PIESYS: A Patient Model-Based Intelligent System for Continuing Hypertension Management

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Abstract. Hypertension is estimated to be the third leading cause of death worldwide and its management is based on guidelines regarding diagnosis, evaluation, risk assessment, treatment and continuing care. This paper presents an intelligent decision support system, which operationalises algorithms for hypertension management using intelligent technologies. PIESYS encourages blood pressure control and recommends guideline-concordant choice of drug therapy in relation to co morbid diseases. Because evidence for best management of hypertension is mostly individualized, PIESYS is designed to help clinical experts to customize their therapeutic strategy with the use of the Patient Response Database (PRDB) incorporating initial or current data with patient responses or side effects, providing response-adaptive continual care. Together with PRDB, PIESYS uses an independent module, called Computerized Patient Model (CPM), reflecting patient's current state, which affects therapy or care modifications for hypertension management. PIESYS introduces personalised (patient-centric) approach in health care systems in contrast to guideline-dependent classical ones.

Keywords: Hypertension management, decision support, patient model.

1 Introduction

Hypertension if one of the major prevalent diseases that influences the prognosis of chronic diseases. The management of hypertension includes not only the use of antihypertensive drugs, but also the modification of unhealthy lifestyles. Multi-dimensional approaches are required for the management of hypertensive patients. Despite the availability of evidence-based clinical practice guidelines in most countries, a lot of hypertensive patients remain inadequately managed. In Greece, in a recent study, 39,2% of hypertensive patients know that they have elevated blood pressure, 6,3% know it but have taken no medication, 27,5% follow a specific medication, but have blood pressure over 140/90 mmHg and only 27% have been found as well controlled. One difficulty lies in the synchronization of a patient's own therapeutic history with the guideline strategy. Doctors, usually provide a typical evaluation and treatment strategy. Several classes of antihypertensive medications are known, the effect of which is based on different mechanisms. Like any

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chronic disease, hypertension is complex to manage. So, the creation of a system to assist doctors in making an initial diagnosis and providing the appropriate treatment is still desirable [1]. Traditionally, an intelligent system that helps clinicians to diagnose and treat diseases is used to identify a patient-specific clinical situation on the basis of key elements of clinical and laboratory examinations and consequently usually refine a theoretical treatment strategy, a priori established in the guideline for the corresponding clinical situation, by the specific therapeutic history of the patient [1]. Depending on the patient's response to the ongoing treatment, it models patient scenarios which drive decision making and are used to synchronize the management of a patient with guideline recommendations [2]. The so-called guideline-based treatment cannot take into consideration the main difference between management of acute and chronic diseases, which is the consideration of time. Time introduces patient-based treatment choice that means that decisions about the care process are dependent mainly on decisions made and actions taken at previous consultations, patient acceptance of recommendations and the outcomes of those actions. The notion of the classification of the state of a disease control over time (‘controlled’, ‘uncontrolled’ or ‘critical’) is as important as that of exhibited trend (‘worsening’ or ‘improving’). The concept of a therapy that persists over time but can be modified is important. Modern medical practice is based on the “axiom” that the focus shouldn’t be on diseases but on patients, thus introducing a “patient-specific model” constructed of a number of genetic and laboratory datasets that represent the current situation of a health care customer. Guideline independence and patient modelling in chronic diseases introduce a new generation of computer-assisted intelligent Decision Support Systems (DSSs), based on technologies that provide to the patient its “personal” instead of the “most likely” treatment scenario [2], [3]. In this paper, we present a DSS for the diagnosis and treatment of Hypertension, called PIESYS. A number of developed systems in the area of Hypertension Management already use more or less intelligent techniques, like HYPERTENZE [3], PRODIGY [4], HyperCritic [5], [6], ARTEMIS [7], [8], [9] and HTN-APT [10] and even those that operate in conjunction with a patient records handling system [11], [12]. PIESYS primarily aims to help in the diagnosis and treatment of hypertension effectively by taking into account a patient-model. Also, it can be used by medical students for training purposes on hypertension management and introduce a computer-assisted environment that is able to synthesise patient specific information with treatment guidelines, perform complex evaluations, and present the results to health professionals quickly.

