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FUZZY MULTICRITERIA APPROACH FOR EVALUATION AND RANKING THERAPEUTIC PROCEDURE

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Key words: drug choice, therapeutic procedure, uncertainty, fuzzy number

SUMMARY:. This paper presents a new fuzzy multicriteria mathematical model for evaluation and ranking therapeutic procedure (in further TP). The choice of adequate therapeutic procedure is an every-day, unsolved problem in medical practice, which has to be worked on and improved constantly. The treatment outcomes depend very much on this choice. The optimization criteria include drug performance and are given either cardinal values or linguistic expressions. Uncertainties are modelled by fuzzy numbers. The algorithm for evaluation and ranking of TP is based on the new mathematical model which is developed in this paper. An illustrative example is given.

INTRODUCTION

With recent attention to the importance of evidence-based medicine in every-day practice, a number of treatment guidelines have emerged to aid clinicians in clinical decision making [8]. If developed properly, treatment guidances lead clinicians to the most optimal treatment decisions, and treatment outcomes are improved with their use. Unfortunately, not all guidelines were developed properly, and only small segment of medical disorders is covered by valid guidelines [5, 7]. The problem is further complicated by the fact that majority of clinicians do not use valid guidelines in their practice, for variety of reasons.

There is clear need for additional modalities of helping clinicians in bringing optimal therapeutic decisions. One of them could be mathematical modelling of the decision-making process. In our work, we have developed fuzzy multicriteria model for deciding about the best treatment strategy among available options.

In this paper, fuzzy multicriteria mathematical model for ranking and evaluation TP has been developed. This model represents mathematical bases of experts system developed by the authors. Generaly, applying of mathematical models in making decision process decreases the subjectivity of experts, doctors in this case and leads to more reliable choice of appropriate solutions. In other words, the risk of choosing inappropriate TP in the treatment of patients is also decreased. This way of selecting TP can have multiple and various usage, including financial effects of treatment.

In this paper we suppose the following:

1. We considered TP relevant for each patient, separately
2. The number of TP defined by doctors is finite
3. The determining of TP is multi-criteria optimization task. Optimization criterions have different relative importance.
4. The optimization criterions have imprecise values for each TP. This assertion is based on the fact that relations between elements TP (drugs) critically depend on patients [4]. This fact is one of main reasons why this problem requires fuzzy system modeling [11]. The values of optimization criteria can be described by fuzzy numbers. The fuzzy approach to treating uncertainties has some advantages over the stochastic approach:
   - Calculating of probability distributions for each stochastic variable requests a lot of evidence,
   - Combining of different uncertainties leads to a complex probability distribution, this results in very complex mathematical expressions.

   In real problems like the one we have been considering, there are a lot of imprecise data. Turk and Fazel Yarandi [1] have summarized advantages of the phases in modeling uncertain values:
   - Fuzzy system models are conceptually easy to understand
   - Fuzzy system models are flexible, and with any given system, it is easy to manage it with system models or layer more functionality on top of it without starting again from scratch
   - Fuzzy system models can capture most nonlinear functions of arbitrary complexity
   - Fuzzy system models are tolerant of imprecise data
   - Fuzzy system models can be built on top of the experience of experts
   - Fuzzy system models can be blended with conventional control techniques
   - Fuzzy system models are based on natural languages
   - Fuzzy system models provide better communication between experts
5. The solution of the problem treated can be found by using real numbers.

This paper is organized in the following way: in Section 2, the problem statement of ranking TP is presented. In Section 3, the optimization criteria are defined and they are described by fuzzy numbers. In Section 4, a new procedure for determination of the best TP is presented. The proposed procedure is illustrated by an example given in Section 5.

PROBLEM STATEMENT

Health services research has documented the magnitude of health care variations in clinical decision making, and therefore, in the treatment outcomes. Few studies focused on the reasons for variations among physicians. However, it was noted that physician adherence with guidelines varies with different types of "patient" and with the length of clinical experience [6]. The variations could be restricted with appropriate software, which would aid in decision-making.

The mathematical problem statement

The mathematical model for evaluation and ranking TP is deceloped within the following assumptions:

1. Therapeutic indications which are being treated in the observed medical institution, formaly are presented by set of index β:

$$\beta = \{1,...,b,...,B\}$$

where B is the total number of possible therapeutic indications. This number is known and we can consider it unchangeable in longer time period.

