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A FUZZY APPROACH TO EVALUATION AND MANAGEMENT OF THERAPEUTIC PROCEDURE IN DIABETES MELLITUS TREATMENT

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Abstract: In this paper a new fuzzy model (FMOTPD2) is developed and by this model the measures of beliefs are determined so that one of the groups of possible therapeutic procedures is optimal for each patient of type 2 diabetes on hospital treatment. The choice of therapeutic procedure on individual level, which is one of the demands of modern medicine, means that each therapeutic procedure is to be evaluated by multiple and different criteria. In this paper, evaluation criteria are classified into two groups: (1) common criteria by which medicines used by the type 2 diabetes patients are being evaluated and (2) specific criteria, by which the patients' 1h state of health with type 2 diabetes mellitus is being estimated. Generally, the relative importance and values of these criteria are different. It is assumed that (a) the relative importance of evaluation criteria is defined by a team of medical experts and described by linguistic expressions and (b) the values of evaluation criteria are determined by evidence data, anamnesis and a diagnostic process. They can be crisp or uncertain. The most often used linguistic expressions describing the relative importance of evaluation criteria are modeled by triangular fuzzy numbers. The rest of uncertainties, which exist in developed model are described by discrete fuzzy numbers. A new algorithm for determining a unified fuzzy portrait of treated therapeutic procedures for each patient is given. It enables calculation of the measures of beliefs that some therapeutic procedures are more optimal than the others. The developed model is illustrated by examples with real word data collected in a hospital.

Keywords: Type 2 diabetes, therapeutic procedure, knowledge-based system, uncertainty, fuzzy set.

1. INTRODUCTION

Diabetes mellitus is a group of metabolic disorders with absolute and/or relative insulin deficit. Making a diagnosis of this disease is based on procedure which is developed by American Diabetes Association [2]. Doctors diagnose diabetes mellitus if fasting blood glucose is higher than 7.0mM and if blood glucose is higher than 11.0mM in 2h oral glucose tolerance test. Patients with diabetes have good glycemic control if HbA1c (as the retrograde parameter of glycoregulation within the past 2 to 3 months) is lower than 7 %.

Diabetes is rapidly increasing in the developed countries, in such a way that the increase can be described as an epidemic. According to data from International Diabetes Foundation in 2005 more than 246 million people worldwide is being treated for this chronical non-contagious disease. According to results of experience of this organization, by the year 2025 over 300 million people worldwide will have diabetes. The actual number of people with diabetes mellitus is definitely higher since by certain epidemiological investigations, on each diagnosed patient there is one non-diagnosed patient. A high percentage of patients with diabetes belong to the group of active population. Health care organization and doctors emphasize the necessity of prevention, which could be carried out through well-planned screening, so that it could delay or reduce the risk of transitioning from prediabetes to outright diabetes. In [11] it is shown that modification of diet and exercise patterns of people at diabetes risk, reduce incidence of diabetes by 58%. Also, the treatment of pre diabetes with drugs (metformine and glitazons) reduces the risk of transitioning to diabetes by 25% to 49%.

The new classification system identifies four types of diabetes mellitus: "type 1", "type 2", "other specific types" and gestational diabetes [18]. In this paper, the author considers patients with type 2 diabetes mellitus, because over 90% of diabetic disorders have this type of diabetes. Type 2 diabetes mellitus is characterized by insulin resistance in peripheral tissue and an insulin secretory defect of the beta cell [24]. Type 2 diabetes mellitus is caused by a combination of genetic and environmental factors. Many genes have been implicated in increasing or causing the likelihood of the disease [7]. Environmental factors contribute to low energy expenditure and obesity [9].

The procedure of diabetes mellitus treatment is defined in clinical guidelines for each type diabetes mellitus. The treatment requires the use of hygiene regime diet (diet, increased physical activity, and weight loss) and the use of pharmacotherapy. Pharmacological options start with 2 monotherapy treatment of patients with type 2 diabetes. If the glucose control is bad during time (as determined by HbA1C), then it is necessary to include other medicines as well. There are standard combination drugs which are defined in clinical guidelines for type 2 diabetes. In [5] it is shown that the complementary actions of the antidiabetic agens metformin hydrochloride and rosiglitazone maleate may main optimal glycemic contro in patients with type 2 diabetes. Therefore, their use may be indicated for patients whose diabetes is poorly controlled by metformin alone. In [20] a consensus algorithm for the initiation and adjustment of therapy is presented. Medical management of hyperglycemia in type 2 diabetes is performed by using this algorithm. Developed algorithm is based on the algorithm which is presented in 2006 by these authors. In this paper, an update to the consensus algorithm specifically addressed safety issues surrounding the thiazolidinediones. In this revision, they focus on the new classes of medications that now have more clinical data and experience.

