An Application of Fuzzy Prototypes to the Diagnosis and Treatment of Fuzzy Diseases

Ruben Romero-Cordoba,[†] Jose A. Olivas,[*] Francisco P. Romero,[‡]
Francisco Alonso-Gonzalez,[§] Jesus Serrano-Guerrero[¶]
SMILe Research Group, Department of Information Technologies and Systems, University of Castilla-La Mancha, Ciudad Real, Spain

Decision support systems, embedded in modern telemedicine applications, are a tool to improve the skills of general practitioners and patients in decision-making in medicine. Nowadays, one of the more challenging problems in this context is how to diagnose those diseases, whose early clinical signs are often subtle, and many of their common signs and symptoms are similar to other. These "fuzzy diseases," even they can have distinctive features, are not diagnosable through a concrete clinical test or symptom, and, thus, they are difficult to recognize, especially in their initial phases when they might be mistaken for other similar ones. Then, the diagnosis of a fuzzy disease set is based on the exclusion of symptoms and tests results, due to the similarity between them. In the present article, it is proposed the development of a Clinical Decision Support System framework to diagnose a set of fuzzy diseases, concretely applied to Fibromyalgia and associated syndromes. For this purpose, in this paper a reasoning method that uses theories about conceptual categorization from the psychology, pattern recognition, and Zadeh's prototypes has been designed. Through the use of this model, satisfactory results in the evaluation of patients were obtained.

1. INTRODUCTION

The growth of the computer applications in medicine and health care has been highlighted in reports such as the "2013 Annual Report of the U.S. Hospital IT Market."[1] It was carried out in the year 2014, and it describes a large growth of these systems in the U.S. hospitals, including the application of artificial intelligence (AI) and knowledge engineering techniques.[2]

One promising line of work in such fields is the development of decision support systems (DSS). The central goal of DSS is to process and provide suitable

[*]Author to whom all correspondence should be addressed: e-mail: joseangel.olivas@uclm.es.
[†]e-mail: ruben.romcor@gmail.com.
[‡]e-mail: franciscop.romero@uclm.es.
[§]e-mail: pacoalonso@gmail.com.
[¶]e-mail: jesus.serrano@uclm.es.

INTERNATIONAL JOURNAL OF INTELLIGENT SYSTEMS, VOL. 0, 1–17 (2016)

View this article online at wileyonlinelibrary.com. • DOI 10.1002/int.21836

information to support individuals or organizations in their decision-making tasks.[3] The concept of clinical decision support system (CDSS)[4] is used if the DSS is designed to assist physicians and other health professionals. Therefore, a CDSS is a DSS designed to achieve clinical advices for patients by incorporating knowledge management techniques (patient data, etc.).

The diagnosis of poorly understood disorders is, nowadays, one of the most challenging goals for this kind of systems. The notion of "fuzzy disease" was introduced by Sadegh-Zadeh,[5] but its interpretation and definition proves to be very complex. Nevertheless, the framework of fuzzy sets, systems, and relations is very useful to deal with the absence of sharp boundaries of the sets of symptoms, diagnoses, and diseases. The application of fuzzy logic techniques in medicine is based on the following suggestion made by L. A. Zadeh: "symptoms and diseases are fuzzy in nature and fuzzy sets are feasible to represent these entity classes of medical knowledge." Taking into account, this approach contributed to medical decision-making and the development of computer-assisted diagnosis in medicine.[6] For example, in Ref. 7 diseases are defined according to fuzzy sets. By making requests of membership degrees of certain symptoms, similarities to existing diseases are calculated and decisions will be made on whether an entered group of symptoms provides an indication of the existence of a disease. Moreover, it should be possible to make requests of new prototypical diseases and symptoms and to modify them. In our work, a "fuzzy disease" is a disease that is not diagnosable through a concrete clinical test or symptom and many of its signs and symptoms are similar to other conditions.

It is proposed a CDSS that may be used to perform a diagnostic with a set of fuzzy diseases. The main task is the creation of a method for representing and performing a diagnostic with a group of diseases whose diagnostic process has not been clearly defined. For this purpose, several techniques related with the prototype concept, the categorization of types and the Zadeh's prototype theory [8] will be used. With the aim of applying these techniques, it has been chosen a set of diseases that have many similarities between them and simultaneously they have a strong similarity with fibromyalgia.

Fibromyalgia and related syndromes are poorly understood disorders often seen in primary care practice. Fibromyalgia is often difficult to diagnose as the symptoms vary considerably and could have other causes. Awareness of common mimics of fibromyalgia and comorbid disorders will increase confidence in establishing a diagnosis of fibromyalgia.[9]

Fibromyalgia prevalence in overall levels is between 2% and 5% of the world population, and it predominates in people about 20 and 50 years old,[10] with a higher proportion of women (10 times more than men).[11] The total amount of affected people in different countries are not negligible[12]: 3.2% in Germany, 2.4% in Spain, 2% in the United States, 1.4% in France, 3.7% in Italy, 3.6% in Portugal, and 2.5% in Sweden. In Spain, 15% of the rheumatology consults and between 5% and 10% of the primary health care are dedicated to these patients, which mean a total expense in public health of about 11 million euros per year. Therefore, it can be determined that the development of a CDSS may reduce costs and improve the health care quality.

This paper is an extended version, including more technical details, of the one presented (granted with the "Best paper award") at the Conference of the Spanish Association for Artificial Intelligence (CAEPIA),[13] mainly focused on the description of the proposed CDSS. The main novelty of this extended version is the detailed description of the background, concepts, and uses proposal of "prototype," "fuzzy deformable prototypes," and "fuzzy diseases."

