance assigned by experts to g_j from the C^h category. The addition of all coefficients $W^h{}_j$ is 1.

$$\mathrm{I}(\mathrm{a}, \mathrm{b}_i^h) \; ? \; (\overset{n}{\underset{j?1}{?}} (W_j^h x C_j(a,b_i^h)) x \overset{n}{\underset{j?1}{?}} (1 ? D_j(a,b_i^h))^{w_j^h}) \qquad (\mathbf{1})$$

Both the concordance $C_j(a, B^h{}_i)$ and the discordance $D_j(a, B^h{}_i)$ indexes are defined by the fuzzy sets from Fig 1. To get over the data inaccuracy the thresholds $d^+{}_j\ (B^h{}_i)$ and $d^-{}_j\ (B^h{}_i)$ are used. In order to indicate incompatibilities the $v^+{}_j\ (B^h{}_i)$ and $v^-{}_j\ (B^h{}_i)$ thresholds are used.

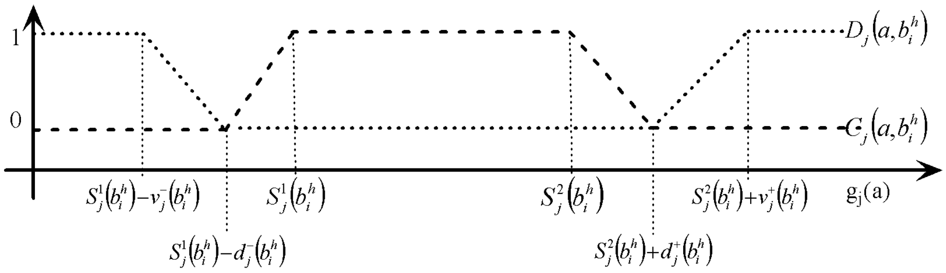


Fig. 1. Graphic for the partial indifference index between the object a and the prototype $b^h{}_i$, and the partial discordance index for that relation.

The fuzzy belonging degree for the object $d(a, C^h)$ from a category is evaluated through (2) using (3) to specifically assign an object to a category.

$$d(a, C^h) = max\{ I(a, B^h{}_1), I(a, B^h{}_2),\ldots, I(a, B^h{}_{Lh})\}, h=1,..,k \qquad (\mathbf{2})$$

$$a?\ Ch\ ?\ \ d(a, Ch) = max\{ d(a, Cl)/\ l?\ I\{1,..,k\}\} \qquad (\mathbf{3})$$

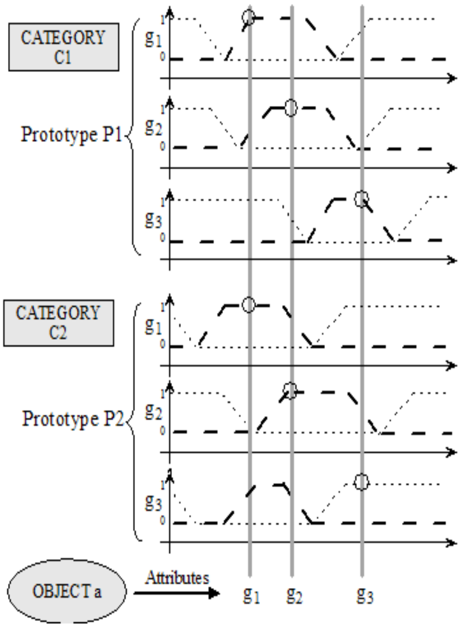


Fig. 2. A simple example of the PROAFTN's performance

To understand how PROAFTN works in an intuitive way, we provide the following example (Fig 2). Initially we have two categories, *C1* and *C2*, which define the prototypes P1 and P2 respectively. Each one of these prototypes has the attributes g1, g2, and g3 with their corresponding concordance and discordance. On the other hand, we have the object we want to classify along with its attributes g1, g2 and g3.
We start by calculating (1)

$$I(a, b1) > 0, \quad I(a, b2)=0$$

In this case we can see that I(a,b2) is zero due to its total discordance with the attribute g3. Next, we calculate (2)

$$d\ (a, C1)=max\{I(a,b1)\}=I(a,b1)>0$$
$$d\ (a, C2)=max\{I(a,b2)\}=I(a,b2)=0$$

Finally, the object a is classified as C1 by applying (3)

