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A multi-criteria decision-making approach for schizophrenia treatment techniques

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Summary

Aim of the study: There are different schizophrenia treatment approaches used to manage the disorder. The objective of this study is to show that the multi-criteria decision-making approach can be applied for selecting the most appropriate schizophrenia treatment. We propose the use of the fuzzy Preference Ranking Organization Method for Enrichment of Evaluations (PROMETHEE) technique for evaluating and comparing schizophrenia treatment techniques.

Methods: The most commonly used therapy techniques for schizophrenia, namely pharmacotherapy, cognitive behavioral therapy, psychoeducation program, transcranial magnetic stimulation, and electroconvulsive therapy were selected. The side effects, efficacy, time of treatment, cost of treatment, and comfort level were used as the criteria for the analysis. Criteria weights and preference function were used while computing the difference of alternatives contribution. After defining the values of each criteria, we set the weights and the preference function, and finally obtained the results with the Decision Lab program for two different cases: high importance is given to the efficacy, side effects, and patient comfort; the same level of importance is given to all criteria.

Results: The results show that pharmacotherapy is the most preferred technique in both cases, while other techniques have different stages in the complete ranking based on the assigned weights.

Discussion: One can easily adapt more treatment techniques and criteria and assign their weights based on a specific patient profile.

Conclusion: The proposed technique for the decision-making process is an important tool that can be considered by clinicians as well as patients/families in selecting the most appropriate treatment technique.

schizophrenia, treatment techniques, multi-criteria, decision-making, fuzzy PROMETHEE

1. INTRODUCTION

There are 26 million schizophrenia patients around the globe [1]. Annually, it is estimated that 1 in 4,000 individuals are schizophrenic [2], which makes it one of the most important mental disorders, affecting the way a person perceives thoughts and interprets the reality around them [3]. By 2013, schizophrenia had become the top cause for disability worldwide [4]. The mortality rate of schizophrenia is two to three times higher than that found in a healthy population [5]. For a family with a schizophrenic member, the costs of managing the condition can be excessive and it is also a burden to the country's economy.

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In 2013, the US government spent 155.2 billion dollars on the treatment of schizophrenia and its complications [6]. Based on a study carried out in the US, the annual cost of treating schizophrenia is 44,773 USD per person [6]. Early detection and treatment of schizophrenia is important for reducing the negative impact on the process of disorder management and in achieving good prognosis outcomes [7]. There are classes of schizophrenia treatment approaches, including antipsychotic drugs, psychotherapy, psychosocial and the newly emerged transcranial magnetic extended brain stimulation. The pharmacological treatment includes the first and second-generation antipsychotic medicines. Once a patient is diagnosed, the targets of the treatment are firstly identified. Treatment targets may include positive and/or negative symptoms such as hallucinations, losing interest in life, and a range of potential community adjustment problems. Then, a treatment plan is formulated and implemented. This formulation includes the selection of the treatment methods and the treatment setting.

For a psychiatrist, making the right decision is significant for patients. Selecting the appropriate treatment option is considerably important and potentially a challenging task. The approach followed to take the right treatment is based on several criteria which are not always crisp. The major factors for evaluation are efficiency and side effects, even though other factors such as cost, comfort, treatment delivery setup for patient need to be considered. Well-characterized treatment modes assist health care professionals to select and deliver better disorder management options. An additional benefit of evaluating treatment modes is that it contributes toward accelerating patient remission and better prognosis results.

The fuzzy preference ranking organization method for enrichment of evaluations (PROMETHEE), a multi-criteria decision-making technique applied for making decisions where there are uncertainties, has become an important tool in assisting professionals to compare and make better alternative selections. Fuzzy systems have been applied in a range of outranking problems which involve uncertainty and multi-criteria scenarios in different fields such as energy, economy, industry, machine tool selection [8-11], and recently proposed to be utilized in oncology and nuclear medicine [12-17]. Its flexibility and efficiency in managing decision scenarios marked by uncertainty make it applicable in clinic. However, its translation to the clinical settings as an effective decision-making tool requires more researches and validations by clinical trials.

In this study, we propose the use of fuzzy PROMETHEE to evaluate, compare, and find the most appropriate treatment techniques for schizophrenia. To our knowledge, there are no studies on the application of fuzzy PROMETHEE or any other multi-criteria decision-making methods in psychiatric disorders in the literature. In fact, the only existing method for selecting the most appropriate treatment technique is that the psychiatrists perform a preoperative assessment by reviewing the patient medical history and overall physical performance based on the clinical practice guideline and their experiences. Applying fuzzy PROMETHEE in evaluating treatment techniques of schizophrenia can contribute to a more accurate decision-making experience for the psychiatrists and result in a better management of the disorder.