The structure of the paper is as follows. Section 2 presents the medical knowledge modelling. In Section 3, the system architecture of PIESYS is described. In Section 4 implementation issued are presented. Section 5 contains evaluation results. Section 6 discusses related work and finally Section 7 concludes.

2 Medical Knowledge Modelling

Appropriate diagnosis of Hypertension requires doctors with long experience in Blood Pressure (BP) management. Therefore, except from the fact that we had a number of interviews with an expert in the field, we also used patient records and bibliographical sources to acquire corresponding knowledge.

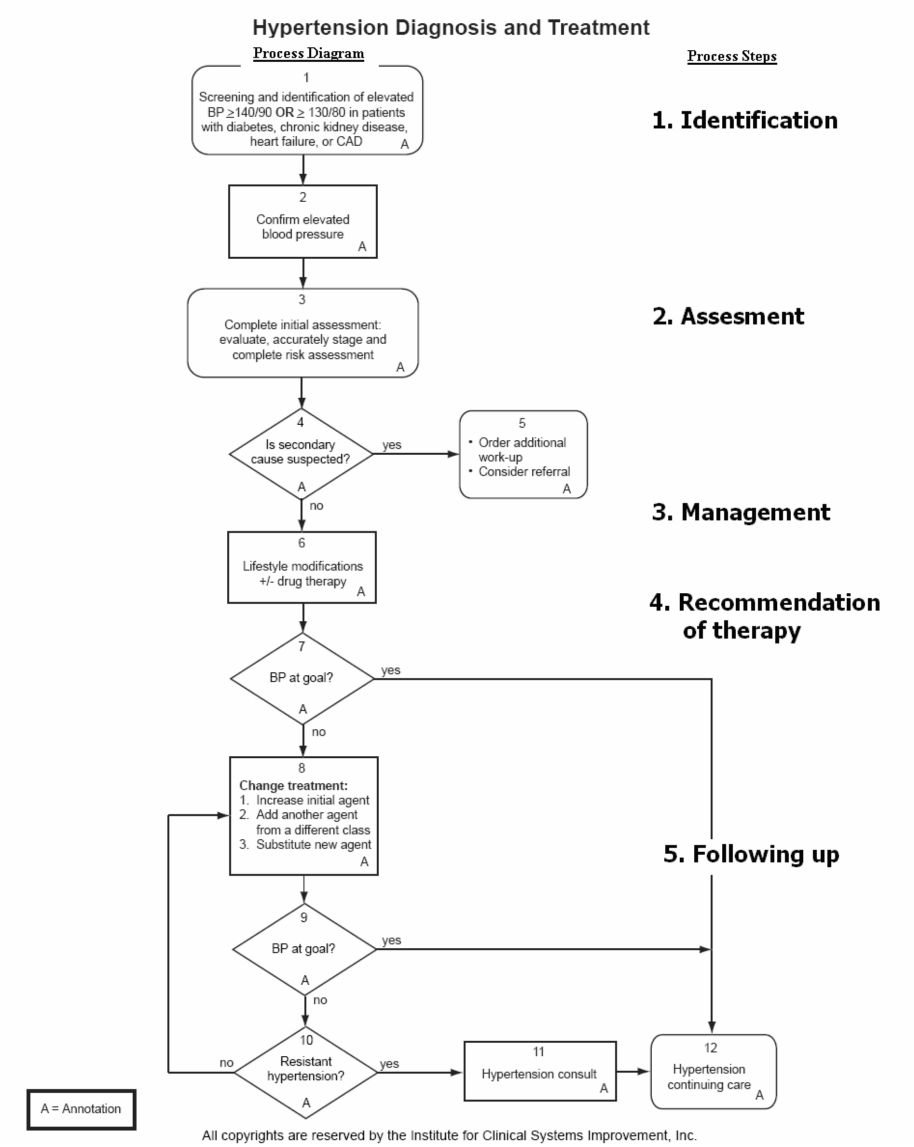

Fig. 1. Hypertension Diagnosis, Treatment and Monitoring Process Model

Our approach to knowledge modeling included three steps. First, we constructed a model of the basic diagnosis and treatment process (a 5-step process described below). We relied on the expert doctor and the literature at this step [15]. Then, we specified the parameters that played a role in each entity of the process model. At this step, we relied on the expert and the patient records. Finally, we determined the hypertension guidelines that are used in clinical practice in our country, according to

Greek Ministry of Health and Welfare [16]. We had, however, to iterate a number of times on this last step to tune a model as shown in Fig. 1.

2.1 Process Model

We used the model of Fig. 1 for the diagnosis and treatment processes. According to that, initially, (*step 1: Identification*) a clinician requires the following information: (a) medical history, (b) social history, (c) medication history, (d) target organ damage and (e) diagnostic tests as blood pressure and cholesterol levels. At this stage, based on the patient history information as well as testing, an initial diagnosis is made, concerning the classification of the problem (1 and 2 in the process diagram in Fig.1). There are two possible initial classifications: (a) optimal, normal or high-normal and (b) grade of hypertension. At the next stage (*step 2: Assessment*) the doctor calculates the risk factor of the disease (mild, moderate, severe, isolated). To confirm the initial diagnosis and be more concrete, the expert requires further information related to diagnostic laboratory tests. Once he gets them, can give the final diagnosis, which can be one of (a) high-normal (b) grade 1 and (c) grade 2-3 