Multi-criteria Decision Making on the Best Drug for Rheumatoid Arthritis

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Abstract
The theory of Multi-Criteria Decision Making (MCDM) was introduced in the second half of the twentieth century and aids the decision maker to resolve problems when interacting criteria are involved and need to be evaluated. In this paper, we apply MCDM on the problem of the best drug for rheumatoid arthritis disease. Then, we solve the MCDM problem via the λ-Sugeno measure and the Choquet integral to provide realistic values in the process of selecting the most appropriate drug. The approach confirms the proper interpretation of multi-criteria decision making in the drug ranking for rheumatoid arthritis.

Keywords: Choquet integral, λ – Sugeno measure, Multi-criteria decision making, Rheumatoid arthritis disease

Introduction
Multi-criteria decision making (MCDA) is a branch of decision theory where acts or alternatives are chosen considering several points of view or criteria, assuming that the decision maker has all the information at his/her disposal concerning the alternatives, i.e. they are fully described by a vector of attributes which is supposed to be known without uncertainty. Over the years, many approaches and underlying theories have been developed for solving decision problems with multiple criteria. In [1], there is a comprehensive coverage of the latest research on MCDM problems that were applied in different scientific fields. Also, there exist some multi-criteria decision making problems in medical applications, especially in medical diagnosis. According to fuzzy decision making models [2] based on utility theory in medical diagnosis, Rakus-Andersson and Jogreus facilitated the choice of the drug, especially in the diagnosis of coronary heart disease [3, 4].
In this paper, we apply multi-criteria decision making on the optimal drug for rheumatoid arthritis by taking the drug values as measures and a special aggregation function to obtain realistic values. Section two introduces the basic definitions needed in our research. Section 3 discusses the MCDM problem on the optimal drug for rheumatoid arthritis. In section 4, we give a study case with results. Lastly, the paper is finished with some conclusions.

**Basic definitions**

A capacity [5] or fuzzy measure [6] is a generalization of classical measure by means of using non-additive property instead of additive property. The definition of the capacity is as follows.

**Definition 1.** [6] Let \( S \) be a finite set and \( 2^S \) is the power set of \( S \). A capacity is a set function \( \mu : 2^S \to [0, 1] \) that satisfies:
1. \( \mu(\emptyset) = 0, \mu(S) = 1 \),
2. for all \( A \subseteq B \subseteq S, \mu(A) \leq \mu(B) \).

There are many types of capacities, one of which is the \( \lambda \)–Sugeno measure [7]. The definition of the \( \lambda \)–Sugeno measure is as follows.

**Definition 2.** Let \( S = \{s_1, s_2, \ldots, s_n\} \) be a finite set, then a function \( \mu_\lambda : 2^S \to [0, 1] \) is called \( \lambda \)–Sugeno measure if it satisfies the following requirements:
1. \( \mu_\lambda(S) = 1 \)
2. If \( A, B \in 2^S \) then \( \mu_\lambda(A \cup B) = \mu_\lambda(A) + \mu_\lambda(B) + \lambda \mu_\lambda(A) \mu_\lambda(B) \) with \( A \cap B = \emptyset \).

In general, it can be shown that

\[
\mu_\lambda(\{s_1, s_2, \ldots, s_n\}) = 1 = \prod_{i=1}^{n} (1 + \lambda \mu_\lambda(\{s_i\})) - 1, \quad \lambda \neq 0
\]

This gives a polynomial equation with respect to \( \lambda \)

\[
1 + \lambda = \prod_{i=1}^{n} (1 + \lambda \mu_\lambda(\{s_i\})). \tag{2}
\]

Moreover, the values of \( \mu_\lambda(\{s_1, \ldots, s_n\}) \) for \( 1 \leq i < n \) may be computed recursively as

\[
\mu_\lambda(\{s_1, \ldots, s_n\}) = \mu_\lambda(\{s_i\}) + \mu_\lambda(\{s_1, \ldots, s_{n-1}\}) + \lambda \mu_\lambda(\{s_i\}) \mu_\lambda(\{s_1, \ldots, s_{n-1}\}) \tag{3}
\]