2. The drugs which are used for illness treatment b (b=1,...,B) can be classified in the different groups, considering their different mechanisms of effects. Generaly, there are G different drug groups which are formaly presented by set of drug index

$$\chi = \{1,...,g,...,G\}$$

Let us suppose, there are N different drugs which belong to different groups in the medical institutions. The drugs are formally presented by the set of drug index ϕ:

$$\phi = \{1^g,...,n^g,...,N^g\}$$

where:

N is the total number of drugs used in the considered medical institution. This number is known according to statistical data and can be considered unchangeable in the time period.

n^g is a note for any kind of drug from the set ϕ; index g (g=1,...,G) is a note to which group the drug belongs to.

Generaly, drugs can be purchased from one or more suppliers. Determing the best supply strategy of drugs for medical institutions, presents a problem for itself. This probles is very significant from the economical aspects.

3. Each lek $n^g \ (n = 1,...,N; g = 1,...,G)$ is described by attributes such as: efficiency, safety of use, drug price, etc. Team of doctors define all the attributes which describe each drug. Their values can be either deterministic or imprecise. The optimization criteria in ranking TP are calculated from these attibutes. In general, we consider K optimization criteria, i.e.:

$$\kappa = \{1,...,k,...,K\}$$

In this paper, only three optimization criterions are associated: drug efficiency, drug safety and price of drug. The procedure for optimization criteria calculation is presented in Section 3.

4. As it is known, the optimization criteria can be either of benefit or cost type. Yoon and Hwang [12] define two criteria types:

(a) Benefit optimization criteria are positively correlated with utility or the preferences of decision maker, which means: if the criteria values increase, so does the utility of decision maker,

(a) Cost optimization criteria are negatively correlated with utility or the preferences of decision maker, which means: if the criteria values increase, so does the utility of decision maker.

According to classification which is given in [12], drug efficiency and drug safety are benefit criteria. Price of drug is cost optimization criterion.

5. In general, the relative importance of each optimization criterion k $(k \in \kappa)$, $w_k \ (k = 1,...,K)$ is different. Determination of criteria weight is a difficult task which presents a problem to itself. There are a number of techniques to assess the weights of optimization criteria. They are normalizes, non-normalizes or linguistic expressions [2].

In this paper, the comparison pair matrix of relative criteria importance $\Omega = [\omega_k / \omega_{k'}]_{KxK}$ is subjectively constructed. Elements of this matrix, $\omega_k / \omega_{k'} \ (k, k' = 1,...,K)$ are importance of optimization criterion k $(k \in \kappa)$ with respect to optimization criterion $k' \ (k' \in \kappa)$. The values of this matrix are positive and within the interval [1,9]. The value 1 marks that the optimization criteria k $(k \in \kappa)$ and $k' \ (k' \in \kappa)$ are equally important. Value 9 shows that the optimization criterion k $(k \in \kappa)$ is extremely more important than optimization criterion $k' \ (k' \in \kappa)$. Elements of this matrix have the following properties [10]:

- Elements of the main diagonal are not defined
- Values of off-diagonal terms are reciprocal to each other
- Consistency index provides a way of measuring how many errors were made when making judgments

Here, the optimization criteria weighted vector is calculated by applying eigenvector method. Optimization criteria weights are ordinal numbers.

MODELLING OF OPTIMIZATION CRITERIA VALUES

Considered optimization criteria are described in this Section.

1. Efficancy of drug

Efficacy of a drug is degree of achievement of a therapeutic goal.

Efficancy of drug can be adequately described by three linguistic descriptors: "small", "medium" i "large". These linguistic expressions are modelled by three triangular fuzzy numbers $\tilde{E}_r\ (r = 1,2,3)$, so:

$$\tilde{E}_r = \left\{ e_j, \mu_{\tilde{E}_r}(e_j) \right\} \quad (1)$$

where:

e_j is a discrete value in the domain of triangular fuzzy number $\tilde{E}_r\ (r = 1,2,3)$. These values are defined in real set of numbers into interval [1,5]. The value 1 presents that the efficiency of drug is very small, and the value 5 indicate that the drug is effitient.

$\mu_{\tilde{E}_r}(e_j)$ is the membership function of fuzzy number $\tilde{E}_r\ (r = 1,2,3)$. In this paper, we have pressumed that it is triangular. Values are determed by doctors judgements. Triangular fuzzy numbers $\tilde{E}_r\ (r = 1,2,3)$ are illustrated in Figure 1.

