A Simple Model for Evaluating Medical Treatment Options

Irosh Fernando, Frans Henskens, Masoud Talebian and Martin Cohen

Abstract One of the key areas of clinical decision making in the field of clinical medicine involves choosing the most appropriate treatment option for a given patient, out of many alternative treatment options. This paper introduces a model that is intuitive to clinicians for evaluating medication treatment options, and therefore has the advantage of engaging clinicians actively in a collaborative development of clinical Decision Support Systems (DSS). This paper also extends the previously introduced models of medical diagnostic reasoning, and case formulation (in psychiatry). Whilst the proposed model is already implemented as a DSS in psychiatry, it can also be applied in other branches of clinical medicine.

Keywords Model for selecting treatment options · Medical decision support · Medical decision support system

1 Introduction

Clinical reasoning in Medicine can be described in relation to four main areas: diagnostic reasoning, case formulation, choosing investigations, and choosing treatment options. Whilst the authors have previously described a theoretical framework for

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diagnostic reasoning, and case formulation [4, 5], this paper mainly focuses on the process of selecting treatment options.

For any given clinical situation, often there are a number of potential treatment options, which are associated with different pros and cons. The process of choosing 'the best' option is typically guided by the clinician's knowledge of the diagnosis and case formulation. Choosing the best option is often a complex process that requires careful evaluation of a number of variables related to each treatment option and the patient's characteristics. Understandably, it is a critical decision that determines the recovery, and considers the risks of potential complications associated with each treatment option. Because of the limitation of human cognitive capacity to process a large number of variables accurately and efficiently in a timely manner, the choice process sometimes results in poor or even adverse outcomes. Therefore, having a theoretical framework for evaluating treatment options in an explicit manner can improve the quality of clinical decision making, and yield benefits to patients.

The first part of the paper explores the process of treatment evaluation at a conceptual level. The next section describes the formalisation of the proposed conceptual model. An example is used to explain the model, and two alternative approaches, namely Analytic Hierarchy Process (AHP) [8], and Genetic Algorithms [6] are briefly compared with the proposed approach. Finally, the paper briefly introduces Treatment Evaluation System (TES), which is an implementation of this model for evaluating treatment options in Psychiatry.

2 Conceptual Model for Evaluating Treatment Options

In order to develop a formal model for evaluating treatment options, it is important to have a conceptual understanding of this process. Gaining such understanding can often be difficult due to the largely implicit nature of clinical reasoning by expert clinicians, and also the domain expertise required in order to conceive the decision making process. The general model often used in modern clinical medicine involves a shared decision making process involving both the clinician and the patient [1]. In this process, the clinician may propose a number of treatment options according to his/her understanding of the diagnosis and etiological formulation, whereas the patient makes an informed decision by evaluating pros and cons associated with each treatment option.

For a given diagnosis, there may be several etiological explanatory models that attempt to explain 'why this patient developed this illness at this point of time?'. Each explanatory model may indicate at least a one treatment option, and collectively there can be a potentially large number of options, out of which a small number of options have to be chosen. As illustrated in Fig. 1, the clinician may look at a large number of variables according to the type of treatment option, and these variables have to be matched against the characteristics of the patient. For example, any given side effect associated with a medication is a one variable, and the matching of this variable with the patient characteristics involves evaluating the risk of this side effect occurring in the patient, and its potential consequences for the patient.