The value of \( \lambda \) can present the following three kinds of interaction between the elements of \( S \):

- a) whenever \( \lambda > 0 \), the interaction is supper-additive, that is,
  \( \mu_\lambda(A \cup B) \geq \mu_\lambda(A) + \mu_\lambda(B) \)
- b) whenever \( \lambda < 0 \), the interaction is sub-additive, that is,
  \( \mu_\lambda(A \cup B) \leq \mu_\lambda(A) + \mu_\lambda(B) \)
- c) whenever \( \lambda = 0 \), the interaction is additive, that is,
  \( \mu_\lambda(A \cup B) = \mu_\lambda(A) + \mu_\lambda(B) \)

A special type of nonlinear integrals is the Choquet integral [5, 6], with respect to capacity. The Choquet integrals are appropriate tools to represent the weights of criteria with non-additive characteristics as the capacities.

**Definition 3.** Let \( \mu \) be a capacity on \( S \), then the Choquet integral of \( f : S \to R^+ \) with respect to the capacity \( f : S \to R^+ \mu \) is defined by

\[
\int_{S} f \, d\mu = \sum_{i=1}^{n} \left( f(\{s_{(i)}\}) - f(\{s_{(i-1)}\}) \right) \mu(A_{(i)}) \tag{4}
\]

where \( f(\{s_{(i)}\}) \) is permuted so that \( 0 \leq f(\{s_{(1)}\}) \leq \cdots \leq f(\{s_{(n)}\}) \leq 1 \), with \( f(\{s_{(0)}\}) = 0 \) and \( A_{(i)} = \{s_{(i)}, \ldots, s_{(n)}\} \).

**MCDM on the optimal drug for rheumatoid arthritis**

Consider an MCDM that depends on \( n \) criteria (or attributes) described by the alternatives \( D_1, \ldots, D_n \) and a set of criteria \( S = \{s_1, \ldots, s_m\} \). The alternatives \( D = D_1 \times \cdots \times D_n \) are the set of potential alternatives. For any \( d_1, d_2 \in D \), \( d_1 \geq d_2 \), the Decision Maker prefers an alternative \( d_1 \) to \( d_2 \), where \( \geq \) is the preference relation of the Decision Maker. Thus, by employing an overall utility function \( u : D \to R \) (1), we obtain:
A classical way to construct $u$ is to consider one-dimensional utility function $u_i$ on each criterion and then to aggregate them by a suitable function:

$$u(d) = F(u_1(d_1), \ldots, u_n(d_n)) \quad \forall d \in D,$$

where $F$ is called an aggregation function.

Aggregation functions (AFs) are mathematical functions to collect helpful data in multi criteria decision making. The input of AFs is several numerical values and its output is a single value. A special type of aggregation functions is the Choquet integral w. r. t. capacity. These integrals have been studied and applied in diverse fields (see, e.g. [8-16]).

Based on the overall score by means of an aggregation function which takes into account the importance of the criteria interaction, the alternatives can be arranged and the best alternative selected.

In this paper, we consider that the alternatives $d_1, \ldots, d_n \in D$ act as medicines for patients, while the set of criteria $s_1, \ldots, s_m \in S$ are symptoms that are typical of the disease. When a rational DM makes a decision $d_i \in D, \quad i = 1 \ldots, n$ (a space of alternatives), concerning states-results $s_j \in S$ (a space of symptoms), $j = 1, \ldots, m$. Hence, we have the ordered triplet $(S, D, U)$, where $S$ is a space of symptoms, $D$ is a set of alternatives, and $U$ is the utility matrix [4].

$$U = \begin{bmatrix} s_1 & s_2 & \cdots & s_m \\ d_1 & u_{11} & u_{12} & \cdots & u_{1m} \\ d_2 & u_{21} & u_{22} & \cdots & u_{2m} \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ d_n & u_{n1} & u_{n2} & \cdots & u_{nm} \end{bmatrix}$$

In this matrix, each value of $u_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, m$, belongs in the unit interval $[0, 1]$. Hence, we associate with each symptom $s_j, \quad j = 1, \ldots, m$, a value (its importance) by using the following rule.