3.1 Resources

For the implementation of the asthma CPG, the written guides from the National Asthma Education and Prevention Program (NAEPP) [16], along with interviews with medical staff from the Cruces Hospital of Barakaldo (Basque Country) were used as information sources.

The development process that we have followed for the CPG ontology is the one defined by METHONTOLOGY [4], which is a methodology for ontology construction developed by the Polytechnic University of Madrid.

Regarding the tools we have used, we should at least mention the following ones. Protégé-2000 (v1.7) is a tool to build knowledge bases using frames that we have used as a development environment for ontologies. JESS (v 6.1) is an extensively known inference engine. FuzzyJESS (v 1.5) is an add-in for JESS that provided fuzzy logic capabilities. JessTab is a plug-in for Protégé that allows its connection to JESS.

4 Results

Our CPG implementation has been integrated into a DSS called Arnasa, which already has two previous releases built by ourselves, and is intended for monitoring asthma patients [24]. Its functionality is organized in several Web modules; each one specialized in a different area (e.g. security, visualisation of evolution data in 2/3D, consulting and localization of the user interface). For its implementation we have used J2EE technology (*Java 2 Platform, Enterprise Edition*).

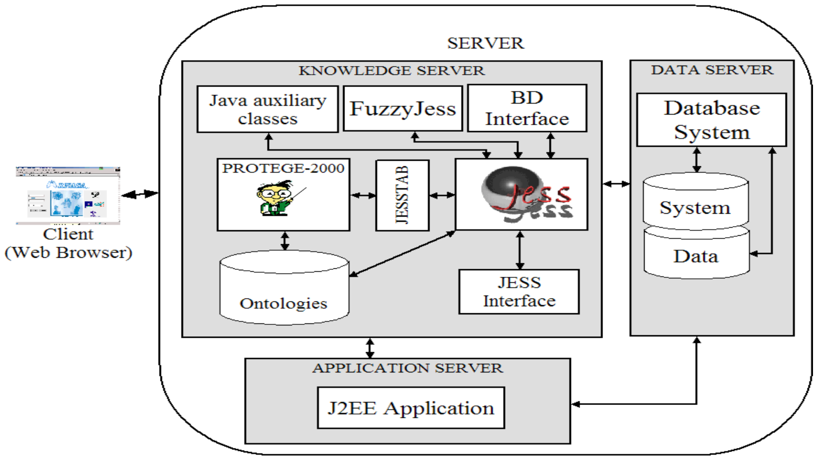


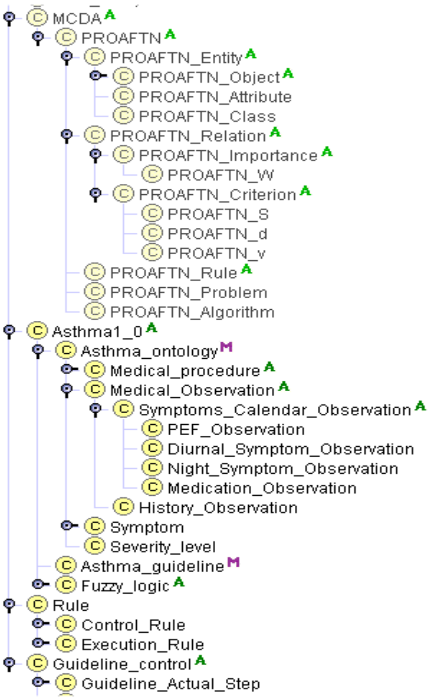
Fig. 3. DSS Arnasa v 3.0 Architecture

The implementation of the CPG as a knowledge server (Fig.3) and its integration into the DSS provide full decision support capabilities. This knowledge server is composed by:

?? Ontologies: a set of ontologies (asthma, CPG, MCDA, and PROAFTN)
?? Protege-2000: a tool for ontology editing.
?? Jess: an inference engine for executing the CPG.
?? FuzzyJESS: a toolkit that provides fuzzy logic in Jess.
?? JessTab plug-in: to link Jess and Protege-2000.
?? Jess Interface: to control the CPG performance from the J2EE application.
?? BD Interface: management of transactions between Jess and the DB.
?? Java auxiliary classes: auxiliary functions used in Jess.

We have developed ontologies for the asthma domain and the multicriteria fuzzy assignment (PROAFTN method) that define a knowledge base. These ontologies (Fig.4) are accessible through Protege-2000 and Jess. Both in the development of the asthma ontology and in the CPG implementation, the application scope has been the sickness severity evaluation. We expect to extend this scope in future releases (medication assignment, management of asthmatic crisis, etc).

GLIF has been used to represent the PROAFTN method and the asthma CPG, at the same time integrating those representations with their respective domain ontologies.



- MCDA
  - PROAFTN
    - PROAFTN_Entity
      - PROAFTN_Object
      - PROAFTN_Attribute
      - PROAFTN_Class
    - PROAFTN_Relation
      - PROAFTN_Importance
        - PROAFTN_W
      - PROAFTN_Criterion
        - PROAFTN_S
        - PROAFTN_d
        - PROAFTN_v
    - PROAFTN_Rule
    - PROAFTN_Problem
    - PROAFTN_Algorithm
- Asthma1_0
  - Asthma_ontology
    - Medical_procedure
    - Medical_Observation
      - Symptoms_Calendar_Observation
        - PEF_Observation
        - Diurnal_Symptom_Observation
        - Night_Symptom_Observation
        - Medication_Observation
      - History_Observation
    - Symptom
    - Severity_level
  - Asthma_guideline
  - Fuzzy_logic
- Rule
  - Control_Rule
  - Execution_Rule
- Guideline_control
  - Guideline_Actual_Step

Fig. 4. View of the developed ontologies with Protege-2000

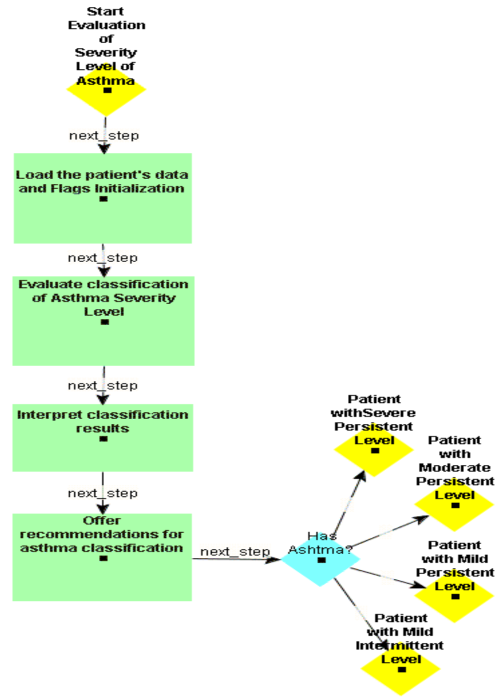


Fig. 5. GLIF representation of a CPG asthma algorithm

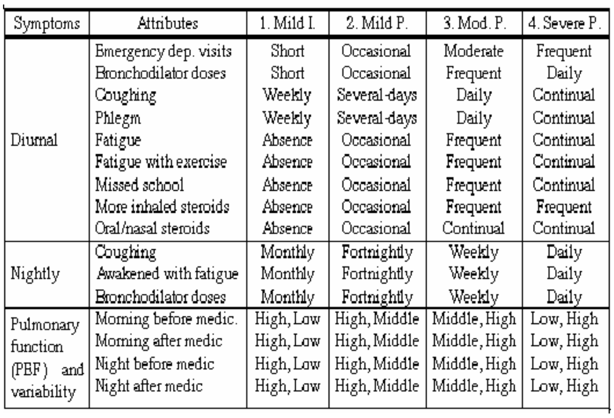
The PROAFTN method has been used inside the CPG in order to diagnose patients' asthma severity level. In order to achieve it, we have used a fuzzy criteria set (Table 2), which is linked to the attributes of the three aspects to look at for each prototype:

?? Diurnal symptoms
?? Nightly symptoms
?? Pulmonary function

The different categories to be assigned to a patient are the severity levels:

1. Mild Intermittent
2. Mild Persistent
3. Moderate Persistent
4. Severe Persistent

Table 2. Symptoms of each prototype, attributes and criteria for each asthma level for the severity diagnosis



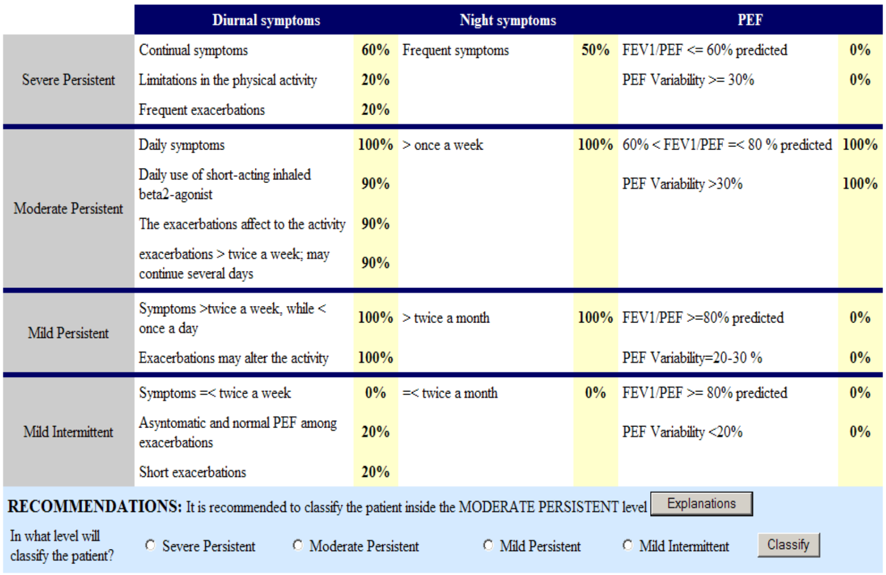
Symptoms	Attributes	1. Mild I.	2. Mild P.	3. Mod. P.	4. Severe P.
Diurnal	Emergency dep. visits	Short	Occasional	Moderate	Frequent
	Bronchodilator doses	Short	Occasional	Frequent	Daily
	Coughing	Weekly	Several-days	Daily	Continual
	Phlegm	Weekly	Several-days	Daily	Continual
	Fatigue	Absence	Occasional	Frequent	Continual
	Fatigue with exercise	Absence	Occasional	Frequent	Continual
	Missed school	Absence	Occasional	Frequent	Continual
	More inhaled steroids	Absence	Occasional	Frequent	Frequent
	Oral/nasal steroids	Absence	Occasional	Continual	Continual
Nightly	Coughing	Monthly	Fortnightly	Weekly	Daily
	Awakened with fatigue	Monthly	Fortnightly	Weekly	Daily
	Bronchodilator doses	Monthly	Fortnightly	Weekly	Daily
Pulmonary function (PEF) and variability	Morning before medic.	High, Low	High, Middle	Middle, High	Low, High
	Morning after medic	High, Low	High, Middle	Middle, High	Low, High
	Night before medic	High, Low	High, Middle	Middle, High	Low, High
	Night after medic	High, Low	High, Middle	Middle, High	Low, High

As it is common in MCDA, some attributes have more weight than others when determining the category. For example: "the patient attends to emergency room".