In classical approach treatment, based on experience and knowledge as well as the patient's state of health, the doctor determines therapeutic procedure which is most suitable for the considered patient. Adequate therapy is important for each patient with type 2 diabetes for:

1. care of health

In theory and clinical practice it is well known that inadequate therapy leads to diabetic complications such as: (1)diabetic retinopathy - nowadays the leading cause of blindness in the working-able population [6], (2) diabetic neuropathy - the leading cause of the lower extremities amputations [19], as well as complications on large blood vessels ([10], [16]) (myocardial infraction, cerebrovascular disease, peripheral vascular disease, and congestive heart failure)- which are major cause of morbidity and mortality for patients with type 2 diabetes.

2. Treatment cost reduction.

In other words, the problem which is considered in this paper is a very actual one in the clinical, social and financial sense.

Patients' state of health with type 2 diabetes is being described by many attributes: blood glucose (fasting blood glucose, HbA1C), lipogerulation, blood pressure, body mass index (BMI), duration of diabetes, etc. In practice, it is known that hypertension in patients with type 2 diabetes is a prevalent condition that leads to substantial morbidity and mortality. In other words , state of health of considered patients could not be determined precisely so the problem of choice of optimal therapeutic procedure for each patient with type 2 diabetes becomes more complex, which leads to the increase of the complex choice optimal therapy for each patient with type 2 diabetes. Due to this we may conclude that the use of medical knowledge–based systems could be a very good solution for the considered problem.

Since the beginning of the second half of the 20th century, as a support to the decision making process in one domain in the area of medicine, is the increasing use of clinical expert systems into which different medical knowledge is built. However, it should be mentioned that the implementation and use of the clinical expert system is linked with many difficulties ([17], [27]). In [1] is developed a low-cost automated knowledge-based system that helps in self-diagnostics and management of this chronic disease for patients as well as doctors. Some real-life experimentations were performed, which confirmed the effectiveness of the developed system.

Any expert knows that his or her medical knowledge consists of nearly 70% of uncertain data [23] for example: symptoms, test analysis, prognostic information, etc. According to data from literature [12] clinical uncertainties can be sufficiently well described by the fuzzy sets theory ([21], [28], [29]). The advantages of the fuzzy approach in modeling of the clinical uncertainties, with respect to other techniques and methods, are numerous. Fuzzy set theory can provide a valuable tool to cope with three major problematic areas of optimal therapeutic procedure determining: imprecision, randomness and ambiguity. As far as imprecision is concerned it provides a powerful tool to weigh evaluation criteria relative importance. As far as randomness is considered, it is more effective than probabilistic approaches in the way that the considered problems can be based on previous events, since each independent case is not repeatable. As far as ambiguity is concerned it copes better than other methods with the treatment of linguistic variables. Fuzzy logic enables us to emulate the human reasoning process and make a decision based on vague or imprecise data [14].

In the literature one can find a large number of papers in which the blood glucose control is done in an exact way, by the mathematical modeling application. In [4] a model is described in which the blood glucose control is done by application of the fuzzy logic principles and neural networks techniques. It was shown that the neuro-fuzzy control system is effective in improving the blood glucose control in critical diabetes patients without increasing either the number of blood control determinations or the risk of hypoglycemia. In [8] is shown application of a neural network approach for development of a prototype system for knowledge classification in domain of diabetes management. The system will further facilitate decision making for patients with diabetes by insulin administration. In particular, a generating algorithm for learning arbitrary classification is employed. The factors participating in the decision making were among others: diabetes type, patient age, current treatment, glucose profile, physical activity, food intake, and desirable blood glucose control. Roudsari [25] developed a web-based diabetes management system (DiabNet). DiabNet offers innovative online diabetes management involving online appointment and consultation. This intelligent system can be personalized to the needs of the individual patient, incorporating appropriate historic trends in blood glucose data and with the potential of including an adaptive capability. In [13] a new method for classification of data of a medical database is developed. One of the aims of classification is to increase the reliability of the results obtained from the data. Authors assumed that values of medical data can be crisp and fuzzy. A hybrid neural network that includes artificial neural network and fuzzy neural network was developed. Determining the applicability of the proposed model is tested on real data.