hypertension and the Cardiovascular Risk Factor is calculated (3 ,4 and 5 in the process diagram in Fig.1). The possible treatments corresponding to the final diagnoses are: (a) life style modifications (*step 3: Management of Modifiable Risk factors*), (b) drug therapy, that can be one (*step 4: Recommendation of therapy*) of (1) antihypertensive therapy, (2) antihypertensive therapy based upon concurrent disease (3) combination therapy, (4) review pharmacotherapy with patient (6 and 7 in the process diagram in Fig.1). The last stage (*step 5: Monitoring and Following-up*) recommends the possible monitoring time, targets the Blood Pressure levels with the patient on each visit, and review steps 2,3 and 4 (8, 9, 10, 11, and 12 in the process diagram in Fig.1). Usually, after the failure of the previous treatment, the severity of current state and patient preferences, recommend changes if necessary [16].

2.2 Input-Output Variables

Based on our expert, we specified a set of parameters that play a role for each of the entities in the process model that represent patient data. Finally, we resulted in the following parameters for each entity in the process model. According to the model, we distinguish between *input*, *intermediate* and *final* parameters at each sub process.

Input parameters: (a) medical history (cardiovascular disease pulmonary disease, diabetes mellitus), (b) social history (patient ID, sex, age, height, weight, smoking), (c) target organ damage (heart insufficiency, left ventricle hypertrophy) and (d) diagnostic tests (blood pressure levels, cholesterol levels)

Intermediate output parameters: (a) hypertension risk factor (HRF), (b) hypertension classification (normal, hypertension).

Intermediate input parameters: (a) hypertension risk factor (mild, moderate, severe, isolated), (b) concurrent diseases (heart, pulmonary, renal).

Final output parameters: (a) Cardiovascular Risk Factor (mild, moderate, severe, low) (b) Blood Pressure Target

Final treatment parameters: Final treatment according to current Blood Pressure Levels and the total Cardiovascular Risk Factor (a) life style modifications and (b) initial drug choices,

Follow-up input parameters: (a) life style modifications, (b) initial drug choices, (c) patient response

Follow-up output parameters: (a) Further life style modifications, (b) Optimization of drug choices dosages according to Goal Blood Pressure and (c) patient reevaluation.