So, in this work, a proposal of a knowledge representation and inference method based on fuzzy deformable prototypes (taking into account the "fuzzy diseases" definition) and its application to a real problem in a real CDSS for the diagnosis and treatment of fibromyalgia and associated syndromes are presented.

The rest of the paper is organized in the following way: Section 2 briefly overviews current reasoning techniques used in CDSS that manage diseases of this type. In addition, short descriptions of the chosen diseases and about the fuzzy techniques used in this work are also included. In Section 3, it is displayed the structure and architecture of the system, showing its main components. In Section 5, a complete example of patient evaluation is depicted. A description of the performed evaluations and their results are shown in Section 6. To finish, some conclusions are presented as well as several possible improvements to the system.

2. BACKGROUND

Medical diagnosis is a difficult and complex task, and CDSS are technologies designed for their potential to improve the quality of health care, including their application to support clinical decisions.[14]

The system proposed in this work is intended to perform a diagnostic and/or treatment of diseases through an exclusion process. Several methods and techniques in the AI context have been applied to this purpose. A classic expert system to help physicians with the diagnosis of memory loss-related diseases (Parkinson, Alzheimer, etc.) [15] has a set for rules based on the symptoms of each type of neurological disease, and they were presented using a decision tree and inferred using a forward-chaining method. Another example of DSS applied to mental disorders [16] is based on the application of different data mining techniques (hierarchical clustering, rule sets, visualization techniques) useful for differential interprofile diagnosis from personality inventories.

Neural networks are also used for the differential diagnosis of different diseases. For example, an expert system for the differential diagnosis of strabismus [17] is based on parallel instances of a multilayer perceptron trained on exemplar data generated in consensus by two clinical experts. Neural networks are also used together with other machine learning techniques such as support vector machines and decision trees with the aim to directly aid clinical decision-making to diagnose soft tissue tumors and microcytic anemia.[18]

Fuzzy logic-based models have proved their efficiency in medical decision support and medical reasoning owing to the characteristics of the fuzzy approach to describe and represent clinical vagueness and to handle the uncertainty related to concepts, such as symptoms and diseases, that are, according to Zadeh's suggestions,[6]

fuzzy in nature because they have imprecise or gray boundaries. For example, fuzzy sets are used to handle the uncertainty inherent in the problem of skin infections differential diagnosis.[19] Also, a fuzzy rule-based system to prevent the coronary heart diseases occurrence in the near future,[20] based on a neurofuzzy classifier, provides interpretable linguistic terms, which could be regarded as a fuzzy version of the decision tree classifier.

Nowadays, the rapid accumulation of data from medical research causes that CDSS systems have to take into consideration issues related to patient data quality like incompleteness or unreliable data. Fuzzy logic techniques like fuzzy cognitive maps [21] or fuzzy prototypes [22] could be a useful tool for modeling medical reasoning in this context.[23] Also, recent techniques combining cloud computing and mobile technologies are used in conjunction of AI techniques like Naïve–Bayes classifiers and fuzzy inference methods are being used to improve the expected results in the automated medical diagnosis process and to offer consistent support and useful information for medical staff.[24]

However, the application of these techniques has been destined for disease diagnostic processes in which there are clearly distinguishing features. In this proposal, the designed system will not have diseases with a distinguishing feature due to the similarity and disparity of symptoms. The illnesses chosen are polymyositis, rheumatoid arthritis, systemic Lupus erythematosus, polymyalgia rheumatic, and hypothyroidism, being the common nexus, and the most difficult to diagnose, fibromyalgia as it is explained in the following section.

2.1. Fibromyalgia

Fibromyalgia is characterized as a chronic disease that affects to the soft parts of the locomotor system and that presents a high sensibility in multiple points of the body in which there is a generalized presence of chronic musculoskeletal pain. The pain symptoms usually coexist with others such as fatigue, sleep disturbances, memory problems, concentration, joint stiffness, headaches, feeling of swelling in the hands, anxiety, depression, and so on.

Many times, fibromyalgia is confounded with other illnesses, because its symptoms are very similar. It does not have any known cause, and it does not produce any type of changes in tissues or cells. The diagnostic is mainly clinic, and the results of the tests are not enough to detect it. To diagnose it, different tests must be performed to rule out diseases such as polymyositis, rheumatoid arthritis, systemic Lupus erythematosus, polymyalgia rheumatic, hypothyroidism, and so on. Once they are discarded, the health records of the patient, as well as his symptomatology, are studied. After that, a process of physical exploration begins where the tender points [25] are detected and those affected are accounted (see Figure 1). These points are called *objective indicators*.

Fibromyalgia treatment is difficult due to the incomplete understanding of the pathogenesis, the disagreement regarding the symptom profile, and the lack of consensus for the definition of treatment response.[27] In the absence of a curative treatment, the aim is to relieve the symptoms through a personalized one, depending on multiple factors as the trigger points affected or the symptoms. The pharmacologic