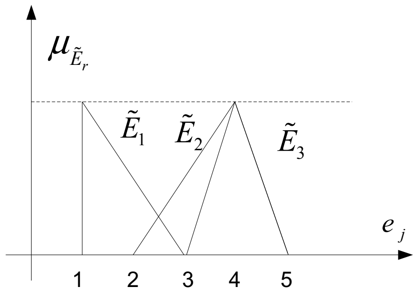

Figure 1 Triangular fuzzy numbers of drug efficiency

2. Safety of drug using

Drug safety encompasses all kinds of adverse reactions of human organism on a drug (harm that the drug could produce in the organism).

Safety of drug using can be adequatelly described by four linguistic expressions: "small", "acceptable", "medium" i "extremely big". They are modelled by four fuzzy numbers $\tilde{B}_s\ (s = 1,2,3,4)$, so:

$$\tilde{B}_s = \left\{ b_j, \mu_{\tilde{B}_s}(b_j) \right\} \quad (2)$$

where:

b_j is a discrete value in the domain of fuzzy number $\tilde{B}_s\ (s = 1,2,3,4)$. These values are defined in real set of numbers into interval [1,9] according to, Saaty's measurement scale [10]. The value 1 presents that the safety of drug usage is extremly small, and the value 9 indicates that it is safe to use the drug.

$\mu_{\tilde{B}_s}(b_j)$ is a membership function of fuzzy number $\tilde{B}_s\ (s = 1,2,3,4)$. In this paper, we have supposed that it is trapezoid shaped. Values of these functions are obtained by subjective doctors judgements.

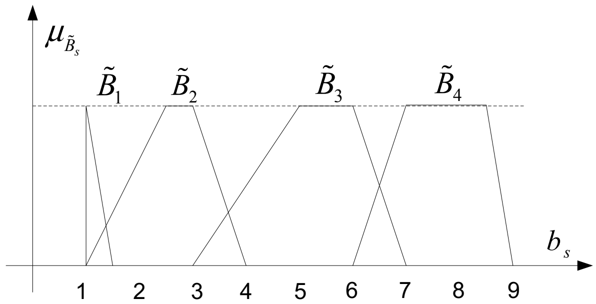

Figure 2 Fuzzy numbers which present safety of drug usage

3. Price of drug

Price of drug, $C_n\ (n = 1,.., N)$ is deterministic. It is calculated according to expression:

$$C_n = c_n \cdot f_d \cdot T \quad (3)$$

where:

c_n is unit price of drug, f_d daly dose, T period of treatment

EVALUATION AND RANKING OF TP

The procedure of evaluation and ranking of TP is realized through following steps.

Step 1. The comparison pair matrix of relative criteria importance is constructed. According to eigen- vector method [10], vector of importance of optimization criteria $W = [w_1, ..., w_K]$ is obtained.

Step 2. The procedure of normalization of optimization criteria is conducted. There are many methods of normalization in the literature [9]. In this paper, linear normalization is used:

a) for benefit optimization criteria, normalized values are calculated according to expression:

$$\left(e_j\right)' = \frac{e_j}{e_j^{max}} \tag{4}$$

e_j^{max} is a maximum value in the domain of fuzzy number broja $\tilde{E}_r$ $(r = 1,2,3)$

$$\left(b_j\right)' = \frac{b_j}{b_j^{max}} \tag{5}$$

b_j^{max} is a maximum value in the domain of fuzzy number $\tilde{B}_s$ $(s = 1,2,3,4)$

b) for cost optimization criteria

$$\left(c_n\right)' = 1 - \frac{c_n - c_n^{min}}{c_n^{max}} \tag{6}$$

where:

c_n^{min} ia a minimum value of unit price and c_n^{max} is a maximum value of unit price.

Step 3. Each drug $n^g \left(n = 1,...,N;\ g = 1,...,G\right)$ is a evaluated respecting each considered criterion and its importance. In this paper, three optimization criteria are considered. Grade of each drug $n^g \left(n = 1,...,N;\ g = 1,...,G\right)$, respecting all three considered optimization criteria and its importance is obtained according to expression:

$$\tilde{O}_n = w_1 \cdot \left(\tilde{E}_r\right)' + w_2 \cdot \left(\tilde{B}_s\right)' + w_3 \cdot \left(C_n\right)' \tag{7}$$

which is also fuzzy number according to rules of fuzzy algebra [13].