3 PIESYS Architecture and Design

The developed system has the structure of Fig. 2, which is similar to the typical structure of such systems [14]. PIESYS consists of two Expert Systems (ESs) and a Patient Database (PRDB).

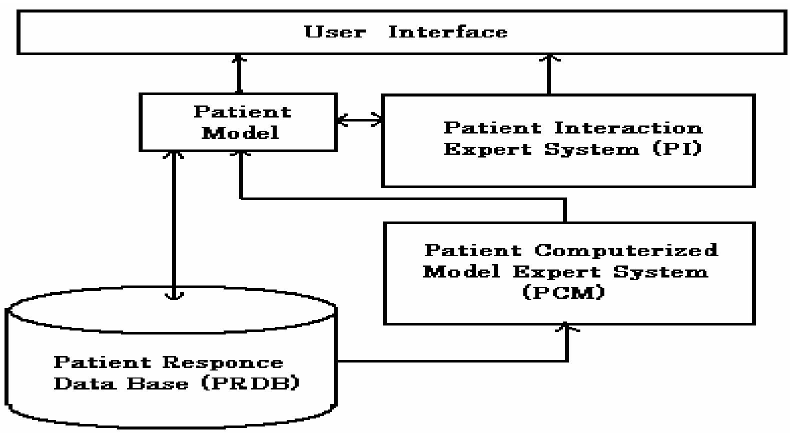

Fig. 2. The general structure of PIESYS

3.1 Patient Interaction Expert System (PI)

The *knowledge base* of the expert system includes *production rules*, which are symbolic (if-then) rules with Boolean or crisp variables (e.g. age, smoke, cholesterol, etc). The variables of the conditions (or antecedents) of a rule are inputs and the variable of its conclusion (or consequent) an output of the system. To represent the process model, we organized production rules in three groups: *classification rules*, *diagnostic rules* and *treatment rules*. The current patient data are stored in the Patient Database, as *facts*. Each time that the reasoning process requires a parameter value, it gets it from the database or the user. Fig.3 presents how the rule groups, Patient Database and the facts/user are used during the reasoning process to simulate the diagnosis process.

Table 1. Computerized Patient Model Rules (part of)

HRF	(BP-TBP) x 100 %/TBP	CRF	Patient model	
Moderate	< 20	Medium	Controlled	Improved
Moderate	< 20	Low	Uncontrolled	Improved
…				
Moderate	< 50	High	Critical	Worsened
Moderate	> 20	High	Uncontrolled	Worsened
…				
Isolated	< 20	Low	Controlled	Improved

3.2 Patient Computerized Model Expert System (PCM)

To represent the process model, we organized production rules in two groups: *Patient Model Rules* and *Computerized Patient Database Rules*. *Patient model rules* classify the current patient data to a specific patient model according to the calculated Hypertension Risk Factor (HRF), Cardiovascular Risk Factor (CRF) and the distance from the Target Blood Pressure (TBP). For example with HRF: "Moderate", CRF: "high" and distance from TBP: < 20 % the patient is characterized as "uncontrolled" and "improved". These values are stored in the patient database. A sample of *patient model rules* can be seen in Table 1.

Table 2. Computerized Patient Database Rules (part of)

Patient Model (old)		CRF (new)	User Response	Update
Uncontrolled	Improved	High	Yes	Yes
Uncontrolled	Worsened	Low	Yes	No
Uncontrolled	Improved	High	Yes	No
Critical	Improved	Low	No	No
…				
Controlled	-	-	Yes	Yes

For each patient dataset that is stored in the Patient Database, *Computerized Patient Database Rules* decide to update the parameter values if the recommended life-style or treatment modifications are accepted by the doctor and the patient. Each time that reasoning process requires a value, it gets it from the database or from user interaction. A sample of the *Computerized Patient Database Rules* can be seen in Table 2. Fig.3 presents how these rules are used/participates during the reasoning process to simulate the patient modelling process.