- If the number is higher, then a greater significance of symptom will be $s_j$.

Hence, we give $w_1, w_2, \ldots, w_m$ as powers-weights to $s_1, s_2, \ldots, s_m, \quad w_j \in W, \quad j = 1, 2, \ldots, m$, where $W$ is a space of weights, then we get the following weighted matrix.

$$U_w = \begin{bmatrix} w_1 \cdot u_{11} & w_2 \cdot u_{12} & \cdots & w_m \cdot u_{1m} \\ w_1 \cdot u_{21} & w_2 \cdot u_{22} & \cdots & w_m \cdot u_{2m} \\ \vdots & \vdots & \ddots & \vdots \\ w_1 \cdot u_{n1} & w_2 \cdot u_{n2} & \cdots & w_m \cdot u_{nm} \end{bmatrix}$$

By employing the quantity $U_w (d_i)$ given in [2], we can approximate the common decisive power of alternative $d_i$.

$$U_w(d_i) = \sum_{j=1}^{m} w_j \cdot u_{ij}$$

Thus, for a final optimal alternative $d^*$, we choose this $d_i$ that satisfies

$$U_w(d^*) = \text{Max}_{1 \leq i \leq n} U_w(d_i).$$

For defining the effectiveness of medicines, each of the following terms determines a linguistic variable, named medicine effectiveness with respect to symptom: $\{E_1 = \text{none}, E_2 = \text{almost none}, \quad E_3 = \text{very little}, E_4 = \text{little}, E_5 = \text{rather little}, E_6 = \text{medium}, E_7 = \text{rather large}, E_8 = \text{large}, E_9 = \text{very large}, E_{10} = \text{almost complete}, E_{11} = \text{complete}\}$, with all sets being defined in the interval $Z=\{0,100\}$, as an index set for supports of $E_1$ to $E_{11}$.

Rakus-Andersson and Jogreus [4] introduced the membership function $M(z)$ for the fuzzy set. We summarize the representatives of effectiveness in the following table (Table 1).
Table 1- The representatives of medicine effectiveness with respect to symptoms

| symptoms          | complete | rather large | little | rather little | medium | rather large | large | very large | almost complete | complete |
|-------------------|----------|--------------|--------|---------------|--------|--------------|-------|------------|---------------|----------|
| non               | 0        | 10           | 20     | 30            | 50     | 60           | 70    | 80         | 90            | 100      |
| almost none       | 0.1      | 0.2          | 0.3    | 0.4           | 0.5    | 0.6          | 0.7   | 0.8        | 0.9           | 1        |
| almost complete   |          |              |        |               |        |              |       |            |                |          |

To compare symptom j with symptom l, we can assign the values $c_{jl}$ and $c_{lj}$ to the pair $(s_j, s_l)$. Hence, for all $j, l = 1, 2, ..., m$:

- $c_{ij} = \frac{1}{c_{ji}}$

- If symptom $j$ is more important than symptom $l$, then $c_{jl}$ gets consigned with one of the numbers $1, 3, 5, 7$ or $9$, due to the difference of importance being equal, weak, strong, demonstrated, or absolute, respectively. While, if symptom $l$ is more important than symptom $j$, then we will assign the value of $c_{lj}$. Hence, we construct a $m \times m$ square matrix $C = (c_{ij})_{i,j=1}^m$. The weights $w_1, w_2, ..., w_m$ are decided as components of the eigenvector corresponding to the largest in magnitude eigenvalue of the matrix; for more details see [4].

For total effectiveness, we solve the MCDM problem by using the $\lambda$-sugeno measure and the Choquet integral for the medicines ranking.