2. MATERIALS AND METHODS

2.1. Alternative treatment options

2.1.1. Pharmacotherapy

It is among the major and highly important schizophrenia treatment options [18]. The treatment delivery is classified into two major parts based on the goal. The first one is aimed at decreasing hostility and returning the patient to healthy activities like sleeping and eating. The second one is delivered as a maintenance treatment, which improves the patient's socialization and self-caring and also enhances their mood. The antipsychotic treatment has two generations: the first and second generation. The first generation is known for extrapyramidal complications compared to the second generation [19]; this treatment lasts for 12 months and aims to keep the condition in remission and allow the patient to resume normal activities [20]. However, the second generation can lead to certain metabolic complications [21].

2.1.2. Non-pharmacological psychotherapy

Although the pharmacological treatments are the main class of schizophrenia treatment, because symptoms may persist, additional non-pharmacological treatments are needed, namely psychosocial treatments [22]. There are two main types of psychosocial treatment of schizophrenia management; cognitive therapy for behavioral remediation and family intervention with psychoeducation [23].

A Cognitive behavioral therapy (CBT)

The major principle is to normalize patient rationale for reasoning [24]. CBT is promising for schizophrenic victims whose symptoms cannot be controlled through medication. It is a well-organized treatment for patients with schizoid personality disorder that enables them to cope with psychotic symptoms by re-examining their perceptive activity progressively. The patient is highly encouraged to become actively involved in developing a rationale, which is acceptable for problem-solving and managing oneself. Through the course of 9-12 months, scholars presented CBT, which is effective in reducing positive symptoms but has not yet been shown to lessen negative symptoms [25].

B Psychoeducation program

Psychoeducation aims to address the patient situation of gating relapse and re-admission to hospital [26]. It has features like component structure, philosophical point of view and aim. This procedure lasts for 9 to 24 months and is administered by professionals. According to the philosophy, the team providing the treatment has to share the burden with the family and they all focus on disorder management and the treatment [27].

2.1.3. Transcranial magnetic stimulation (TMS)

This relatively complicated device is used to deliver a magnetic force to the scalp surface. The main aim of the pulse is to inhibit or stimulate neurons and their network [28]. It can be deduced from the description that it is a non-invasive and painless mode of treatment. The device applies Faraday's law. During the procedure, an electromagnetic coil is placed on the scalp to convert the incoming electrical signal into magnetic energy. The field effects come either through inhibition or excitation and it is defined based on the frequency of the pulse. Low frequency produces inhibition and high-frequency yields an excitatory effect. Side effects can include a mild and self-limited headache after the procedure. Pain can be experienced on the scalp, and there is a hearing effect due to the machine noise [29].

2.1.4. Electroconvulsive therapy (ECT)

This is the pioneering model for schizophrenia treatment. The manner in which it affects the activity has not fully been determine but it is suggested that it has an enormous effect on the central nervous system (CNS) components, including neurotrophic, hormones, neuropeptides, neurotransmitters and factors. It helps to alleviate the signs of the disorder. ECT is a precise electric current administered to the anesthetized patient's brain, and the current forms convulsive act with the CNS and gives relief. The well-known adverse effects are confusion and memory loss for activities before and after the treatment, which may last for one month [30].

2.2. Fuzzy PROMETHEE

From the inception of the fuzzy system, the design aims to handle vague and questionable issues [8]. The fuzzy system can be easily defined as a method to imitate human reasoning capability for decision making on uncertainties. It is based on consequent theories and is highly applicable and appropriate in creating a knowledge-based system in the field of health science.

We propose the use of the fuzzy PROMETHEE method to evaluate the treatment techniques of schizophrenia. The PROMETHEE approach was first introduced by [31]. They aimed to prove that it can be used as multi-criteria decision-making technique for outranking. In

this approach, the notion of criteria is extended and considered for a ranking problem which includes a decision-making method based on multi-criteria and on pair comparison of presented alternatives [31]. The extension of criteria is simply developed by the subject taking the problem easily through considering the situational weight of the preferences. While solving a ranking problem using the PROMETHEE approach, a pair of possibilities is generated. To implement the method, we need two types of information, criteria weight and preference function while computing the difference in the alternatives' contribution for individual criteria. The preference function is mainly the difference between options. A detailed explanation of fuzzy PROMETHEE can be found at [14].