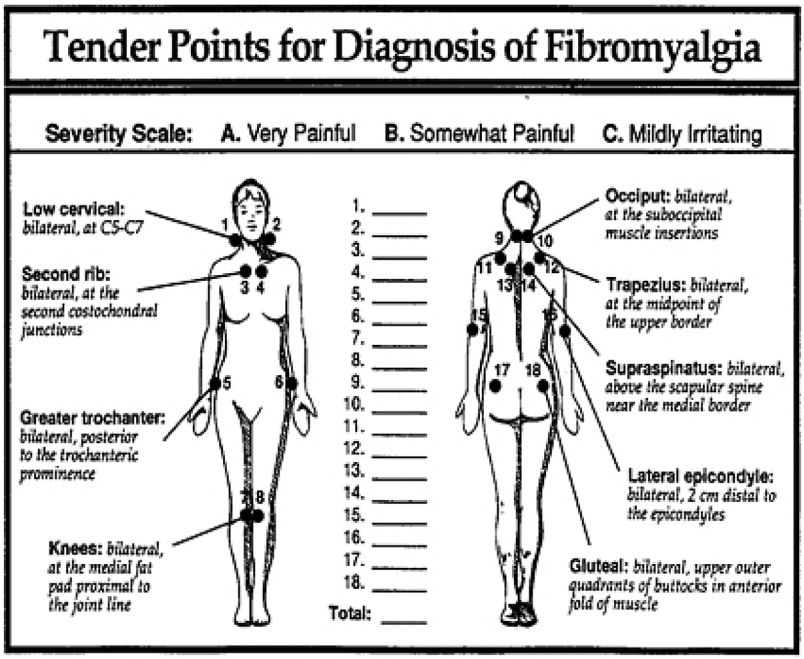

Figure 1. American College of Rheumatology 1990 criteria for the classification of fibromyalgia.[26]

treatments are usually combined with other alternatives like acupuncture.[28] In a nutshell, fibromyalgia is present with a high incidence in many countries and affects patients with a large amount of different symptoms. However, there is very little information about its causes, which has a negative impact, both physically and psychologically on patients who have to be constantly monitored. Moreover, for health institutions it is a relevant problem, owing to the high presence of patients with a disease not clearly defined, not correctly treated, or wrongly diagnosed.

2.2. Fuzzy Prototypes

Medical reasoning, as well as some kinds of scientific and technical reasoning, follows a logic of conjectures and refutations; that is, the physician from his encounter with the patient starts with different hypothesis which can be verified, or on the contrary, be refuted. If the hypothesis is refuted by experimental facts, it is subsequently replaced by other hypotheses that are better adapted to the facts. Thus, for each disease you can have, on the one hand, a degree of confirmation (i.e., the degree to which the evidence supports the hypothesis under consideration) and, on the other hand, a degree of refutation (i.e., the degree to the facts refute the

hypothesis). The result of combining these two factors is the degree of credibility of this hypothesis. Therefore, each disease being considered by the system includes a set of facts that confirm or falsify. The logic model to present the factors confirmation, falsification, and credibility is based on fuzzy techniques, in extensions of the theory of prototypes of Zadeh.[8]

According to the prototype resemblance theory of disease,[29] the nosological class that comprises such fuzzy human conditions as diseases cannot be based on and represented by, a classical, reductively definable concept of disease. Nevertheless, the class of diseases can be defined as an irreducible category that is constituted by some prototypes to which the remaining members of the category, the diseases, are similar to different extents. It is possible to consider that ideal types prototypically describe a disease, but in fact only approximate the ideal to a degree. Some kinds of diseases show some kinds of uncertainty or vagueness associated with the fulfillment of this ideal. Therefore, to develop this theory it is essential to measure the similarity between a member of a category and its prototype.

Fuzzy deformable prototypes (from now on FDPs) can provide an adequate formal framework for working with this idea. FDPs come from the confluence of two interesting approaches to the concept of prototype: the "deformable prototypes" of Bremermann,[30] introduced in the late 1970s from the field of pattern recognition (in the framework of "deformable prototypes" a real element is classified according to the minimum energies required for physically deforming the closest prototype) and the fuzzy prototypes of Zadeh,[8] result of a controversy with cognitive psychologists [31] where a fuzzy prototype is not an element—usually the best representative of a set or class—but a reunion of good, bad, and borderline elements of a category.

Taking into account these approaches, FDP [32] can be defined as a linear combination of fuzzy prototypical categories (described as tables of attributes) able to be adapted to (describe) any new real situation, where the coefficients are the degrees of membership of this real situation to each of these fuzzy prototypical categories. This approach has been implemented in several applications, including those related to information systems and software engineering,[33] traffic control,[34] document management,[35] social sciences,[36] information retrieval, Web search,[37] and forest fire prediction.[38]

3. DESIGN OF A CDSS FOR FUZZY DISEASES

CDSS can be defined as any piece of software that takes information about a clinical situation as inputs and that produces inferences as outputs that can assist practitioners in their decision-making and that would be judged as "intelligent" by the program's users.[39]

As can be seen in Figure 2, every CDSS has at least two core components: the knowledge base and inference engine. The knowledge base is a structured collection of expert medical knowledge which can be built through data- or expert-driven approaches. In this version of the system, the CDSS depends only on a knowledge base derived from expert knowledge. The first step to build the CDSS is the conceptualization of each disease in a prototype (explained below) by the expert

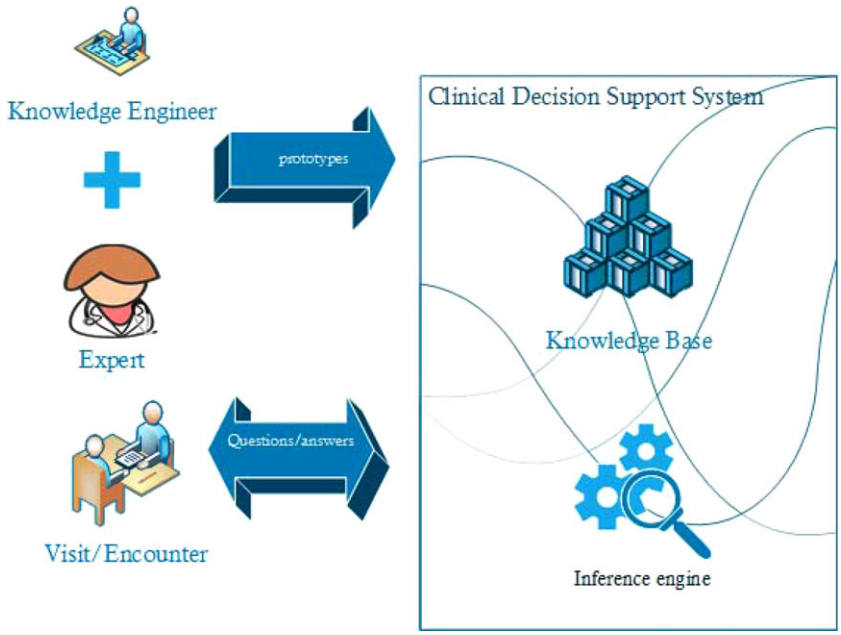

Figure 2. CDSS architecture.