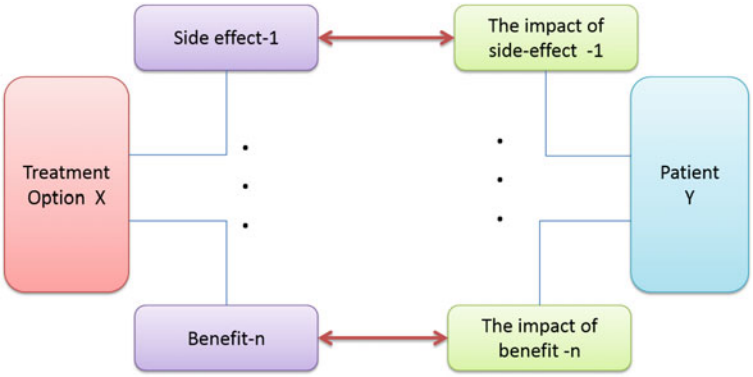

Fig. 1 Conceptual model of treatment evaluation

3 Formal Model

All possible diagnoses consists of a finite set $D = \{d_1, d_2, \ldots\}$, and for any given diagnosis d_i, there exists a set of etiological explanatory models $M(d_i) = \{m_1, m_2, \ldots\}$. For any given explanatory model m_j, there exists a finite set of treatment options $T(m_j) = \{t_1, t_2, \ldots\}$. For each treatment option t_k there exists a finite set of profile items $E(t_k) = \{e_1, e_2, \ldots\}$.

Associated with each treatment option, t_i there exists a row vector of n dimensions $V(t_k) = (v(e_{k1}), \ldots\ v(e_{kn}))$ where v is a function defined as follows:

$$v : E(t_k) \rightarrow [0 \ldots 1]$$

The reason for this is that the likelihood of the occurrence of any outcome, desirable or undesirable, can be described in terms of their probabilities (e.g. probability of having a successful surgical outcome, probability of having a particular side effect etc.). For example, consider $v(e_{kj}) = 0.6$ representing the probability of the occurrence of the outcome associated with the profile item e_{kj} of the treatment t_k. On the other hand, profile items that are not associated with the probabilities of occurrence (e.g. cost associated with a treatment option) can be assigned a ratio with respect to the largest possible value. For example, consider the profile item e_1 as the treatment cost, and that there are three treatment options: t_1 costs $\$_1$, t_2 costs $\$_2$ and t_3 costs $\$_3$. Then the value of the profile item for each treatment option can be calculated as follows:

$$v(e_{11}) = \frac{\$_1}{(\$_1 + \$_2 + \$_3)} \text{ for } t_1$$

$$v(e_{21}) = \frac{\$_2}{(\$_1 + \$_2 + \$_3)} \text{ for } t_2$$

$$v(e_{31}) = \frac{\$_3}{(\$_1 + \$_2 + \$_3)} \text{ for } t_3$$

The product $v(e_{kj}).p_j$ can be interpreted as the impact of the profile item e_{kj} of the treatment t_k considering its level of significance p_j to the patient. Therefore, the overall 'fitness' of the treatment t_k can be approximated as a summation of all such products, using a fitness function defined as:

$$f(t_k) = \sum_{j=1}^{n} v(e_{kj}).p_j$$

Suppose there are m of such treatment options, from which at least one needs to be chosen. Collection of the corresponding row vectors associated with these treatment options can be represented as a matrix:

$$M = \begin{pmatrix} v(e_{11}) & \cdots & v(e_{1n}) \\ \vdots & \ddots & \vdots \\ v(e_{m1}) & \cdots & v(e_{mn}) \end{pmatrix}$$

A patient profile corresponding to a treatment option with a profile row vector of n dimensions, can be represented as a column vector of n dimensions:

$$P = \begin{pmatrix} p_1 \\ \vdots \\ p_n \end{pmatrix}$$

where $p_1, \ldots p_n$ represents the relative importance assigned to the profile items $e_{i1}, \ldots e_{in}$ associated with the treatment option t_i. Each p_j is an integer value in the interval $[-9 \ldots 9]$. This is because each treatment option is associated with only two categories of profile item: desirables and undesirables. Negative values correspond to the magnitude of the significance associated with undesirable characteristics of the patient profile (e.g. side effects and adverse complications) whereas positive values correspond to the magnitude of the significance associated with desirable characteristics of the profile (e.g. desirable treatment outcomes). The scales shown in Figs. 2 and 3 can be used to choose a value for desirable and undesirable profile items respectively. The positive scale is somewhat similar to the fundamental scale of absolute numbers used in the Analytic Hierarchy Process (AHP) [8].