Case study
In this section, we will study the case of rheumatoid arthritis disease. The clinical data, with respect the medical diagnosis, treatment, and symptoms of rheumatoid arthritis, were collected from Al Kindy Teaching Hospital, Baghdad, Iraq.

We take the most substantial symptoms, which include $s_1 =$"joints pain", $s_2 =$"swollen joints", $s_3 =$"joints stiffness", $s_4 =$"fatigue", $s_5 =$"fever", $s_6 =$"loss of weight", $s_7 =$"rheumatoid nodules under the skin".

The drugs recommended for improving the patient’s state are $d_1 =$non-steroidal anti-inflammatory drugs (NSAID$_s$), $d_2 =$corticoids, $d_3 =$cyclooxygenize, $d_4 =$disease-modifying anti-rheumatic drugs (BMARD$_s$), and $d_5 =$ biological factors. The relationship between the medicine action and the retreat of symptoms is shown in Table 2.

Table 2- The relationship between the drugs action and the retreat of symptoms

| symptoms          | $s_1$     | $s_2$     | $s_3$     | $s_4$     | $s_5$     | $s_6$     | $s_7$     |
|-------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| drug action       |           |           |           |           |           |           |           |
| $d_1$             | complete  | rather large | almost none | almost none | almost none | almost none | almost none |
|                   | $u_{11} = 0.8$ | $u_{12} = 0.4$ | $u_{13} = 0.3$ | $u_{14} = 0.1$ | $u_{15} = 0.1$ | $u_{16} = 0.1$ | $u_{17} = 0.1$ |
| $d_2$             | Very large | Very large | little    | little    | almost none | almost none | almost none |
|                   | $u_{21} = 0.8$ | $u_{22} = 0.8$ | $u_{23} = 0.3$ | $u_{24} = 0.3$ | $u_{25} = 0.1$ | $u_{26} = 0.1$ | $u_{27} = 0.1$ |
| $d_3$             | large, $u_{31} = 0.7$ | large, $u_{32} = 0.7$ | very large | rather little | little    | almost none | almost none |
|                   | $u_{33} = 0.8$ | $u_{34} = 0.4$ | $u_{35} = 0.3$ | $u_{36} = 0.1$ | $u_{37} = 0.1$ | $u_{38} = 0.1$ | $u_{39} = 0.1$ |
| $d_4$             | large, $u_{41} = 0.8$ | large, $u_{42} = 0.7$ | very large | very large | large    | almost none | almost none |
|                   | $u_{43} = 0.7$ | $u_{44} = 0.8$ | $u_{45} = 0.8$ | $u_{46} = 0.7$ | $u_{47} = 0.3$ | $u_{48} = 0.3$ | $u_{49} = 0.3$ |
| $d_5$             | rather large, $u_{51} = 0.8$ | large, $u_{52} = 0.9$ | large    | very large | almost complete | almost complete | very large |
|                   | $u_{53} = 0.8$ | $u_{54} = 0.8$ | $u_{55} = 0.8$ | $u_{56} = 0.8$ | $u_{57} = 0.8$ | $u_{58} = 0.8$ | $u_{59} = 0.8$ |
Next, we note that the physical status of a patient is subjectively better if the symptom "joints pain" disappears. The case is assigned to "swollen joints", "joints stiffness", "fatigue", "fever", "loss of weight", and "rheumatoid". Thus, we construct the following matrix $C$, which represents the comparison of symptoms.

$$
C = \begin{bmatrix}
1 & 3 & 5 & 5 & 7 & 7 & 9 \\
\frac{1}{3} & 1 & 3 & 3 & 7 & 7 & 9 \\
\frac{1}{5} & \frac{1}{3} & 1 & 5 & 7 & 7 & 9 \\
\frac{1}{5} & \frac{1}{3} & \frac{1}{5} & 1 & 5 & 7 & 9 \\
\frac{1}{7} & \frac{1}{7} & \frac{1}{5} & 1 & 7 & 9 & 1 \\
\frac{1}{7} & \frac{1}{7} & \frac{1}{7} & \frac{1}{7} & 1 & 3 & 1 \\
\frac{1}{9} & \frac{1}{9} & \frac{1}{9} & \frac{1}{9} & \frac{1}{3} & 1 & 1 \\
\end{bmatrix}
$$