domain. Thus, the knowledge base consists on a series of prototypes, each one with a set of questions about clinical signs, symptoms, laboratory tests, etc., and their possible answers. It is used to generate quantification (degree) of the similarities in the clinical case of a patient with the prototypes.

As it is mentioned in the preceding section, the approach given to the detection and treatment of diseases that are highly similar comes from theories of prototypes. The prototype concept turns around the notion of membership of an element in relation to a class. The prototypes theory of psychology, enunciated by some scientists such as Eleanor Rosch [40] suggests that an item belongs to a class or prototype, if it resembles, in a high level, the maximum representative of the class. Later and carrying on this idea, Zadeh introduced the concept of fuzzy prototype [8] to reformulate the basic ideas exposed by the psychology scientists. The main improvements exposed are based on the fact that an element belonging to a group is not always a good representative of the class to which it belongs.[41] Moreover, a prototype is not an element with a defined limit and simple features, but rather, a fuzzy schema or object and then, it may possess certain "degree" of membership to one or more classes. Therefore, he determined that not only the most characteristic element defines a prototype but that it establishes a system of membership to determine the similarity of an object with a prototype.

Then, based on these ideas, the fact that an element has a higher proximity with some classes or others have allowed devising a method for detecting and treating diseases with a high similarity index. The diseases would be then the prototypes and

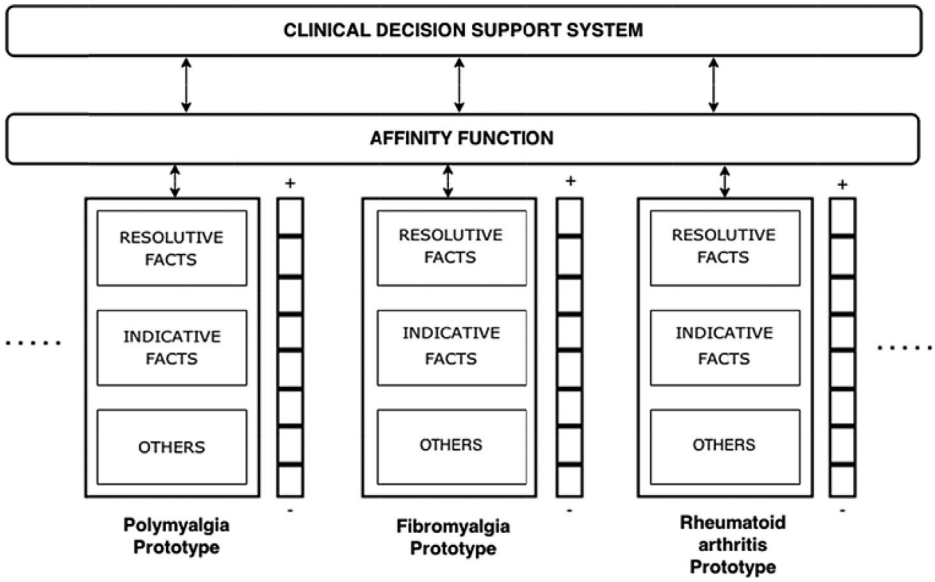

Figure 3. Affinity function structure.

the symptoms their features. The prototypes may have an internal classification of its features:

- *Resolute facts:* If a prototype represents a disease, the resolute facts or hallmark symptoms would constitute the evidences that confirm or refute the disease. For example, the value of TSH (*thyroid*-stimulating hormone) in a blood analysis determine whether the patient suffer or not hypothyroidism, it is enough to diagnose the disease.
- *Indicative facts*: The indicative facts would suspect that it may have some similarities due to the symptoms and the results of the patients' tests. For example, an excerpt of the facts that can make us suspect that the patient has hypothyroidism could be the following: hair loss, bradypsychia, arthralgias, asthenia, lethargy, and paresthesia.
- *Others*: This group may contain special conditions imposed by experts in the field, and from their experiences, comments about the disease, etc.
- Once you have identified the types of facts, it is required to define the range values that can take each of the symptoms, signs or tests described in the prototype. Another important detail of the prototype design would be the classification of symptoms or evidences that would be part of it, giving them a category of importance (this being a linguistic or numerical label), which will determine the degree of compliance with the prototype. Therefore, some symptoms are common to different diseases but they are not equally important for all of them. For example, muscle weakness is more important when you study the possible presence of hypothyroidism than when you are studying the presence of fibromyalgia.

As shown in Figure 3, introducing a set of symptoms and tests results associated with a patient, the affinity function mission is to find the greatest similarity among the multiple prototypes defined. These contain input values: "known," "unknown," or "nonexistent" of the different prototypes that represent the diseases. The "known"

one will create an assessment based on their affinity with each of the prototypes. The fact of lack of certain symptoms will also be treated in a favorable or unfavorable way in terms of affinity, and the "nonexistent facts" would have a different treatment. With all this, the affinity function maintains a vector of the prototypes ordered by affinity.