3.3 The Patient Response Database (PRDB)

In the Patient Response Database the current patient *input, intermediate* and *final* parameter values are stored, as well as the patient model and possible text recommendations under strict chronological order. After each new entrance the database is used in combination

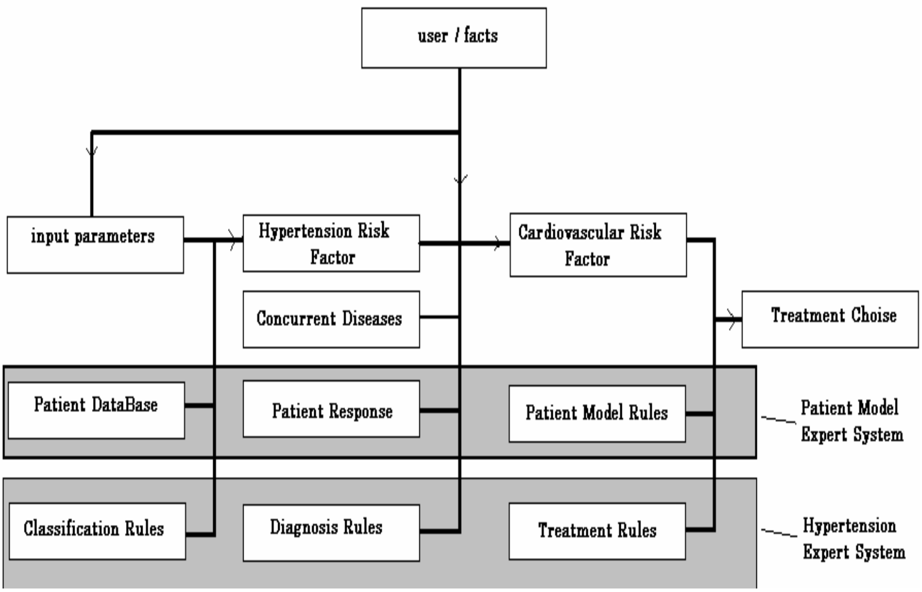

Fig. 3. The reasoning process of PIESYS

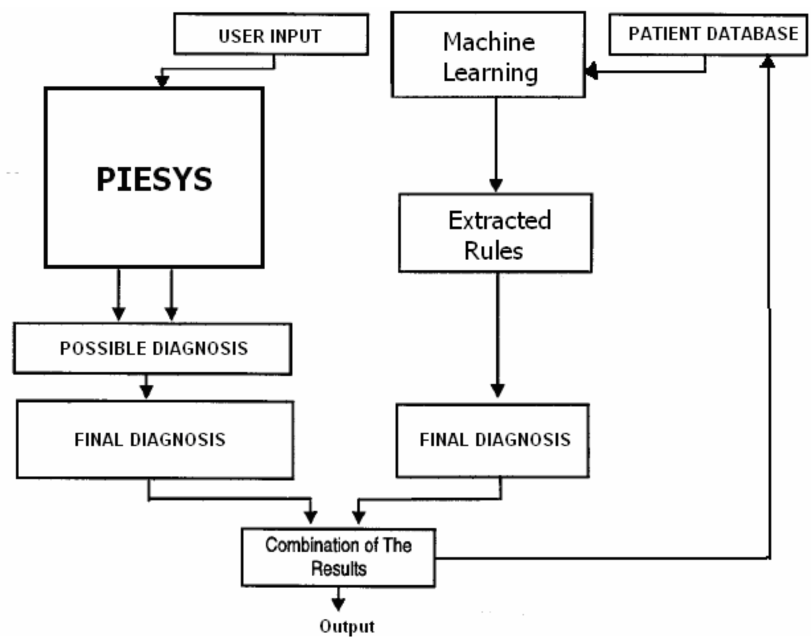

Fig. 4. Hybrid PIESYS

with the patient response (i.e new *input* or *intermediate* parameters) for revaluation and treatment modifications with the use of PI ES. The PCM ES additionally recalculates the patient model that is also stored. If the modifications are acceptable from both doctor and patient the PRDB is updated. Additionally machine learning techniques can be used to improve the knowledge base of the Hypertension Expert System [17]. A knowledge-base development methodology using machine learning, statistical analysis, and validation techniques according to sensitivity and specificity is already under development to analyze patient datasets in order to give the final output at each processing step after the combination of the two approaches as can be seen in Fig. 4 [18].