The largest eigenvalue of $C$ is $8.5179$, and the corresponding eigenvector $V = (0.7656, 0.4601, 0.4740, 0.2117, 0.1183, 0.0489, 0.0307)$. Hence, the coordinates of $V$ are the weights $w_1, w_2, w_3, w_4, w_5, w_6$, and $w_7$. Therefore, we have the following single $\lambda$-sugeno measures: $\mu_1(s_1) = 0.7656, \mu_2(s_2) = 0.4601, \mu_3(s_3) = 0.3740, \mu_4(s_4) = 0.2117, \mu_5(s_5) = 0.1183, \mu_6(s_6) = 0.0489, \mu_7(s_7) = 0.0307$.

Using equation (2): $1 + \lambda = \prod_{i=1}^{n}(1 + \lambda \mu_i(s_i))$, we obtain

$$
\lambda + 1 = (0.7656\lambda + 1)(0.4601\lambda + 1)(0.3740\lambda + 1)(0.2117\lambda + 1)(0.1183\lambda + 1)
\times (0.0489\lambda + 1)(0.0307\lambda + 1).
$$

Thus,

$$
\lambda = \{0, -0.9282, -10.78869, -20.1590, -32.6007, -3.9384 - 3.9308i, -3.9384 + 3.9308i\}
$$

Since $\lambda \not\in (-1, \infty)$, we choose $\lambda = -0.9282$ only.

If $\lambda = -0.9282$, then we can calculate other $\lambda$-Sugeno measure values from equation (3):

$$
\mu_3(s_1, ..., s_n) = \mu_4(s_1, ..., s_{n-1}) + \lambda \mu_5(s_1, s_n)
$$

Then,

$$
\mu_3(s_1, s_2) = 0.8987, \mu_3(s_1, s_3) = 0.8738, \mu_3(s_2, s_3) = 0.6727, \mu_3(s_1, s_4) = 0.8269, \mu_3(s_3, s_4) = 0.4782, \mu_3(s_2, s_4) = 0.5814, \\
\mu_3(s_1, s_5) = 0.7998, \mu_3(s_2, s_5) = 0.5279, \mu_3(s_3, s_5) = 0.4512, \mu_3(s_4, s_5) = 0.3068, \mu_3(s_1, s_6) = 0.7798, \mu_3(s_2, s_6) = 0.4881, \\
\mu_3(s_3, s_6) = 0.4059, \mu_3(s_4, s_6) = 0.2510, \mu_3(s_5, s_6) = 0.1618, \mu_3(s_1, s_7) = 0.7745, \mu_3(s_2, s_7) = 0.3478, \mu_3(s_3, s_7) = 0.3940, \\
\mu_3(s_4, s_7) = 0.2364, \mu_3(s_5, s_7) = 0.1456, \mu_3(s_6, s_7) = 0.0782, \mu_3(s_1, s_2, s_3) = 0.9607, \mu_3(s_1, s_2, s_4) = 0.9338, \mu_3(s_1, s_2, s_5) = 0.9183, \\
\mu_3(s_1, s_2, s_6) = 0.9068, \mu_3(s_1, s_2, s_7) = 0.9038, \mu_3(s_1, s_3, s_4) = 0.9138, \mu_3(s_1, s_3, s_5) = 0.8962, \mu_3(s_1, s_3, s_6) = 0.8830, \mu_3(s_1, s_3, s_7) = 0.8796, \\
\mu_3(s_1, s_4, s_5) = 0.8544, \mu_3(s_1, s_4, s_6) = 0.8381, \mu_3(s_1, s_4, s_7) = 0.8340, \mu_3(s_1, s_5, s_6) = 0.8124, \mu_3(s_1, s_5, s_7) = 0.8077, \mu_3(s_1, s_6, s_7) = 0.7883, \\
\mu_3(s_2, s_3, s_4) = 0.7522, \mu_3(s_2, s_3, s_5) = 0.7171, \mu_3(s_2, s_3, s_6) = 0.6911, \mu_3(s_2, s_3, s_7) = 0.6842, \mu_3(s_2, s_4, s_5) = 0.6359, \mu_3(s_2, s_4, s_6) = 0.6039, \\
\mu_3(s_2, s_4, s_7) = 0.5955, \mu_3(s_2, s_5, s_6) = 0.5528, \mu_3(s_2, s_5, s_7) = 0.5436, \mu_3(s_2, s_6, s_7) = 0.5049, \mu_3(s_3, s_4, s_5) = 0.5440, \mu_3(s_3, s_4, s_6) = 0.5054
$$
Now, we apply Choquet integral (Equation (4)) for the choice of an optimal drug for the rheumatoid arthritis disease. The Choquet integral of non-steroidal anti-inflammatory drug (NSAID$_{x}$) is