The main idea is to give a numerical value to the relation of a patient with each of the patterns; in this case, several diseases are related to fibromyalgia. The objective is broadly taking all those questions that have been exposed to the user (in this case, the primary care physician) and that has tried to answer with the help of the patient. The answers to these questions can be classified according to the information provided or the result of the evaluation:

- It is founded an indicator that can give a positive or negative answer to an open question. For example, the patient has fever 37ºC at the time of the evaluation.
- The question has not been answered. For example, the physician does not believe that the answer to that question is relevant and he does not taken it into account during the evaluation.
- The answer is not conclusive: For example, when the patient is asked if he remembers having had a fever the last 3 days in the afternoon.

Based on these ideas, an algorithm that evaluates these parameters and takes the already answered questions (previous appointments or evaluations) and is intended to give a numerical value for the relation of the patient's symptoms with each of the diseases of the framework is proposed (Figure 4).

Once all the evaluations were done and changed the score, the patterns are resorted returning the list of diseases in order of affinity with the user symptoms.

As we can see, the algorithm evaluates each response obtained with the questions and answers of each prototype. These have been obtained after the process of knowledge engineering in which, physicians intervened to build the conceptualization of each disease in a prototype. In this way, it was built a database of questions and answers and the assessment of them, depending on the conditions above described: "known," "unknown," and "nonexistent." For example, some initial questions about the diagnosis could be as follows: Do you feel Muscle Pain?, Do you have skin lesions?, Do you feel pain in the morning more than 30 min?, etc.

The knowledge base is used by the algorithm to generate a quantification of the similarities in the clinical case of a patient with the different prototypes registered in the system based on the importance of each symptom, sign, or test result in the disease. Finally, the order of the prototypes depends on the weight given and they are returned in a vector, obtaining an ordered list of the most favorable diagnosis for a patient at a particular time of diagnosis. This would allow both, the doctor and the system, to determine what may be the next step in the patient evaluation.

The process of choosing the questions is set in the knowledge acquisition process, interviews with experts who help in designing the system. Each disease frame has a number of questions/symptoms/associated tests. After identifying all of them, a classification is generated based on its importance in the diagnosis itself. In addition, to rate them and establish ranges that can take (facing assess the degree of similarity of the state of a patient with a disease) a second oriented three large

1. Go through all the questions that the system has suggested to the system user. For each:
    1. Evaluate in areas or diseases where this response affects the outcome of a diagnosis.
        1. Get the answers pre-set in the stages of system design, which allow increase or decrease "suspicion" the patient has the disease.
        2. If the question that has been evaluated and has an outcome:
            1. The numerical value is added according to the expert judgment (Knowledge acquisition process) if it fits with the frame (prototype) of this disease.
            2. If, on the contrary, does not fit, the numerical value rest proximity to the patient with the disease.
        3. If the answer does not have a valid value as is expected (do not know / no answer, empty, etc.):
            1. If the value is not known because there has been no way to evaluate it, it is scored according to defined parameters (Knowledge acquisition process).
            2. If the value has not been evaluated, the score differs, since the question despite being exposed, has not been assessed.

Figure 4. Rates prototypes algorithm.

groups classification is generated:

- The first group are the questions/tests, etc. decisive,
- The second are those that can guide the user to a decision without going to confirm, and
- Last (group 3) are symptoms/tests that would provide less significance but are included within the disease frame.

The procedure for submitting questions to the user is given in Figure 5.

When does the system know whether the answers are enough to move to the next group? It is decided in the knowledge acquisition process and stored in the diseases frames. While the answers to the questions of a pattern are filled, they are filling the rest of patterns containing these questions. So you may have answered almost all questions in group 1 of an X pattern and when reordering patterns go and start with the group 2 of questions of another different one.

1. An initial questionnaire which will make a first assessment of the similarity of different diseases is presented.
2. The questions of the most similar pattern are presented.
    1. System presents all first group questions (can be answered all or just some).
    2. Because they can be answered only some, in the second step, two things can happen:
        1. If there are not enough questions answered in the first wave, it insists showing all except the first group already answered.
        2. If answers are sufficient, the group 2 and left unanswered of the group 1 are shown.
3. Group 3, the same as for groups 1 and 2.

Figure 5. Procedure for submitting questions to the user.

4. EXAMPLE OF PATIENT EVALUATION

In this section, it is described first the basic workflow of a patient evaluation, then it is presented a complex clinic case for study, with details about how the system behaves in a real reasoning process.

4.1. Evaluation of Workflow

The procedure followed by the CDSS in the process of patient evaluation and reasoning is shown in Figure 6.

As shown in Figure 5, the first step is the choice of questions to ask. On it, the system evaluates what questions choose to ask, for extracting the key responses at each point of diagnosis. For example, if diagnosis is in a starting point, it shows the initial questions chosen to know where to guide the process: Do you feel pain for more than 6 months ago?, Do you feel joint pain?, Do you feel muscle pain?, Do you feel located or generalized pain?, Do you feel pain in the morning for more than 30 min?, Does it improve with medication?, Do you have skin lesions?, and so on.

In later iterations, the disease set is ordered by similarity for each patient and it is used to choose the questions to ask belonging to the prototype which has more similarity. For example, the questions related to the prototype "polymyalgia rheumatica" are, among others, as follows: How old is he?, Do you have pain and stiffness ?, Does it improve with medication?, Does he respond well to steroids?, Has he electromyography alterations?, Is it high the PCR value ?, and so on.

This process also enables that the evaluation of the questions will be at the same time in all prototypes.