2.2.1. Treatment techniques and criteria

In using fuzzy PROMETHEE to evaluate alternatives, we should firstly decide the appropriate comparison criteria. Among the available criteria for characterization, we have selected the cost of treatment (full and per session), time required to complete the respective treatment mode defined as time per single session and time for full treatment, degree of side effects, efficacy (which is the degree of treatment ability to produce the desired outcome), and finally, comfortability of the treatment during the process. These criteria are mapped to numerical values with respective weighting. People begin treatment with the intention of obtaining relief for their pain and to be happy in their lives. Victims of schizophrenia may follow one or a combination of treatment modes explained in the previous section. While following their treatment and fighting to manage their problem, there is a possibility that the patient will be affected by the side effects of the respective treatment modality. We assigned the weights for the side effects based on their levels of risk. Some of the treatments such as the use of an antipsychotic drug may cause moderate and manageable side effects like losing weight, dizziness, nausea, constipation etc. On the other hand, treatments like ECT result in serious side effects ranging from confusion to memory loss. For any treatment mode, the subject feels a different level of comfort in the process. Different treatments have different levels of efficacy, which refers to how effective the treatment mode and if it results in the desired outcome. It is obvious that treatments have different levels of effectiveness in managing the disorder. Table 1 shows the treatment modes and their respective criteria along with their corresponding values. The evaluating criteria and corresponding values are determined after an extensive literature search.

Table 1. Treatment alternatives and their respective criteria with corresponding values (VH: very high, H: high, M: medium, L: low, VL: very low)

Therapy techniques	Cost of treatment ($)	Cost of a session ($)	Time for treatment (weeks)	Time for a session (min.)	Side effect	Efficacy	Comfort level
ECT	23,067	1817	3	60	H	M	L
TMS	10,333	312	5	35	L	M	L
Pharmacotherapy	6,048	17	6	10	M	H	M
CBT	3333	133	15	45	VL	M	H
Psychoeducation program	6657	74	30	60	VL	M	H

2.2.2. Treatment alternatives' criteria weighting

In imitating the human decision-making approach through fuzzy PROMETHEE on schizophrenia treatment alternatives, we have applied a fuzzy triangular numbers. The weights are assigned by analyzing treatments characterizing the features, side effects, efficacy, time of treatment, cost of treatment, and comfort of the pa-

tient as presented in the rank that is taken to give weight. We assigned the highest weight to side effects and efficacy to the patient suffering from schizophrenia so as not to provide an additional source of problems for their health. Weighting side-effects and controlling them while making decisions helps in preventing treatments with adverse side-effects becoming the first line of choice. The goal of treatment is to manage the illness adequately and to prevent it from increasing in severity. The capability of a treatment approach to handle and manage an illness is measured by the efficacy of the alternative. There is no doubt about weighting efficacy to be on the first line compared to the other criteria since the goal of the treatment is to enable persons with schizophrenia to live productively and minimize the effects of their illness. Even if side effects and efficacy are ranked first in weighting, the treatment is also characterized by cost-effectiveness and affordability by the patient. Since schizophrenia has become an economic burden for a country's economy, as explained in the introduction, including the cost of treatment is professionally and logically acceptable. In this example, we have decided to assign low importance to cost in the scale, while the time of treatment has been set to high. However, patients/clinicians are responsible for making decisions on the selection of the weights based on their own specific conditions. Table 2 shows the assigned weights in triangular fuzzy numbers.

Table 2. The linguistic scale of importance, corresponding fuzzy numbers and assignment of weights

Linguistic scale for evaluation	Triangular fuzzy numbers	Importance ratings of criteria
Very high (VH)	(0.75, 1, 1)	Side effects, efficacy, patient comfort
High (H)	(0.50, 0.75, 1)	Time for treatment, time for session
Medium (M)	(0.25, 0.50, 0.75)	
Low (L)	(0, 0.25, 0.50)	
Very low (VL)	(0, 0, 0.25)	Cost of treatment, cost of session

The weight of the criteria is selected in a very careful approach taking into consideration the most important one to be superior to other criteria. It is interesting to see how the computed ranking changes when the importance of weight changes. It was shown in the methodology section that computing the outranking ratio depends on the weight assigned to the criteria. Assume we have assigned the same weights to all criteria as shown in Table 3. After taking the same weight for each of the criteria, the importance of each criteria will be equal for the decision makers. This means for all alternatives, efficacy has equal weight and importance as patient comfort and others. This is done to demonstrate the applicability of the method to the schizophrenia treatment techniques and show how the ranking changes when the weights change.