The paper is organized in the following way: In Section 2 is given the setup of the choice problem of the optimal therapeutic procedure under multi-criteria with respect to its relative importance for each patient with diabetes mellitus type 2, separately; in the third Section the uncertainties modeling by the fuzzy numbers is presented; in Section 4 the new model (FOTPD2) is given and the corresponding algorithm for evaluation and choice of the optimal therapeutic procedure on individual level for patients with diabetes mellitus type 2; in Section 5 an example in which real data exist is presented. The authors consider that the developed model should be a mathematical basis for development of an expert system for automatic choice of the optimal therapeutic procedure for each patient with type 2 diabetes.

2. PROBLEM STATEMENT

2.1 Basic Assumptions

Assumptions for evaluation and management of therapeutic procedure treatment for each patient with type 2 diabetes are:

-A group of patients is being observed, which did not have regulated glycemia, though they are taking the Metformin therapy.

-Considered therapeutic procedures which are defined in clinical guidelines for diabetes mellitus; they are determined according to algorithm of type 2 diabetes treatment.

-There are genetic names of drugs for use in type 2 diabetes:

1. **Biguanides** (exemplified by metformin), decreases hepatic glucose production and has some effect on peripheral glucose uptake.
2. **Sulfonylureas**, enhance insulin secretion (the oldest agents used to treat type 2 diabetes)
3. **Thiazolidinediones** which are peroxisome proliferator-activator receptor (PPAR)-gamma activators (for example pioglitazone), act at number of sites to lower blood glucose levels by increasing insulin sensitivity in muscle and adipose tissue and have some effect on lowering hepatic glucose production.
4. **Alpha-glucosidase inhibitors** (Inhibitori alfa-glukopzidaze) are used to slow the digestion of starches and the absorption of glucose from the gastrointestinal tract.
5. DPP IV inhibitors
6. **Insulin** is only available through injections. It reliably decreases blood glucose but increases the risk of weight gain and symptomatic low blood sugar episodes.

-Generally, each therapy can be consisted of one or more drugs; in the considered problem, therapies are consisted of more drugs and they are:

1. Metformin and Insulin
2. Metformin and Sulfonylureas
3. Metamorfin and Glitazoni
4. Metformin, Sulfonylureas, and Insulin
5. Metformin, Sulfonylureas, and Glitazoni
6. Metformin and DPP IV inhibitors
7. Metformin and Alpha- inhibitors glitazonate.

-Criteria for evaluation of drugs (in further common criteria) which are used for type 2 diabetes are:

1. Unit price of a drug, monetary unit
2. Efficiency of a drug
3. Side effect of a drug

The choice of therapy depends of temporary patient's state of health. Criteria on which the state of health for each patient with type 2 diabetes can be determined (in further specific criteria) are:

1. fasting blood glucose, mM
2. HbC1, mM
3. time length of the illness, years
4. obesity (BMI)

-To each considered criteria an ordered pair is associated (relative importance, value).

Relative importance of considered criteria does not depend on patient and they change rarely. Generally, the relative importance of considered criteria is different and determined on the basic of knowledge and experience of doctors. In this paper, they are described by linguistic expressions which are modeled by triangular fuzzy numbers.

Values of common criteria, that is specific criteria, are being determined for each drug, in other words for each patient individually. These values can be crisp or uncertain. In this paper, modeling of uncertain criteria is based on fuzzy set theory.

2.2 Notation

l drag which use for type 2 diabetes, l=1,..,L

L the total number of treated drugs

i crisp criterion according to evaluate drug l, i=1,..,I

j uncertain criterion according to evaluate drug l, j=1,..,J

I, J, (I+J), number of crisp criteria, number of uncertain criteria and the total number criteria for evaluating of treated drugs, respectively

p index for patient, p=1,..,P

P the total number of treated patients with type 2 diabetes

c crisp criterion according to evaluation of patient's state of health with type 2 diabetes, c=1,..,C

u uncertain criterion according to evaluation of patient's state of health with type 2 diabetes , u=1,..,U

C,U, (C+U)-number crisp criteria, number of uncertain criteria and the total number of criteria according to evaluation of each treated patient's state of health with type 2 diabetes, respectively

$\tilde{W}_i, \tilde{W}_j$, $\tilde{W}_c$, -triangular fuzzy number representing relative importance of each considered criteria