With the purpose of having the entire knowledge stored in the KB, a set of rules has been added to the previously developed ontologies (Fig.4). These rules allow the execution and control of the different PROAFTN and CPG algorithms (processes) in JESS. It includes the creation of the *Rule* class and its subclasses (Fig.4), and the implementation of the rules as instances of those classes. On the other hand, to complete the PROAFTN method assignation process, we need a set of fuzzy rules. We have created for this purpose the class *PROAFTN_Rule* (Fig.4) and added it to the method ontology. Therefore, all the needed knowledge for the representation and execution of the CPG and the PROAFTN method is part of the ontologies.

The follow up of each algorithm should be possible. The results of each execution should be available in a justified and reasoned way for the user. In order to attain it, we have created the *Guideline_Control* classes and subclasses. Their instances hold the status information of the algorithm nodes used in each execution.

In order to show the CPG performance results, the physician receives a page containing information about the performed evaluation of the severity level. An example can be seen in Fig.6. It displays the results obtained after the application of the PROAFTN method to the patient data for each severity level. Based on those results, the system gives several recommendations to help the physician to classify the severity level of the patient. Finally, the system waits for the physician decision.



	Diurnal symptoms		Night symptoms		PEF	
Severe Persistent	Continual symptoms	60%	Frequent symptoms	50%	FEV1/PEF <= 60% predicted	0%
	Limitations in the physical activity	20%			PEF Variability >= 30%	0%
	Frequent exacerbations	20%				
Moderate Persistent	Daily symptoms	100%	> once a week	100%	60% < FEV1/PEF =< 80 % predicted	100%
	Daily use of short-acting inhaled beta2-agonist	90%			PEF Variability >30%	100%
	The exacerbations affect to the activity	90%				
	exacerbations > twice a week; may continue several days	90%				
Mild Persistent	Symptoms >twice a week, while < once a day	100%	> twice a month	100%	FEV1/PEF >=80% predicted	0%
	Exacerbations may alter the activity	100%			PEF Variability=20-30 %	0%
Mild Intermittent	Symptoms =< twice a week	0%	=< twice a month	0%	FEV1/PEF >= 80% predicted	0%
	Asyntomatic and normal PEF among exacerbations	20%			PEF Variability <20%	0%
	Short exacerbations	20%				

RECOMMENDATIONS: It is recommended to classify the patient inside the MODERATE PERSISTENT level

In what level will classify the patient? ○ Severe Persistent ○ Moderate Persistent ○ Mild Persistent ○ Mild Intermittent

Fig. 6. Severity evaluation results according to the PROAFTN method.

5 Conclusions

The effective CPG implementation can be achieved by means of the formalism GLIF, the application of ontologies, and support tools for their edition and execution. The CPG representation through Protege-2000 is easily understandable for the physicians. The complexity of the domain information, including both the asthma treatment and the MCDA, recommends using domain ontologies that later will be integrated into the processes represented by GLIF.

Determining recommendations can bring different classification problems up for every decision node of the CPG. Because each determination is based on multiple fuzzy criteria, the implementation of additional MCDA or Soft-Computing methods is needed. This can be achieved in an effective and maintainable way by defining their classification processes with the method proposed in this work. When determining the asthma severity level, the PROAFTN implementation is effective on the Web.

Our solution is better that the Iowa proposal because: 1) The Java technology we use is more powerful than the CGI technology they use. 2) Recommendations based on the information extracted from patient’s medical records instead of entered manually by the user. 3) Knowledge representation based on domain ontologies and a specific formalism to represent a CPG, such as GLIF, instead of decision trees.

In conclusion, the effectiveness of the CPG implementation through both GLIF and the utilisation of efficient classification methods make it applicable to the real world when it is integrated into a Web-based DSS. It provides recommendations for the physicians that helps them in the decision making process.

Acknowledgments

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