Step 4. For illness treatment b (b=1,..,B) more TP can be used. For each illness, a doctor deternines kind and a number of possible TP. Generally, for each illness b (b=1,...,B) we have different TP. The total number of TP for illness b (b=1,...,B) is marked as I_b. The grade of each TP is obtained by the following expression:

$$\tilde{A}_i^b = \sum_{n=1}^{N} \tilde{O}_n \quad \left(i = 1,..., I_b;\ b = 1,..., B\right) \tag{8}$$

which is also fuzzy number [13].

Step 5. In this paper, representative scalar of fuzzy number $\tilde{A}_i^b$ is calculated by moment method [3].

ILLUSTRATIVE EXAMPLE

Developed model is illustrated by an example: Selection of TP in the migrene treatment

Input data

The doctor has determined five possible TP which are defined in the following a way:

TP_1-combination of ergotamine tartrate 1 mg and coffein 100 mg, orally

TP_2-dihydroergotamine 1 mg i.v.

TP_3-prochlorperazine 25 mg, rectally

TP_4-sumatriptan 6 mg, subcutaneous injection

TP_5-zolmitriptan 5 mg, orally

Each TP is described respecting considered optimization criteria, as it is presented in Table 1.

Tabela 1 Description of TP with respects efficinecy, usage safety and price

	Usage efficinecy	Usage safety	Price
TP_1	"medium"	"small"	100
TP_2	"medium"	"medium"	100
TP_3	"small"	"velika"	100
TP_4	"large"	" acceptable "	500
TP_5	"large"	"small"	500

The procedure of evaluation and ranking of possible TP for migrene treatment is presented.

Step 1. The comparison pair matrix of relative criteria importance is constructed by team of doctors (pharmacologists and neurologists). In this example, these values are:

$$\begin{bmatrix} - & 3 & 6 \\ & - & 4 \\ & & - \end{bmatrix}$$

A measure inconsistency is C.I.=0.082, meaning that expert team has made good evaluation.

The importance of each considered ctiterion is: $w_1 = 0.627$, $w_2 = 0.28$ and $w_3 = 0.094$.

Step 2. Normalized values of optimization criteria are presented:

$$\mu_{(\tilde{E}_1)'} = \begin{cases} 1 & e_j^{'} = 0.2 \\ -2.5 \cdot e_j^{'} + 1.5 & 0.2 \le e_j^{'} \le 0.6 \end{cases},$$

$$\mu_{(\tilde{E}_2)'} = \begin{cases} 2.5 \cdot e_j^{'} - 1 & 0.4 \le e_j^{'} \le 0.8 \\ -5 \cdot e_j^{'} + 5 & 0.8 \le e_j^{'} \le 1 \end{cases}$$

$$\mu_{(\tilde{E}_3)'} = \begin{cases} 2.5 \cdot e_j^{'} - 1.5 & 0.6 \le e_j^{'} \le 1 \\ 1 & e_j^{'} = 1 \end{cases}$$

$$\mu_{(\tilde{B}_1)'} = \begin{cases} 1 & 0.11 \le b_s^{'} \le 0.2 \\ -9.09 \cdot b_s^{'} + 3 & 0.22 \le b_s^{'} \le 0.33 \end{cases},$$

$$\mu_{(\tilde{B}_2)} = \begin{cases} 9.09 \cdot b_s^{'} - 2 & 0.22 \le b_s' \le 0.33 \\ 1 & 0.33 \le b_s' \le 0.44, \\ -8.33 \cdot b_s^{'} + 4.67 & 0.44 \le b_s' \le 0.56 \end{cases}$$

$$\mu_{(\tilde{B}_3)} = \begin{cases} 8.33 \cdot b_s^{'} - 3.67 & 0.44 \le b_s' \le 0.56 \\ 1 & 0.56 \le b_s' \le 0.78, \\ -8.09 \cdot b_s^{'} + 8.09 & 0.78 \le b_s' \le 0.89 \end{cases}$$

$$\mu_{(\tilde{B}_4)'} = \begin{cases} 9.09 \cdot b_s^{'} - 7.09 & 0.78 \le b_s^{'} \le 0.89 \\ 1 & 0.89 \le b_s^{'} \le 1 \end{cases}$$