V_{lj} parameter of criterion i of considered drug l, i=1,..,I; l=1,..,L

$(V_{li})^n$ normalized value of V_{lj}, i=1,..,I;l=1,..,L

$\tilde{V}_{lj}$ parameter of criterion j for drug l, j=1,…,J;l=1,..,L

b_{lj} transformed value of $\tilde{V}_{lj}$, j=1,..,J; l=1,..,L

$\tilde{\Phi}_{li}$ represents value of criterion i for drug l with respect to relative importance of criterion i, i=1,..I; l=1,..,L

$\tilde{\Phi}_{lj}$ represents value of criterion j for drug l with respect to relative importance of criterion j, j=1,..,J; l=1,..,L

$\tilde{\Phi}_{l}$ fuzzy portrait of drug l, l=1,..,L

t combined therapeutic procedure which is used for treatment of patients with type 2 diabetes, t=1,..,T

T the total number of considered therapeutic procedure

$\tilde{\Phi}_{t}$ fuzzy portrait of therapeutic procedure t, t=1,..,T

v_{cp} parameter of criterion c of treated patient p, c=1,..,C; p=1,.,P

v_c^r reference value of criterion c, c=1,...,C

v_{cp}^n normalized value of v_{cp}, c=1,..,C; p=1,.,P

$\tilde{\Phi}_{cp}$ represents value of criterion u with respect to their relative importance for treated patient p, u=1,..,C;p=1,..,P

$\tilde{\Phi}_{p}$ fuzzy portrait of patient state of health p, p=1,..,P

$\tilde{\Phi}_{tp}$ fuzzy portrait of therapeutic procedure t i for patient p, t=1,..,T; p=1,..,P.

3. MODELLING OF UNCERTAINTIES

In this Section, the modeling procedure of uncertainties which exist in the developed model is described. Modeling of all uncertainties is based on the fuzzy set theory ([28],[29]).

3.1 Relative importance of criteria

The number and type of linguistic expressions by which the relative importance of criteria (common and specific) is described according to choice of the optimal therapeutic procedure for patient with diabetes mellitus type 2, are determined by the team of doctors. In this paper, we use five linguistic expressions: *very low importance, low importance, medium importance, high importance,* and *very high importance.* These linguistic expressions are modeled by the triangular fuzzy numbers, $\tilde{W}_1,\tilde{W}_2,\tilde{W}_3,\tilde{W}_4,\tilde{W}_5$, respectively.

The domain of each triangular fuzzy number $\tilde{W}_1,\tilde{W}_2,\tilde{W}_3,\tilde{W}_4,\tilde{W}_5$ is defined over the set of real numbers, which belong to the interval [0,10]. The value 0 denotes that the relative importance is the lowest and value 10 that it is the highest.

In the literature, there are six classes of experimental methods which are used for determining membership functions [21]. According to the problem that is considered here, the authors have used the horizontal method of membership estimation.

The triangular fuzzy numbers by which the relative importance of causes due to which diabetes complications occur is described, are shown in Fig.1.

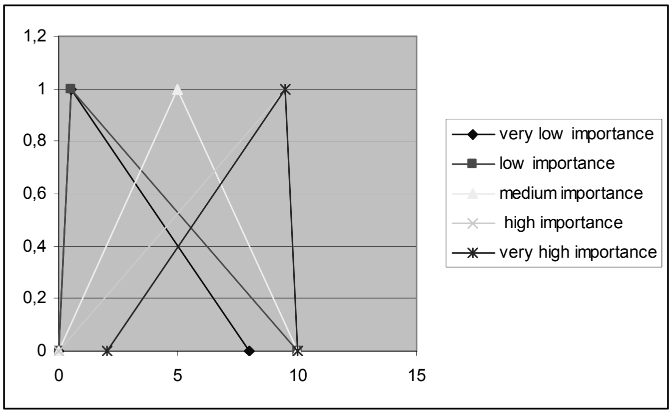

Figure 1: Relative importance of causes

3.2 Modeling of Side Effect of Drugs

The uncertain criteria such as side effect of drugs and existence of diabetic complications and presence of joined illnesses are described by different linguistic expressions. The number and kind of these linguistic expressions are determined by doctors. They are modeled by discrete fuzzy numbers. Why we opted for discrete fuzzy numbers? We used discrete membership function in order to avoid analytic considerations and to apply "digital way of thinking" [15]. According to evidence data and/or results in practice (for instance by applying DELFI method) it is possible to determine membership function of each discrete fuzzy numbers.