The results of these experiments will be evaluated by the medical expert for their soundness with respect to the existing knowledge in the domain and potential for the generation of new and useful medical knowledge. The experiments to be performed will demonstrate how the synergy of medical and machine learning expertise helps in the inference of a new knowledge and potentially could increase efficiency and reliability of the medical diagnostic process [17].

4 Implementation Issues

The user interface has been developed with Macromedia Flash 8.0, the patient database with SQL database and the two expert systems have been developed in CLIPS 6.1b Expert System Shell. CLIPS is a productive development and delivery expert system tool which provides a complete environment for the construction of rule and/or object based expert systems with many advantages as variety of Knowledge Representation, Portability, Integration/Extensibility, Interactive Development, Verification/Validation, Fully Documented and Low Cost. Finally, about 125 rules have been constructed for PIESYS. Patient data in the Database are organized in the form of CLIPS templates. For example, the following rule:

Rule 13:
If *patient_smokes is yes and*
over_weight is yes and
cholesterol is high or
user_classification is grade-2
then danger is middle

Rule 13 has been implemented in CLIPS as follows:

```
(defrule danger-middle

(declare(salience 100))
(not(and(user-smoke y)(user-overweight y)(upper-cholest y)))
(or(and(user-organ n)
 (user-disease n)
 (user-SD n)
 (or(user-taxinomisi stadio-1)(user-taxinomisi stadio-2))
 (or
      (or(user-smoke y)(user- overweight y)(upper-cholest y))
          (or (and(user-smoke y)(user-paxisarkia y))
```

```
                    (and(user- overweight y)(upper-cholest y))
                     (and(user-smoke y)(uper-chol y))
=>
 (assert (danger middle))))
```

To implement reasoning flow, different priorities have been used for different rule groups (Fig. 3).

5 Experimental Results

We used PIESYS for a number of 60 (well managed) patient records from a Hospital Database with different types of hypertension. The PIESYS treatment results were compared to the results of our expert doctor on the basis of the factual information included in the patient records. To evaluate PIESYS, we used three metrics, commonly used for this purpose: *accuracy, sensitivity and specificity*. The evaluation results are presented in Table 3 and show an acceptable performance.