Step 3. The value of each considered TP for migrene treatment is calculated according to expression (7), which is equal to the expression (8). Evaluation value of ecah TP is calculated for the following membership function values: $\alpha = 0;0.25;0.5;0.75;1$. The following results are given:

$$\tilde{O}_1 = \begin{Bmatrix} (0.313,0),(0.383,0.25),(0.454,0.5),(0.524,0.75),(0.688,1), \\ (0.719,1),(0.665,0.75),(0.744,0.5),(0.745,0.25),(0.784,0) \end{Bmatrix},$$

$$\tilde{O}_2 = \begin{Bmatrix} (0.374,0),(0.445,0.25),(0.516,0.5),(0.587,0.75),(0.753,1), \\ (0.814,1),(0.759,0.75),(0.836,0.5),(0.837,0.25),(0.876,0) \end{Bmatrix},$$

$$\tilde{O}_3 = \begin{Bmatrix} (0.594,0),(0.54,0.25),(0.483,0.5),(0.43,0.75),(0.468,1), \\ (0.499,1),(0.43,0.75),(0.483,0.5),(0.54,0.25),(0.594,0) \end{Bmatrix},$$

$$\tilde{O}_4 = \begin{Bmatrix} (0.466,0),(0.523,0.25),(0.58,0.5),(0.634,0.75),(0.676,1), \\ (0.709,1),(0.634,0.75),(0.58,0.5),(0.523,0.25),(0.466,0) \end{Bmatrix},$$

$$\tilde{O}_5 = \begin{Bmatrix} (0.436,0),(0.509,0.25),(0.5804,0.5),(0.648,0.75),(0.738,1), \\ (0.769,1),(0.696,0.75),(0.642,0.5),(0.587,0.25),(0.533,0) \end{Bmatrix}$$

Step 5. In this step, scalar values of TP are obtained. According to these values, the ranking of TP is simply performed.

$O_1 = \text{defuzz}\,\tilde{O}_1 = 0.636$, $O_2 = \text{defuzz}\,\tilde{O}_2 = 0.715$,

$O_3 = \text{defuzz}\,\tilde{O}_3 = 0.473$,

$O_4 = \text{defuzz}\,\tilde{O}_4 = 0.635$, $O_5 = \text{defuzz}\,\tilde{O}_5 = 0.68$.

Rank of TP for migrene treatment is presented in Figure 3.

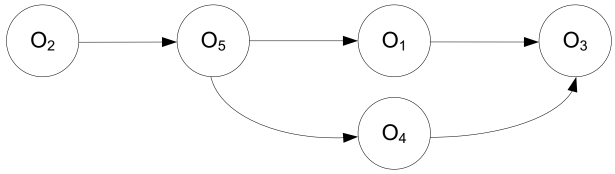

Figure 3 Rank of TP for migrene treatment

The best TP for migrene treatment respecting all three considered optimization criteria, simutaneously, and their importance is TP_2 - dihidroergotamin 1 mg intravenski. The worst is TP_3 - prohlorperazin 25 mg, rektalnim putem.

CONCLUSION

In this paper, a new fuzzy model for evaluation i ranking the TP za svaku bolest, separatno is presented.The advantages of developed model according to literal sources are shown, primary, in the more realistic statement of the problem. Team of doctors define different TP alternatives. By developing model, the best alternative with respect of multi-criteria is found. Also, the developed model is flexible according to the possibility of number change, kind of optimization criteria change and also importance of optimization criteria change. The proposed fuzzy model is suitable for softver development.

The following conclusion is made:

(i) It is possible to describe the problem of solving the best TP as multi-criteria optimizaton task by formal language that enables to look for the solution by exact method.
(ii) The uncertainties which exit in the model can be described by fuzzy numbers.
(iii) The importance of the selecting the best TP is primary shown in the adequate patient treatment. All the changes, as the changes in the number of criteria or its importance, can be easily incorporated into the model.
(iv) Ranking of finite number of TP, with respect to many optimization criteria, simultaneously, is obtained by comparing scalar values of fuzzy numbers.
(v) The developed methodology gives the possibilities through simulation to get the answer if there would be the result change if the input data change.
(vi) The developed methodlogy is illustrades by numerical example. The values of input data and possible alternatives are defined by doctors.

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