In this paper, the domain of each discrete fuzzy number is defined over the set of real numbers, which belong to the interval [0-5]. The value 0 denotes that the value of considered uncertain criteria is the lowest and value 5 that it is the highest.

Side effects of drugs are described as negative effects which are caused by the drug. These side effects are numerous and different and they are described for each drug separately. Some of the most recent side effects which may occur are: feeling of nausea, weakness, psychomotor abilities disorder.

In this paper it is assumed that values of side effects are able to describe through three linguistic expressions: "low", "moderate" and "high". These linguistic expressions are modeled by discrete fuzzy numbers which are shown in Figure 2.

Defined discrete fuzzy numbers which are used for describing of values of uncertain criteria are shown in Fig. 2.

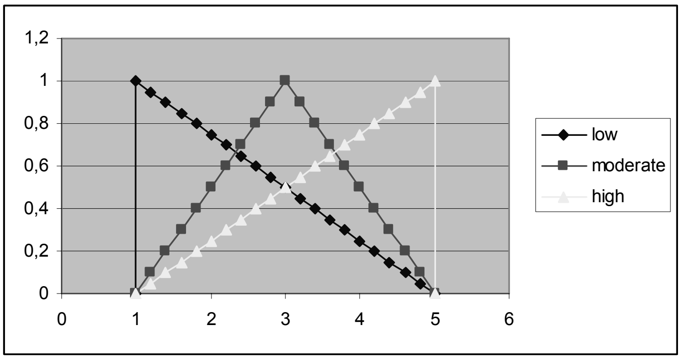

Figure 2: Values of uncertain criteria

4. A NEW DEVELOPED FUZZY MODEL

Based on clinical and epidemiology researches type 2 diabetes is widely spread in population of 20 years of age and over. In other words, a large number of active labor population is being treated of considered disease. Type 2 diabetes treatment is primarily based on medical therapy. The choice of optimal therapy on individual level is the most important issue in type 2 diabetes patient treatment.

In the first step, in determining of the optimal therapeutic procedure for each treated patient with type 2 diabetes, normalized and transformed values of criteria are being determined by which medicines from the defined group of possible medicines are evaluated. The normalization of parameters v_{lj} by applying the linear normalization procedure [22] is performed and thus the normalized parameters $(v_{lj})^n$ which belong to a common scale [0,1] are obtained. Transformation of the linguistic criteria values $\tilde{v}_{lj}$, into degrees of belief b_{lj} is expressed on a common scale [0,1] by applying a fuzzy set comparison method [22]. In the following step, to each normalized and transformed value of considered criteria we join the relative importance of criteria $\tilde{W}_i, \tilde{W}_j$, respectively, and thus values $\tilde{\Phi}_{li}$ and $\tilde{\Phi}_{lj}$ are obtained. $\tilde{\Phi}_l$ is the aggregated sum of the criteria according to evaluate drugs pondered by the relative importance of these criteria. In practice, it is known that patients with type 2 diabetes use combined therapy almost every time, in the next step we define fuzzy portrait of each defined therapeutic procedure $\tilde{\Phi}_t$. Accordingly, $\tilde{\Phi}_t$ is a triangular fuzzy number and it is a base for determining optimal therapeutic procedure on individual level.

In order to choose optimal therapeutic procedure it is necessary to determine type 2 diabetes patient state of health. In this paper, state of health of each considered patient is described by deterministic parameters v_{cp}. These values are different for each patient and they are different from the corresponding referent values of those parameters v_c^r in healthy persons. As the first step in determining of patient state of health with type 2 diabetes, the normalization of parameters v_{cp} is performed in such way that each value is divided by the reference values v_c^r and thus the normalized parameters v_{cp}^n are obtained. Those are, as a rule, numbers greater than 1. If value v_{cp}^n is higher than 1, it is worse and vice versa.

The reference values are:

$v_1^r = 7.5\,mM$, $v_2^r = 7\,mM$, $v_3^r = 10\,year$, $v_4^r = 25$

Fuzzy model for determining the optimal therapeutic procedure for each patient with type 2 diabetes, separately it is based on determining the unique fuzzy portrait of therapeutic procedure on individual $\tilde{\Phi}_{tp}$ which describes predisposition that therapeutic procedure t, t=1,..,T is optimal for patient p, p=1,..,P. $\tilde{\Phi}_{tp}$ is calculated as cross section of the following triangular fuzzy numbers $\tilde{\Phi}_t$ and $\tilde{\Phi}_p$.