Evaluation of the set of m treatment options represented by the $m \times n$ matrix M against the patient profile vector P involves multiplication of M by P resulting in the column vector O of m dimensions, as follows:

$$MP = O$$

Level of importance associated with achieving a desirable outcome	Score
Not important	0
Slight importance	1
Moderate importance	2
Moderate plus importance	3
Strong importance	4
Strong plus importance	5
Very Strong importance	6
Extreme importance	7
Must	8
Absolute Must	9

Fig. 2 Scale for scoring desirable profile items

Level of importance associated with avoiding an undesirable outcome	Score
Not important	0
Slight importance	-1
Moderate importance	-2
Moderate plus importance	-3
Strong importance	-4
Strong plus importance	-5
Very Strong importance	-6
Extreme importance	-7
Must	-8
Absolute Must	-9

Fig. 3 Scale for scoring undesirable profile items

$$\begin{pmatrix} v(e_{11}) & \cdots & v(e_{1n}) \\ \vdots & \ddots & \vdots \\ v(e_{m1}) & \cdots & v(e_{mn}) \end{pmatrix} \begin{pmatrix} p_1 \\ \vdots \\ p_n \end{pmatrix} = \begin{pmatrix} o_1 \\ \vdots \\ o_m \end{pmatrix}$$

The outcome vector O consists of elements representing the relative utility of each treatment option.

4 An Example

In order to explain the model let us consider the following example. Suppose there are three treatment options available for a patient who has a particular diagnosis. Each treatment is associated with a profile vector consisting of five items: probabilities of

Profile items	Treatment 1	Treatment 2	Treatment 3
Probability of having side effect 1	0.1	0.4	0.6
Probability of having side effect 2	0.4	0.5	0.2
Relative cost	0.2	0.4	0.4
Probability of achieving the desirable outcome 1	0.6	0.3	0.9
Probability of achieving the desirable outcome 2	0.7	0.6	0.8

Fig. 4 An example of a matrix of treatment profiles

having each of two side effects, relative cost, and the probabilities of achieving each of two desirable outcomes as described in Fig. 4.

The matrix M corresponding to this table is given as follows:

$$M = \begin{pmatrix} 0.1 & 0.4 & 0.2 & 0.6 & 0.7 \\ 0.4 & 0.5 & 0.4 & 0.3 & 0.6 \\ 0.6 & 0.2 & 0.4 & 0.9 & 0.8 \end{pmatrix}$$

Now, consider the patient profile outlined in Fig. 5. The column vector corresponding to the patient profile is given as:

$$P = \begin{pmatrix} -8 \\ -5 \\ -2 \\ 9 \\ 8 \end{pmatrix}$$

Fig. 5 An example of a patient profile

Profile items	Patient X
Relative impact having the side effect 1	-8
Relative impact of having the side effect 2	-5
Impact of the associated cost	-2
Relative impact of achieving the desirable outcome 1	9
Relative impact of achieving the desirable outcome 2	8

Evaluation of the three treatment options involves the following calculation:

$$MP = O$$

$$\begin{pmatrix} 0.1 & 0.4 & 0.2 & 0.6 & 0.7 \\ 0.4 & 0.5 & 0.4 & 0.3 & 0.6 \\ 0.6 & 0.2 & 0.4 & 0.9 & 0.8 \end{pmatrix} \begin{pmatrix} -8 \\ -5 \\ -2 \\ 9 \\ 8 \end{pmatrix} = \begin{pmatrix} 7.8 \\ 1.0 \\ 7.9 \end{pmatrix}$$

The evaluation outcome vector:

$$O = \begin{pmatrix} 7.8 \\ 1.0 \\ 7.9 \end{pmatrix}$$

represents the relative fitness of the three treatment options. Accordingly, Treatment 3, which has the highest outcome value of 7.9, can be considered the best treatment option.

5 Model Behaviour

Representing the dynamics of the treatment evaluation process as a system of linear equations leads to the advantage that it is more easy to study the behaviour of the system. Understanding of the model's behaviour is necessary for answering some of the important questions in relation to choosing a treatment option.

For example, consider two treatments t_1 and t_2, and that clinician and patient are primarily focused on a particular profile item e_k and its probability of occurrence in this patient in relation to t_1 and t_2. Let us assume that the respective probabilities are $v(e_{1k}) = 0.6$ and $v(e_{2k}) = 0.8$. In this situation the summation of the products $v(e_{1j}).p_j$ and $v(e_{2j}).p_j$ for $i = 1 \ldots n$ and $i \neq k$, are constants; let us assign the values $C_1 = 12$ and $C_2 = 10$ respectively to these sums. This means, without considering the profile item e_k, that treatment t_2 is superior to treatment t_1. One of the useful questions to answer is 'How high a level of significance do you need to assign to profile item e_k so that the treatment t_1 is superior to the treatment t_2'?