Table 3. The linguistic scale of importance with equal weights

Linguistic scale for evaluation	Triangular fuzzy numbers	Importance ratings of criteria
Very high (VH)	(0.75, 1, 1)	
High (H)	(0.50, 0.75, 1)	
Medium (M)	(0.25, 0.50, 0.75)	Side effect, efficacy, patient comfort, time for treatment, time for session, cost of treatment, cost of session
Low (L)	(0, 0.25, 0.50)	
Very low (VL)	(0, 0, 0.25)	

Finally, we applied the fuzzy inputs to the Decision lab program, as can be seen in Table 4 and Table 5 for different and equal weights, respectively.

Table 4. Different preferences for the criteria

Criteria	Cost of treatment ($)	Cost of a session ($)	Time for treatment (weeks)	Time for a session (min.)	Side effect	Efficacy	Comfort level
min/max	min	min	min	min	min	max	max
Weight	0.08	0.08	0.75	0.75	0.92	0.92	0.92

Table 5. Equal preferences for the criteria

Criteria	Cost of treatment ($)	Cost of a session ($)	Time for treatment (weeks)	Time for a session (min.)	Side effect	Efficacy	Comfort level
min/max	min	min	min	min	min	max	max
Weight	0.50	0.50	0.50	0.50	0.50	0.50	0.50

3. RESULTS

Table 6 and Figure 1 present the complete ranking with the different weights assigned for the criteria selected to be considered in the evaluation. Side effects, efficacy and patient comfort have been assigned higher weights, followed by cost and time for treatment. The results in the table indicate that pharmacotherapy outranks the rest followed by TMS, electroconvulsive, cognitive and psychoeducation program in order. The outranking for the first two alternatives has a positive net flow, unlike the rest of the treatment alternatives, as shown in Figure 1.

Table 6. Complete ranking results for different weights.

Ranking	Therapy techniques	Positive outranking flow	Negative outranking flow	Net flow
1	Pharmacotherapy	0.2870	0.0251	0.2619
2	TMS	0.2240	0.0800	0.1440
3	ECT	0.1100	0.1687	-0.0587
4	CBT	0.1579	0.2205	-0.0626
5	Psychoeducation program	0.0261	0.3107	-0.2846

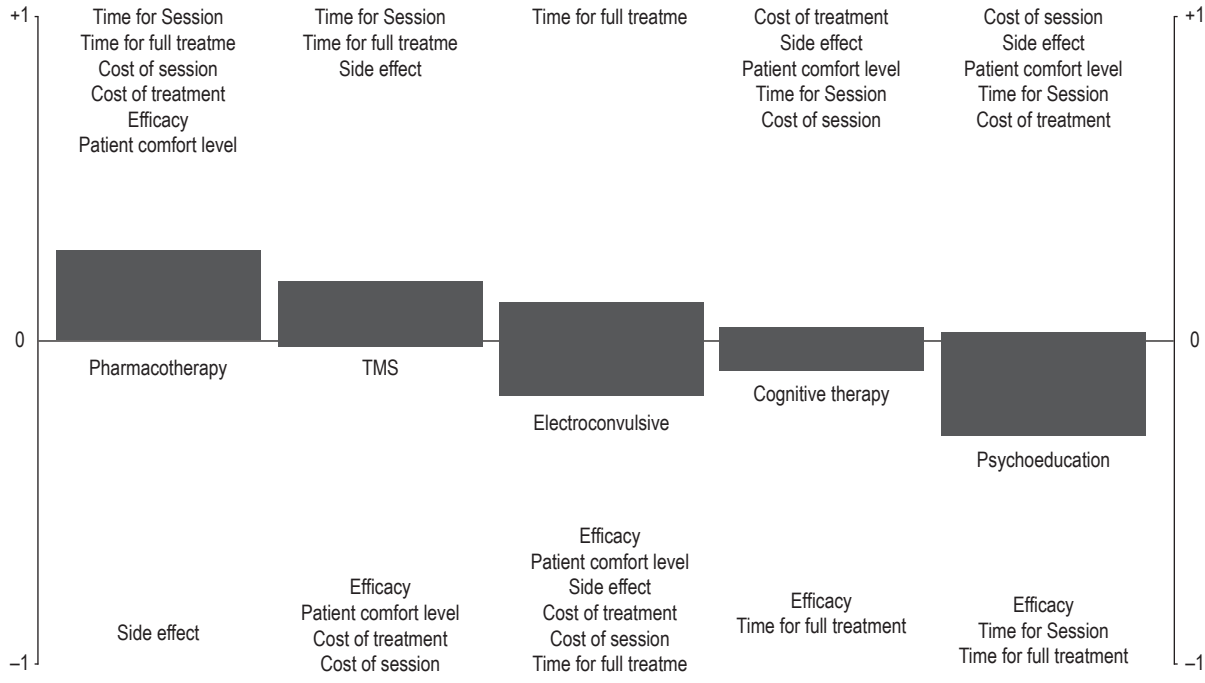

Figure 1. Positive and negative sides of each technique (different weights).