The structure of the questions in each prototype will follow the scheme explained above, being the most urgent symptoms assessed before the others. This

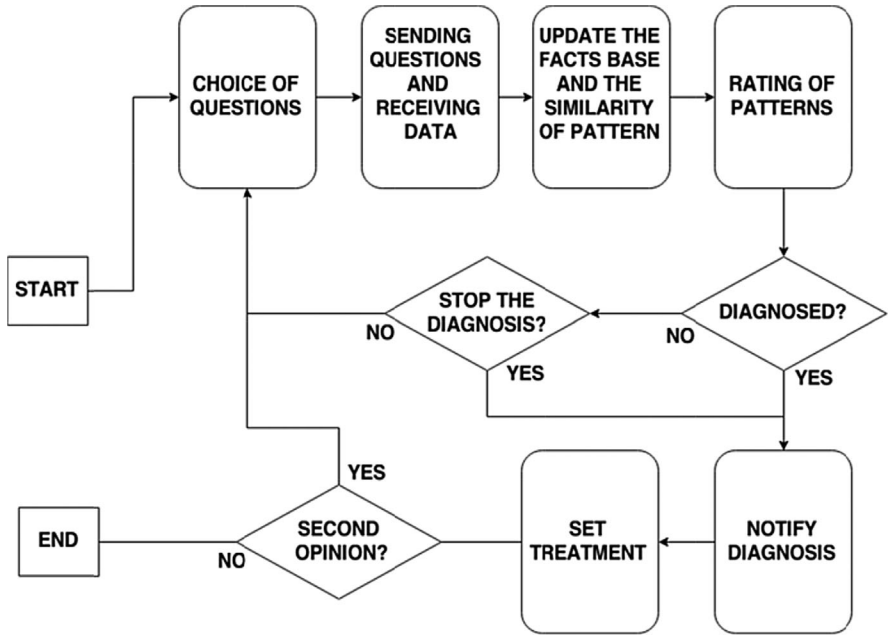

Figure 6. Process of a patient evaluation.

is what the system uses at each iteration to choose the most appropriate questions in each case. Then, the answers to the questions asked will be received and are used for performing the quantification of the similarity of input data with respect to the prototypes. And finally, prototypes are ordered by similarity. If the patient has been diagnosed, the diagnosis is notified, and a treatment, depending on the symptoms reported, is established, giving the possibility to the physician to make a second diagnosis. In the case that the patient has been sufficiently evaluated or the data are contradictory, this question is not performed and the system itself gives information about the most likely diagnosis.

4.2. A Complex Clinical Case

To illustrate in more detail the process undertaken by the core reasoning system, a real clinic case of a patient will be presented (Table I):

At the start of the interview, the practitioner begins to establish rapport with the patient by asking opening questions about the patient's condition and concerns. For this purpose, the system provides the list of initial questions except for those that are in the Patient Electronic Health Record because they have been automatically included in the patient facts, for example, age, genre, number of visits, and so on.After the evaluation of the algorithm described (Figure 4), the system determines that the more viable prototype is Lupus (Table II).

Table I. Overview of the presented complex clinical case

Patient	The patient is a 52 year-old resident in Ciudad Real (Spain) who has attended high frequency of primary care consultations, describing a symptom that could be framed within the scope of the system.
Clinical Case	It is proposed an evaluation for the CDSS designed for a case with a number of symptoms such as skin affectations nonspecific, unspecific blood disorders (including leucopenia and lymphopenia), presence of debility proximal muscle (typical of patients with polymyalgia) and poor response to corticosteroids. With this symptomatic frame, it is wanted to perform a check for a positive diagnosis of Fibromyalgia, given the high proximity with polymialgia, hypothyroidism, polymyositis, and dermatomyositis.
Results	The expected result is a positive diagnosis for fibromyalgia and several alternative diagnoses: polymyalgia rheumatica, hypothyroidism, polymyositis, or dermatomyositis. As for the results obtained by the CDSS, the main diagnostic is the same that the expert formulated. Among the alternatives, the system has determined, by order of similarity: hypothyroidism, dermatomyositis polymyalgia rheumatica.

Table II. Situation after the initial questions

Prototype	Diagnosed	Rejected	Value
Fibromyalgia	No	No	−0.28
Dermatomyositis	No	No	−2.00
Lupus	No	No	−0.22
Rheumatoid arthritis	No	No	−0.64
Hypothyroidism	No	No	−0.78
Polymyositis	No	No	−0.41
Polymyalgia rheumatica	No	No	−1.09

Not having detected a fact that ratifies or disproves the hypothesis, it asks a series of data with which it continues working on this hypothesis. Then, it determines that Lupus cannot be, because there are facts which lead to the rejection of this hypothesis (the no presence of anti-native DNA antibodies). Therefore, the similarity function has changed the order of prototype's vector because now there is a higher affinity with other prototype, in this case, rheumatoid arthritis.

In a subsequent iteration, it detects that it could be a case of hypothyroidism and it continues asking only two questions, the value of TSH and if the patient suffers from frequent fatigue. After the answers, the order of the vector is readjusted, and the system suggests the patient could have fibromyalgia. At that time, it evaluates its indicative facts and later, the tangential (others/secondary) facts. Finally, it determines that the prototype with more similarity with respect to the patient's clinical case corresponds with the fibromyalgia prototype. That is when a new process begins to establish a treatment.

To finish, it recommends to closely monitoring three diseases highly related, by the similarity of his symptoms in this clinic case: hypothyroidism, dermatomyositis, and polymyalgia rheumatica, in this order.