$$d_1 = (c) \int f \, d\mu$$

$$d_1 = f(s_4) \cdot \mu_x([s_1, s_2, s_3, s_4, s_5, s_6, s_7]) + (f(s_3) - f(s_4)) \cdot \mu_x([s_1, s_2, s_3]) + (f(s_2) - f(s_3)) \cdot \mu_x([s_1, s_2])$$

$$d_1 = 0.1 \cdot 1 + 0.2 \cdot 0.9607 + 0.1 \cdot 0.8987 + 0.4 \cdot 0.7656$$

$$d_1 = 0.68825.$$  

Also, we can apply the Choquet integral on corticoid drug, as follows

$$d_2 = (c) \int f \, d\mu$$

$$d_2 = f(s_7) \cdot \mu_x([s_1, s_2, s_3, s_4, s_5, s_6, s_7]) + (f(s_4) - f(s_5)) \cdot \mu_x([s_1, s_2, s_3, s_4]) + (f(s_2) - f(s_3)) \cdot \mu_x([s_1, s_2])$$

$$d_2 = 0.1 \cdot 1 + 0.2 \cdot 0.9836 + 0.5 \cdot 0.8987$$

$$d_2 = 0.74607.$$  

Similarly, we can apply Choquet integral for other drugs.

**Results and Discussion**

The results of Choquet integrated values are shown in Table 3.

**Table 3** The results of Choquet integral in the drug ranking

| No. | $s_1$ | $s_2$ | $s_3$ | $s_4$ | $s_5$ | $s_6$ | $s_7$ | Choquet Integrated Values |
|-----|------|------|------|------|------|------|------|---------------------------|
| 1   | 0.8  | 0.4  | 0.3  | 0.1  | 0.1  | 0.1  | 0.1  | 0.68825                   |
| 2   | 0.8  | 0.8  | 0.3  | 0.1  | 0.1  | 0.1  |      | 0.74607                   |
| 3   | 0.7  | 0.7  | 0.8  | 0.3  | 0.1  | 0.1  |      | 0.72275                   |
| 4   | 0.8  | 0.7  | 0.8  | 0.8  | 0.7  | 0.3  |      | 0.78452                   |
The interpretation of Choquet integral for the drug ranking confirms that the preference relation of the Decision Maker is $d_5 > d_4 > d_2 > d_3 > d_1$. Therefore, the drug 5 is the optimal drug according to the ranking of drugs used to treat rheumatoid arthritis.

**Conclusions**

In this paper, we applied multi-criteria decision making on the optimal drug for rheumatoid arthritis to provide realistic values in the process of selecting the most appropriate drug. The basis of the application is based on the decision of the effect of the drug on the medical symptoms of the disease. For total effectiveness, we solved multi-criteria decision making problem by using the $\lambda$-Sugeno measure and the Choquet integral, which confirmed the optimal drug ranking of rheumatoid arthritis.

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