Similarly, Table 7 and Figure 2 show the complete ranking and positive/negative sides respectively for equal weights. Even though we have assigned equal weights for each criteria, pharmacotherapy is still the first choice outranking the rest, followed by CBT, TMS, psychoeducation program, and ECT.

Table 7. Complete ranking results for equal weights.

Ranking	Therapy techniques	Positive outranking flow	Negative outranking flow	Net flow
1	Pharmacotherapy	0.4151	0.0473	0.3678
2	CBT	0.2900	0.2227	0.0672
3	TMS	0.2252	0.2316	-0.0064
4	Psychoeducation program	0.1624	0.3190	-0.1566
5	ECT	0.0827	0.3548	-0.2722

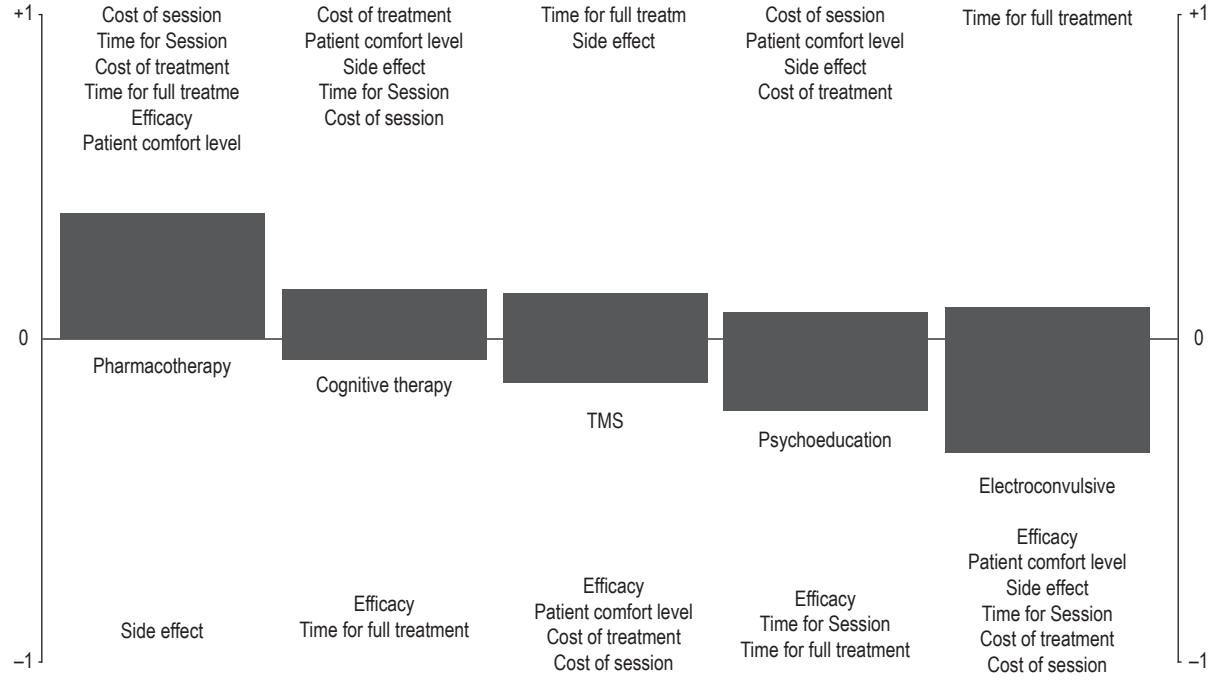

Figure 2. Positive and negative sides of each technique (equal weights).