Table III. Cases evaluated

Case	Clinic-verified case	CDSS diagnostic
1	Rheumatoid arthritis	Rheumatoid arthritis
2	Dermatomyositis	Dermatomyositis
3	Polymyositis	Polymyositis
4	Hypothyroidism	Hypothyroidism
5	Lupus	Lupus
6	Polymyalgia rheumatica	Polymyalgia rheumatica
7	Clinic case between Lupus y Rheumatoid Arthritis (alt.)	*Rheumatoid arthritis*, Alt: dermatomyositis, polymyalgia rheumatica.
8	Clinic case of a patient who is expected to have polymyalgia rheumatica and their symptoms might be confused with polymyositis and dermatomiositis	*Polymyalgia rheumatica*, Alt: polymyositis, dermatomyositis or A. rheumatoid arthritis
9	Clinic case of hypothyroidism. Owing to the symptoms of this case, the diagnosis may be confused with polymyositis or even with fibromyalgia.	*Hypothyroidism*, polymyositis, polymyalgia rheumatica or fibromyalgia.
10	Clinic case whose diagnosis could be polymyalgia rheumatica, Hypothyroidism, polymyositis or dermatomyositis.	*Fibromyalgia*, Alt: hypothyroidism, polymyalgia rheumatica, dermatomyositis.

4. SYSTEM EVALUATION

The verification of the results of the proposed system was carried out by evaluating 10 patients at the Health Center of Daimiel (Spain), through the supervision of Francisco Alonso, MD. The patients have been diagnosed earlier, and it has been proven that the medication chosen by the expert for each disease is the correct dose levels that allow them to lead a relatively normal life. The summary of the assessment for patients is presented in Table III:

As it can be seen, it has reached a high degree of similarity between the medical diagnosis, verified by the expert, and the provided by the CDSS (about 98%). The case of the patient 7 has been partially verified by the CDSS, as it has detected one of the two pathologies with greater similarity between the symptoms: rheumatoid arthritis.

However, it has not detected the possible presence of Lupus in the patient. Nevertheless, the reasoning followed was verified and accepted by the expert. Considering the recorded data in the time of diagnosis and tests conducted by the expert without system help, it can be determined that the CDSS has been a tool, in combination with the physician, that has reduced the time of diagnosis, the number of consultations, and the cost of testing for the health care institution.

The proposed CDSS has been designed as a question/answering system to support ease of use in navigating and retrieving information. To assess the usability of the proposed system, a usability study inspired in Ref. 42 has carried out. Therefore, the expert was asked to prepare two clinic visits on the basis of fictitious patient scenarios, one simple and one complex. The expert physician validated the scenario descriptions and verified the system reasoning process and the asked questions

for each scenario. After these tests, the expert defines the system as well designed, robust, and with a good level of usability. The reasoning mechanism has been valued by our expert as a natural and logical reasoning and close to physician behavior. Moreover, it is demonstrated that he use of the proposed approach reduces time to diagnose these fuzzy diseases in terms of number of medical visits and the time between the first appointment and the start of the right treatment.

5. CONCLUSIONS AND FUTURE WORK

The main goal of this paper is to propose a CDSS as a powerful and essential tool for a doctor as a stethoscope and that it may be useful in the diagnostic and treatment of fuzzy diseases. In this sense, it has been worked using several AI techniques that have allowed to model each disease as a fuzzy prototype for giving to diagnostic and treatment processes a higher flexibility, using the degrees of compatibility for "deformation" of these fuzzy diseases. In this case, the system described aims to improve the health care assistance of the patients with difficult identifiable diseases, enhancing the standard of living of each one. Moreover, for health care institutions, it supposes a considerable cost saving, taking into account the information provided in the introduction of this document.

Finally, with regard to future works, several improvements related to improve the system are proposed. Among others, it includes the extraction of conclusions of medical reports, written through a linguistic processing of unstructured text, to increase the independence of the system, and in terms of patient data extraction. Moreover, it is proposed a generalization of the defined model, for building several interconnected CDSS allowing the diagnostic and treatment of diseases in multiple groups. This lets also an easy way for a disease definition, using the prototype concept.

References

1. HIMSS: 2013. Annual report of the U.S. hospital IT market. Technical report, 2014.
2. Peek N, Combi C, Marin R, Bellazzi R. Thirty years of artificial intelligence in medicine (AIME) conferences: A review of research themes. Artif Intell Med 2015;65(1):61–73.
3. Power DJ. Understanding data-driven decision support systems. Inform Syst Manag. 2008;25(2). 149–154.
4. Berner ES. Clinical decision support systems: Theory and practice. New York: Springer; 2007.
5. Sadegh-Zadeh K. Fuzzy health, illness, and disease. J Med Philos 2000;25(5):605–638.
6. Seising R. From vagueness in medical thought to the foundations of fuzzy reasoning in medical diagnosis. Artif Intell Med 2006;38(3):237–256.
7. Limberg J, Seising R. Fuzzy health, illness, and disease Sadegh-Zadeh's framework and a program to identify diseases. In Proc. FUZZ-IEEE 2007 Conference; 2007. pp 1–6.
8. Zadeh LA. A note on prototype set theory and fuzzy sets. Cognition1982;12:291–297.
9. Arnold LM, Clauw DJ, McCarberg BH. FibroCollaborative. Improving the recognition and diagnosis of fibromyalgia. Mayo Clinic Proc 2011;86(5):457–64.
10. Wolfe F, Brähler E, Hinz A, Häuser W. Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. Arthritis Care Res. (Hoboken) 2013;65(5):777–785.