Table 3. Evaluation results for treatment choice of Hypertension patients

Metrics	EXPERT (%)	PIESYS (%)
ACCURACY	91	78
SENSITIVITY	97	93
SPECIFICITY	95	79

6 Discussion and Related Work

According to the existing literature there are in use a number of computerized systems in the area of Hypertension Management that use more or less intelligent techniques. The first one, HYPERTENZE [3], gives a sequence of decisions based on clinical experience using a series of parameters. It offers the user essential information and explanation of the decisions in a graded form. The price list of equivalent medications can be updated by the user himself. The second is PRODIGY [2], designed to assist general practitioners in England to choose the appropriate therapeutic action encoding clinical guidelines for managing patients with chronic diseases such as asthma and hypertension. It models patient scenarios which drive decision making and are used to synchronize the management of a patient with guideline recommendations. The third one [4] administers the clinical database, which includes symptoms and signs, laboratory data, and prescriptions. The database deals with the temporal course of the patient's status. The system that evaluates the patient's condition and the decision support system have some knowledge bases. The knowledge bases consist of the evaluation of the patient's condition, the appropriate selection of laboratory examinations, and suggestions for treatments, which involve a lifestyle modification and the proper prescription of medication. This system supports only the standard protocol care for hypertensive patients and the database for clinical epidemiology. Additionally, HyperCritic [5] can audit general practitioners' treatment of hypertension by analyzing computer-based patient records. HyperCritic reviews the electronic medical records and offers unsolicited advice. To determine which unsolicited advice might be perceived as inappropriate, builders of programs such as HyperCritic need insight into providers' responses to computer-generated critique of their patient care. In another approach [6], authors deal just with hypertension diagnoses: essential hypertension and five types of secondary hypertension. Only blood pressures, general information and general biochemical data are taken into account. ARTEMIS [7], [8], [9] system, which is in use since 1975, is described as a computerized management of hypertensive patients. From a medical point of view, computerized medical record programs can be used to memorize patients' individual records and profiles, to facilitate patient management and follow-up, to store medical knowledge about hypertension and to provide facilities for decision making at the level of either the individual patient or the population followed up. From a technical point of view, the methodology used integrates data and knowledge management facilities into the same software with the use of an expert system (ES). The ES produces only diagnostic hypotheses (possible causes of hypertension) and a kind of therapeutic suggestions before and after requiring additional information (patient supplementary interrogation, biological or radiological investigations). Finally HTN-APT [10] is a system that aids the physician in managing the hypertensive patient by keeping a record of the patient's progress, allowing easy access to drug information, and generating a number of recommendations and critiques about treatment options. In the most interesting work [11] authors focus on the synchronization of a patient's own therapeutic history with the guideline strategy. The first level of their approach is used to identify a patient-specific clinical situation on the basis of key elements of clinical examination (complication of hypertension, associated diseases). The second level aims at dynamically refining the theoretical strategy, a priori established in the guideline for the corresponding clinical situation, by the specific therapeutic history of the patient. Finally, depending on the patient's response to the ongoing treatment, the system provides a recommendation still consistent with the guideline strategy, whatever the patient's past treatments. Finally, in [12] the computer based clinical decision support system was built for the two most commonly used practice computing systems EMIS and AAH Meditel so that it could be incorporated into routine clinical care. The system is identical to the New Zealand guidelines for the management of hypertension, except that absolute risk is presented numerically rather than pictorially. The system finally calculates the patient's five year risk of a fatal or non-fatal cardiovascular event. According to the previous descriptions successful or less successful systems have been implemented as aids for hypertension treatment and some of them are designed using intelligent approaches acting on medical record databases. PIESYS is an autonomous system designed to help clinical experts to customize the therapeutic strategy with the use of the included Patient Response Database incorporating initial or current data with patient responses or side effects, providing response-adaptive continuing care, because evidences for best management of hypertension is mostly individualized [13], introducing patient-dependent in contrast to guideline-dependent [15], [16] computerized medical systems.

PIESYS is now under testing and has been run for real patient cases, whose records were in a hospital database, and its results are compared to the results the expert doctor. For example, PIESYS has a mean 78% diagnostic and treatment success compared to the expert (Table 3). Long-term metrics according to Monitoring Time and individualized Blood Pressure Level Targets will help for better experimental evaluation of the presented approach.

7 Conclusions

In this paper, we present the design and implementation of PIESYS, an intelligent system that deals with treatment of hypertension. The process was modeled based on expert's knowledge and existing guidelines for hypertension management. PIESYS uses an intelligent system that specifies the management eligibility criteria, thus providing risk justifications, life-style modifications, blood pressure targets, relevant co morbid diseases, guideline-recommended initial drug choices, preferred drugs, additionally with clinical patient-specific messages. Together with PRDB, PIESYS uses an independent module, called CPM, reflecting patient's current state, which affects therapy or care modifications for hypertension management. So, the strongest point of our approach lies in the fact that, contrary to other approaches, PIESYS introduces a patient-dependent generation of medical care systems in contrast to guideline-dependent classical ones. PIESYS can additionally be used by medical students for training purposes on hypertension management and introduce a computer-assisted environment that is able to synthesise patient specific information with treatment guidelines improving the acceptability of such systems [7], [8], [9]. On the other hand, the use of more advanced representation methods, like hybrid ones [17], [18], which are in our future plans, may give better results.

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