Accordingly, $\tilde{\Phi}_{tp}$ is a triangular fuzzy number and it is a base for determining the optimal therapeutic procedure on individual level. Representative scalar of triangular fuzzy number $\tilde{\Phi}_{tp}$ in this paper is given by maximum method (ZZ, 1996). The optimal therapeutic procedure t for patient p is the one to which the highest value Φ_{t^*p}, t=1,..,T; p=1,..,P is joined.

4.1 Developed Algorithm

In this Section, algorithm for choosing the optimal therapeutic procedure for treatment patients of type 2 diabetes is given.

The developed algorithm is realized through the following steps:

Step 1. Calculate normalized values of crisp criteria for drugs:

a) for benefit criterion type

$$V_{li}^n = \frac{f_{li}}{\sum_{l=1}^{L} f_{li}} \tag{1}$$

b) for cost criterion type

$$V_{li}^{n} = 1 - \frac{V_{li} - V^{\min}}{V^{\max}} \text{, l=1,...,L; i=1,..,I} \tag{2}$$

where:

$$V^{\min} = \min_{l=1,..,L} V_{li},\ V^{\max} = \max_{l=1,..,L} V_{li},\ l = 1,..,L; i = 1,..,I$$

Step 2. Calculate measures of beliefs of uncertain criteria according to evaluation of treated drugs. In this paper, degree of belief $b_{l'j}$ is found that $\tilde{V}_{l'j}$ is less or equal to all other $\tilde{V}_{lj}$, l=1,..,L; $l \neq l'$.

Step 3. Calculation of triangular fuzzy numbers:

$$\tilde{\Phi}_{li} = \tilde{W}_i \cdot V_{li}^{n} \tag{3}$$

for all columns i, i=1,..,I which correspond to the cardinal criteria,

$$\tilde{\Phi}_{lj} = \tilde{W}_j \cdot b_{lj} \tag{4}$$

for all columns j, j=1,..J which correspond to the linguistic criteria.

Step 4. Calculate triangular fuzzy number $\tilde{\Phi}_l$:

$$\tilde{\Phi}_l = \frac{1}{I} \cdot \sum_{i=1}^{I} \tilde{\Phi}_{li} + \frac{1}{J} \cdot \sum_{j=1}^{J} \tilde{\Phi}_{lj} \tag{5}$$

Step 5. Calculate a triangular fuzzy number $\tilde{\Phi}_t$:

$$\tilde{\Phi}_t = \frac{1}{L'} \cdot \sum_{l=1}^{L'} \tilde{\Phi}_l,\ L' \leq L \tag{6}$$

Step 6. Calculate normalized values of criteria according to define patient state of health:

$$v_{cp}^{n} = \frac{v_{cp}}{v_c^{r}} \tag{7}$$

Step 7. Calculate a triangular fuzzy number $\tilde{\Phi}_{cp}$:

$$\tilde{\Phi}_{cp} = \frac{1}{C} \cdot \tilde{W}_c \cdot v_{cp}^{n} \tag{8}$$

Step 8. Calculate a triangular fuzzy number $\tilde{\Phi}_p$:

$$\tilde{\Phi}_p = \sum_{c=1}^{C} \tilde{\Phi}_{cp} \tag{9}$$

Step 9. Calculate triangular fuzzy number $\tilde{\Phi}_{tp}$:

$$\tilde{\Phi}_{tp} = \tilde{\Phi}_t \cap \tilde{\Phi}_p \tag{10}$$

Step 10. Calculate a scalar value of triangular fuzzy number $\tilde{\Phi}_{tp}$, Φ_{tp} by applying maximum method (Zimmerman, 1996).

According to calculated scalar values, Φ_{tp} for each patient p rank of possible therapeutic procedure is being determined. The optimal therapeutic procedure for patient p is the one to which the highest scalar value Φ_{tp} is being joined.

5. ILLUSTRATIVE EXAMPLE

The developed procedure is illustrated in example with real data. The relative importance criteria according to which drugs and type 2 diabetes are being ranked are evaluated upon based knowledge and experience of team of doctors (endocrinologists and pharmacologists). The values of criterion joined to each drug are determined in the following way: (1) value of unit price of drug is estimated as total monthly expense for treated drug; as price depends on amount of grams and manufacturer, in this paper we are considering the price of a drug of certain amount of grams which is being prescribed most often and a drug of the manufacturer which is widely spread in the domestic market of oral antidiabetici, (2)efficiency of a drug is defined as expected proportional reduction HbA1c due to use of treated drug; very often proportional reduction HbA1c is assigned interval, in this paper in these cases the medium interval value is considered due to simpler calculation; introduced assumption makes calculation simpler but does not affect the change of the result, (3) side effect of drugs is defined according to recommendations of pharmaceutical companies- manufacturers and the experience of doctors in practice.