The above question can be answered by solving the resulting pair of linear equations:

$$f(t_1) = v(e_{1k})p_k + c_1$$

$$f(t_2) = v(e_{2k})p_k + c_2$$

Setting $f(t_1) = f(t_2)$ and substituting the values for the above problem in these equations gives the following result:

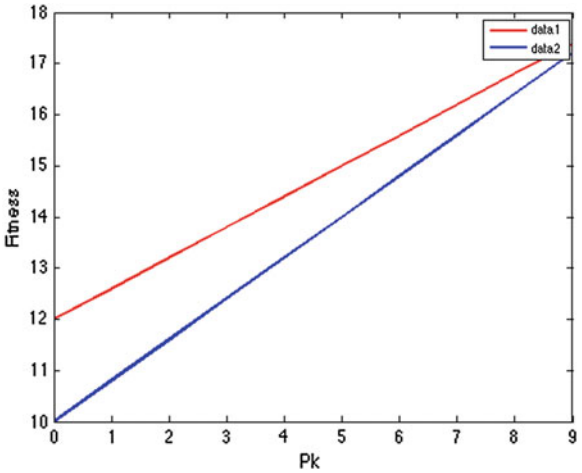

Fig. 6 Behaviour of $f(t_1)$ and $f(t_2)$ according to p_k

$$0.6p_k + 12 = 0.8p_k + 10$$

$$0.2p_k = 2$$

$$p_k = 10$$

Given the above value is out of the range $[-9 \ldots 9]$ the conclusion is that, no matter how important the profile item e_k, treatment t_2 is always superior to treatment t_1. Behaviour of the fitness of each treatment $f(t_1)$ and $f(t_2)$ according to p_k can also be described graphically as shown in Fig. 6.

Now, suppose $v(e_{2k}) = 0.8$ changes to $v(e_{2k}) = 0.85$, whilst $v(e_{1k}) = 0.6$, $C_1 = 12$ and $C_2 = 10$ remain the same (i.e. the level of the evidence base associated with a given treatment property may change slightly over time). Solving the equations for these new values gives:

$$0.6p_k + 12 = 0.85p_k + 10$$

$$0.25p_k = 2$$

$$p_k = 8$$

The above value is within the range $[-9 \ldots 9]$, and according to the scale given in Fig. 2, profile item e_k is a 'must' to achieve. This new result can be interpreted as saying that both treatments have the same degree of fitness, if the patient considers e_k as a 'must' to achieve. Nevertheless, if the patient changes his/her mind and assigns e_k as an 'absolute must' to achieve (i.e. $p_k = 8$), then treatment t_1 is superior to

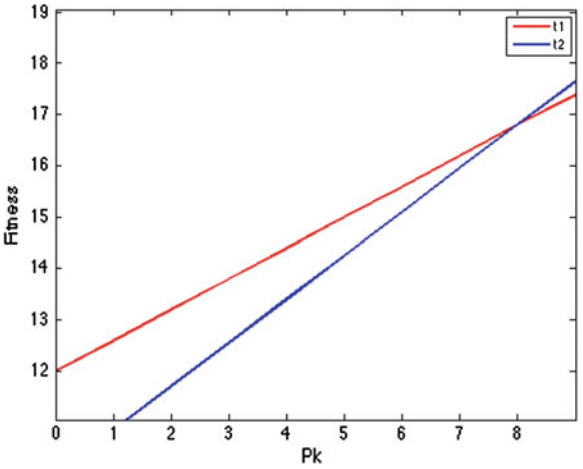

Fig. 7 Behaviour of $f(t_1)$ and $f(t_2)$ according to p_k

treatment t_2, and indeed is the only treatment that can satisfy the 'absolute must' requirement. Figure 7 describes this situation.