4. DISCUSSION

The outcome after evaluating the alternatives by selecting the important criteria and assigning preferential weight shows that the right treatment with the appropriate characterization of the selected criteria outranks the rest of the alternatives in the process. The criteria in the table with the weight are assigned carefully thereby prioritizing lower side effects, higher efficacy and minimizing time requirement. The implemented decision system was expected to suggest and prioritize the pharmacological approach so as to manage the mental illness at the expressed level of severity. The outcome from the fuzzy PROMETHEE method prioritizes pharmacotherapy with few deviations from TMS, ECT and non-pharmacotherapy. Through such an approach, we can fit the demand for alternative decisions desired for certain stages of an illness. Unlike [32], which compared schizophrenia treatment alternatives exclusively for pharmacological treatment through the Markov network approach and showed the economic advantage of several classes of drugs, our study includes existing treatment alternatives without

focusing on a single approach and implemented the fuzzy PROMETHEE approach in selecting a better treatment alternative. A clinician review treatment guide for selecting an appropriate treatment alternative that is mainly based on the symptom severity and stage of the disease was presented in [26].

According to [33], there are variations across the patients, as well as across the drugs. We considered an average patient (did not consider the disease stage or patient profile) and average recovery time (usually it covers a range) to show the method's applicability, but this study can be extended to include all possible factors since fuzzy PROMETHEE supports large number of criteria. Treatment selection might be different for patients in acute phase than those in stable phase. Antipsychotics selection among different drugs can be a separate study given that many criteria affecting the decision-making process such as adverse effects (weight gain and extrapyramidal symptoms, myocarditis, diabetes mellitus, contraindications like parkinsonism, tardive dyskinesia), stage of the disease and patient profile. Age, ethnicity, gender and genetic factors are other limitations not considered in this study. Patient-physician discussions are very important to make a shared and improved decision. Therefore, preferences and opinions of patients or their families should also be considered in the process of decision-making.

Modern guidelines such as The American Psychiatric Association [34] or UK National Institute for Health and Clinical Excellence [35] recommend an initial psychiatric evaluation of the patient for an accurate diagnosis and proper treatment selection. This evaluation reviews the patient's previous psychiatric diagnosis, response/adherence to the previous treatments and other complications such as cognitive decline. It is also recommended to assess the patient's families/caregivers in terms of their knowledge about the disease and impact of the disease on them [36]. Inpatient treatment can be considered for patients with attempt of suicide, exhibit severe violence or need constant supervision. Pharmacological management which is the primary option for schizophrenia despite the fact that it causes metabolic abnormalities such as cardiovascular diseases [37], can be applied based on the past treatment response, past experience of side effects, cost, comorbidity, patient preference, preferred route of administration, availability, current metabolic profile, and treatment resistance, while ECT might be considered for patients with persistent symptoms such as catatonia, suicidal behavior or do not response to Clozapine. Although CBT which the first non-pharmacological intervention included in the guidelines, has been considered an effective therapy and applied along with antipsychotics, there is still a debate about its efficacy [38]. Treatment targets should also be considered when formulating a treatment plan. These targets usually include suicidal behaviors, depression, substance use, and community adjustment problems. The patient history is one of the most important criteria for selecting the treatment technique and should be included in the evaluation criteria. Furthermore, the treatment plan should continuously be re-evaluated and modified as the new information is available. Therefore, it is sensible that a mathematical method can aid in evaluating the specific condition of a patient to find the most appropriate treatment technique when there are so many criteria affecting the treatment selection procedure and when these criteria are not quantitative. Fuzzy PROMETHEE can process qualitative and quantitative data at the same time and it supports a large number of inputs and mimics human thinking to make preferences. Such a method can be used in the clinic for the treatment selection effectively considering the treatment plan is updated iteratively.

In this study, we included only the most common treatment techniques. However, in the future studies, new psychological interventions such as attention training technique, acceptance and commitment therapy, hallucinations focused integrated therapy, art therapy, music therapy and competitive memory training will be evaluated. The combination of the treatments, for instance applying a nonpharmacological treatment in addition to medications is other limitation which was not considered when applying fuzzy PROMETHEE. Therefore, further studies are needed to evaluate the effect of combination of different techniques including more criteria and for personalized treatment selection.

5. CONCLUSIONS

Implementing the multi-criteria decision-making technique through fuzzy PROMETHEE in the evaluation of schizophrenia treatment alternatives has shown that the performance of fuzzy input data and the PROMETHEE outranking approach works well in handling uncertainty and can aid health-care professionals in multi-criteria decision-making problems. The study was able to show the simplicity and feasibility of the proposed technique for multi-criteria decision-making problems in healthcare. It is clear that the current study should be updated and advanced through the inclusion of more treatment approaches and criteria and psychiatrist's opinion is essential in defining the importance of each criteria.

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