Patients data are taken from the data base of 3344 patients with diabetes in the Internal Clinic Center Kragujevac, Serbia. The patients are randomly chosen without repeating.

In order to make tabular review more clear let us introduce the following notation:

v_{1p} - glycorequlation	l=1, Metformin	i=1, Unit rice of drug
v_{2p} - lipogeregulation	l=2, Sulfonylureas	j=1, Efficiency of drug
v_{3p} -obesity (BMI)	l=3, Glitazoni	j=2, Side effect of drug
v_{4p} - duration of diabetes	l=4, DPP IV inhibitors	
	l=5, Alpha- inhibitors glitazonate	
	l=6, Insulin	

T=1, Metformin and Insulin
T=2, Metformin and Sulfonylureas
T=3, Metamorfin and Glitazoni
T=4, Metformin, Sulfonylureas, and Insulin
T=5, Metformin, Sulfonylureas, and Glitazoni
T=6, Metformin and DPP IV inhibitors
T=7, Metformin and Alpha- inhibitors glitazonate

Input data

Table 1: The relative importance and values of drugs which are used for patients with type 2 diabetes treatment

	i=1	i=2	j=1
l=1	168	1.5	Low
l=2	217	1.5	moderate
l=3	2800	0.95	High
l=4	500	0.65	Moderate
l=5	5272	0.65	Moderate
l=6	1970	2	Low
Relative importance	low importance	very high importance	medium importance

Table 2: The relative importance and values of criteria according to evaluation of patient state of health patients with type 2 diabetes

	v_{1p}	v_{2p}	v_{3p}	v_{4p}
p=1	11	3	1	25
p=2	8	5	26	31
p=3	10	6	20	24
p=4	4	1	3	38
Relative importance	high importance	very high importance	high importance	low importance

By applying the developed algorithm we got the results shown in table 5.3, 5.4, 5.5.

Table 3: The relative importance, transformed values of drugs which are used for patients with type 2 diabetes treatment and fuzzy portrait of drug l, l=1,..,L, $\tilde{\Phi}_l$:

	i=1	i=2	j=1	$\tilde{\Phi}_l$
l=1	1	0.21	0.71	[0.14, 3.28, 6.4]
l=2	0.99	0.21	0.29	[0.14, 1.18, 4.97]
l=3	0.5	0.13	0.13	[0.09, 0.65, 2.53]
l=4	0.94	0.09	0.29	[0.06, 0.78, 4.4]
l=5	0.03	0.09	0.29	[0.06, 0.78, 1.37]
l=6	0.66	0.28	0.71	[0.19, 2.12, 5.5]
Relative importance	$\tilde{W}_2$	$\tilde{W}_5$	$\tilde{W}_3$	

Table 4: Fuzzy portrait of therapeutic procedure t, t=1,..,T, $\tilde{\Phi}_t$:

Therapeutic procedure	$\tilde{\Phi}_t$
T=1	[0.16, 2.74, 5.95]
T=2	[0.14, 2.23, 5.68]
T=3	[0.11, 1.96, 4.46]
T=4	[0.16, 2.19, 5.62]
T=5	[0.12, 1.7, 4.63]
T=6	[0.1, 2.03, 5.4]
T=7	[0.1, 2.03, 3.88]

Table 5: The relative importance, transformed values of criteria according to evaluation of patient state of health with type 2 diabetes and fuzzy portrait of patient state of health p, p=1,..,P $\tilde{\Phi}_p$:

	v_{1p}^n	v_{2p}^n	v_{3p}^n	v_{4p}^n	$\tilde{\Phi}_p$
p=1	1.47	0.43	0.1	1	[0.21, 5, 7.5]
p=2	1.07	0.71	2.6	1.24	[0.36, 10.95, 14.05]
p=3	1.33	0.86	2.0	0.96	[0.43, 10.47, 12.87]
p=4	0.93	0.14	0.3	1.52	[0.07, 3.42, 7.22]
Relative importance	$\tilde{W}_4$	$\tilde{W}_5$	$\tilde{W}_4$	$\tilde{W}_2$	

By applying the procedures which are defined in steps 9 and 10 of the developed algorithm we get the following results.