11. Busse JW, Ebrahim S, Connell G. Systematic review and network meta-analysis of interventions for fibromyalgia: a protocol. Syst. Rev. 2013;2(1):18.
12. Branco JC, Bannwarth B, Failde I. Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum 2010;39:448–453.
13. Romero-Cordoba R, Olivas JA, Romero FP, Alonso-Gomez F. Clinical decision support system for the diagnosis and treatment of fuzzy diseases. In J.M. Puerta et al., editor. CAEPIA 2015. LNAI 9422; 2015. pp 128–138.
14. Peleg M, Tu S. Decision support, knowledge representation and management in medicine. Methods Inform Med 2006; 45(1):72–80.
15. Ameri A, Moshtaghi H. Design and development of an expert system in differential diagnosis of maxillofacial radio-lucent lesions. In: Proc. IRCSE '08: IDT Workshop on Interesting Results in Computer Science and Engineering. Mälardalen University, Västerås, Sweden, 2008.
16. Gomula J, Pancerz K, Szkola J. Computer-aided diagnosis of patients with mental disorders using the copernicus system. In: Proc. 4th Int Conf on Human System Interactions (HSI); 2011; pp 274–280.
17. Cunninghamb I, Fishera A, Lakea S, Chandnab A. Web-strabnet: a webbased expert system for the differential diagnosis of vertical strabismus (squint), Comput Math Methods Med 2010;11(1):89–97.
18. Vicente J, Garcia-Gomez JM, Vidal C, Marti-Bonmati L, del Arco A, Robles M. SOC: a distributed decision support architecture for clinical diagnosis. In: Biological and medical data analysis. LNCS, Vol 3337. Berlin: Springer; 2004. pp 96–104.
19. Maseleno A, Hasan M. Skin infection detection using Dempster-Shafer theory. In: Proc Int Conf on Informatics, Electronics Vision (ICIEV); 2012. pp 1147–1151.
20. Marateb HR, Goudarzi S. A noninvasive method for coronary artery diseases diagnosis using a clinically-interpretable fuzzy rule-based system. J Res Med Sci 2015;20(3):214–223.
21. Douali N, Roo JD, Papageorgiou EI, Jaulent MC. Case based fuzzy cognitive maps (CBFCM): new method for medical reasoning. In: Proc IEEE Int Conf on Fuzzy Systems; 2011.
22. Romero FP, Olivas JA, Oruezabal MJ. Enhancing knowledge management capabilities in web-based decision aids using fuzzy prototypes and Data Quality criteria. In: Proc IFSA/NAFIPS 2013 Conference; 2013; pp 519–524.
23. Lin Lin PJ., Jen-Hwa H, Olivia R, Sheng L. A decision support system for lower back pain diagnosis: uncertainty management and clinical evaluations. Decis Support Syst 2006;42(2):1152–1169.
24. Cucu R, Avram C, Astilean A, Farcas IG, Machado J. E-health decision support system for differential diagnosis. In: Proc IEEE Int Conf on Automation, Quality and Testing, Robotics; 2014., pp 1–6.
25. Harth M, Nielson WR. The fibromyalgia tender points: use them or lose them? A brief review of the controversy. J Rheumatol 2007;34(5):914–22.
26. Wolfe F, Smythe HA, Yunus MB. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33(2):160–172.
27. Lawson K. Are complex therapies required as pharmacological treatments of fibromyalgia?. Futur Rheumatol 2007;2(6):599–605.
28. Papadopoulou D, Fassoulaki A, Tsoulas C, Siafaka I, Vadalouca A. A meta-analysis to determine the effect of pharmacological and non-pharmacological treatments on fibromyalgia symptoms comprising OMERACT-10 response criteria. Clin Rheumatol 2016 Mar;35(3):573–586.
29. Sadegh-Zadeh K. The prototype resemblance theory of disease. J Med Philos 2008;33(2):106–39.
30. Bremermann HJ. Pattern recognition by deformable prototypes. Systems Theory in the Social Sciences; 1976, pp. 116–159.
31. Rosch E. Cognitive representation of semantic categories. J Exp Psychol 1975;104(3):192–233.

32. Olivas JA. Contribution to the experimental study of the prediction based on fuzzy deformable categories. Ph.D. Thesis, University of Castilla-La Mancha, 2000.
33. Genero M, Olivas JA, Piattini M, Romero FP. Using metrics to predict OO information systems maintainability.In: Proc 13th Int Conf on Advanced Information Systems Engineering (CAiSE 2001). Interlaken, Switzerland, 4–8June, 2001, Springer. LNCS Vol. 2068. pp 388–401.
34. Angulo E, Romero FP, García-Ródenas R, Serrano-Guerrero J, Olivas JA. An adaptive approach to enhanced traffic signal optimization by using soft-computing techniques, Expert Syst Appl 2011;38(3):2235–2247.
35. Romero FP, Caballero I, Serrano-Guerrero J, Olivas JA. An approach to web-based personal health records filtering using fuzzy prototypes and data quality criteria. Inform Process Manage 2012;48(3):451–466.
36. Sobrino A, Puente C, Olivas JA. Extracting answers from causal mechanisms in a medical document. Neurocomputing, 2014;135:53–60.
37. Garcés PJ, Olivas JA, Romero FP. Concept-matching IR systems versus word-matching information retrieval systems: Considering fuzzy interrelations for indexing web pages. J Am Soc Inform Syst Technol 2006;57(4): 564–576.
38. Olivas JA. Applications of fuzzy prototypes: Forest fire prediction and medical diagnosis. In: Proc Int Conf on Artificial Intelligence (IC-AI '99). CSREA Press, Las Vegas, NV, United States, 1999. Vol 2, pp 662–668.
39. Musen MA, Middleton B, Greenes RA. Clinical decision-support systems. In: Biomedical informatics. Berlin, Germany: Springer; 2014. pp 643–674.
40. Rosch E. Natural categories. Cogn Psychol 1973;4:328–350.
41. Armstrong SL, Gleitman LR, Gleitman H. What some concepts might not be. Cognition 1983;13:363–308.
42. Kilsdonk E, Peute LW, Riezebos RJ, Kremer LC, Jaspers MW. From an expert-driven paper guideline to a user-centred decision support system: a usability comparison study. Artif Intell Med 2013;59(1):5–13.