p=1	$\Phi_{11} = 3.647$ $\Phi_{21} = 3.681$ $\Phi_{31} = 3.003$ $\Phi_{41} = 3.363$ $\Phi_{51} = 2.952$ $\Phi_{61} = 3.257$ $\Phi_{71} = 2.858$	p=2	$\Phi_{12} = 4.649$ $\Phi_{22} = 4.373$ $\Phi_{32} = 3.677$ $\Phi_{42} = 4.333$ $\Phi_{52} = 3.705$ $\Phi_{62} = 4.183$ $\Phi_{72} = 3.357$
p=3	$\Phi_{13} = 4.613$ $\Phi_{23} = 4.337$ $\Phi_{33} = 3.657$ $\Phi_{43} = 4.298$ $\Phi_{53} = 3.681$ $\Phi_{63} = 4.151$ $\Phi_{73} = 3.343$	p=4	$\Phi_{14} = 3.073$ $\Phi_{24} = 2.034$ $\Phi_{34} = 2.584$ $\Phi_{44} = 2.812$ $\Phi_{54} = 2.502$ $\Phi_{64} = 2.727$ $\Phi_{74} = 2.525$

Rank of therapeutic procedures for each treated patient is presented in the following.

p=1	Metformin and Sulfonylureas Metformin, Sulfonylureas, and Insulin Metformin and Insulin Metformin and DPP IV inhibitors Metamorfin and Glitazoni Metformin and Alpha- inhibitors glitazonate Metformin, Sulfonylureas, and Glitazoni	p=2	Metformin and Insulin Metformin and Sulfonylureas Metformin, Sulfonylureas, and Insulin Metformin and DPP IV inhibitors Metformin, Sulfonylureas, and Glitazoni Metamorfin and Glitazoni Metamorfin and Glitazoni glitazonate

p=3	Metformin and Insulin Metformin and Sulfonylureas Metformin, Sulfonylureas, and Insulin Metformin and DPP IV inhibitors Metformin, Sulfonylureas, and Glitazoni Metamorfin and Glitazoni Metamorfin and Glitazoni	p=4	Metformin and Insulin Metformin, Sulfonylureas, and Insulin Metformin and DPP IV inhibitors Metamorfin and Glitazoni Metamorfin and Glitazoni Metformin, Sulfonylureas, and Glitazoni Metformin and Sulfonylureas

Due to these results we can conclude that optimal therapeutic procedure for first considered patient is Metformin and Sulfonylureas. Also, as numerical values joined to therapeutic procedures in the first three places are very close we can say that therapeutic procedures Metformin, Sulfonylureas and Insulin are equally good as Metformin and Sulfonylureas.

For the second patient optimal therapeutic procedure is Metformin and Insulin. If the considered patient is not in the using insulin condition, the optimal therapeutic procedure is Metformin and Sulfonylureas for this kind of patient.

For the fourth patient optimal therapeutic procedure is Metformin and Insulin. If intellectual status of patient is not satisfactory in the sense of taking insulin therapy than the following therapy Metformin and DPP IV inhibitors is prescribed.

6. CONCLUSION

In this paper, a new fuzzy model for evaluation and choice of optimal therapeutic procedure on individual level for patients with type 2 diabetes is presented. The advantages of developed model according to literal sources are shown, primary, in the more realistic statement of the problem. Teams of doctors define: (a) criteria according to which a drug is being evaluated, (b) criteria according to which a state of health of each patient is being determined, (c) the relative importance of defined criteria, (d) possible drugs and possible therapeutic procedures according to Clinical Guidelines for Diabetes and (e) values of uncertain criteria. By developing fuzzy multi-criteria model, the rank of considered therapeutic procedures for each treated patient is determined. Also, the optimal therapeutic procedure for each patient is the one to which the highest numerical value is joined. The developed model is flexible according to the possibility of number change, kind of optimization criteria change and importance of optimization criteria change. The proposed fuzzy model is suitable for software development.

The following conclusion is made:

1. It is possible to describe the problem of solving the optimal therapeutic procedure as multi-criteria optimization task by formal language that enables to look for the solution by exact method.
2. The uncertainties which exist in the model can be described by fuzzy numbers.
3. The importance of selecting the optimal therapeutic procedure is primarily shown in the adequate patient treatment. All the changes such as the changes in the number of criteria or its importance can be easily incorporated into the model.
4. The developed methodology gives the possibilities through simulation to get the answer if there would be the result change if the input data change.
5. The developed methodology is illustrated by numerical example with real data.

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