The above example can easily be extended to study the behaviour of more than two treatments, and also for more than one profile item. Studying the model's behaviour is important to gaining deeper understanding of the treatment evaluation process. Importantly, the model incorporates the clinician's expertise by supporting him/her in adjusting the values of profile items in order to make fair and effective decisions.

6 Alternative Approaches

It is important to recognise that there are problems in other domains that require similar mathematical models at an abstract level, and therefore there exist alternative strategies that could potentially be applied for evaluating treatment options.

For example, Analytic Hierarchy Process (AHP) is a well-established and mathematically rigorous procedure [8]. AHP has been widely applied in various application domains including clinical practice [7]. For example, application of AHP has been described in relation to optimal management of pharyngitis [9], and also estrogen replacement therapy and cosmetic eye lid surgery [10]. Application of AHP requires a pairwise comparison of profile items, and for n profile items, $n(n-1)/2$ (i.e. $O(n^2)$) judgments have to be made. The proposed approach only requires n (i.e. $O(n)$) judgments to be made.

For example consider a treatment profile with a vector of four desirable outcomes. Formulation of the problem in terms of AHP requires rating the relative importance of these profile items using a scale of absolute numbers. Suppose the resulting pairwise

comparison matrix is:

$$[a_{ij}] = \begin{pmatrix} 1 & 3 & 6 & 7 \\ 1/3 & 1 & 1/5 & 1/4 \\ 1/6 & 5 & 1 & 3 \\ 1/7 & 4 & 1/3 & 1 \end{pmatrix}$$

Then, for this example, the item $a_{12} = 3$ is interpreted as saying that profile item 1 is three times more important than profile item 2.

Whilst comparison of profile items of the same category (e.g. undesirable profile item with another undesirable, or desirable property with another desirable property) is clearly meaningful, in the context of the evaluation of treatment choices, comparison of profile items in different categories (e.g. cost of the treatment with a side effect, or an undesirable property with a desirable property) is difficult and sometimes not meaningful.

On the other hand, the pairwise matrix has to be a positive matrix, and if the matrix of treatment profile vectors with positive and negative values is transformed into a positive matrix its interpretation become less intuitive to clinicians. Also, the AHP algorithm requires many complex calculations (e.g. the principal eigenvector, Perron vector, and their eigenvalues) and therefore requires more computational resources. More importantly, as the authors have previously emphasised, engagement of clinicians in a collaborative development environment is a critical step for successful development of Clinical Decision Support Systems [3]. AHP would be less appealing due to its complexity, and may appear less intuitive to clinicians.

Genetic Algorithms (GA) can also be applied to solve problems of similar nature. In GA, for example, profile items can be encoded as genes with their initial values, and the genetic operations such as cross over and mutations can be applied to produce a pool of profile vectors with different values. A fitness function can be designed to select the 'the fittest' profile.

GA is better suited to situations which require selecting a best solution out of a large number of solutions. For example, consider a hypothetical situation in which a pharmaceutical treatment can be designed by adjusting the doses of different chemical components that are correlated with corresponding profile item values. This may result in a potentially infinite number of possible combinations of different chemical components, and thus an infinite number of treatment profiles. Given n different chemical compounds required to synthesise a treatment, a gene can be encoded as a vector $g_0 = (w_1, \ldots, w_n)$ where w_i is the amount of the ith required chemical component. Using the above-mentioned genetic operations a very large (infinitely many) pool of genes can be replicated. Suppose the functions Ω_i where $i = 1 \ldots n$ determines the corresponding values of the profile items e_i such that:

$$v(e_i) = \Omega_i(w_i)$$

Then the fitness of any given gene g_k can be evaluated using a fitness function f as follows:

$$f(g_k) = \sum_{i=1}^{n} \Omega_i(w_i)$$

The 'best' treatment option can be chosen out of any given set of treatment options that are encoded in genes by choosing the corresponding gene with the highest fitness value.

Evaluation of medical treatment options often involves only a few options, and therefore GA is less desirable.

7 Model Implementation in Psychiatry

The new model described above has been implemented as Treatment Evaluation System (TES) in psychiatry, and used for choosing psychiatric treatment options. The design, implementation and its application is presented elsewhere in a separate paper [2]. Figure 8 shows a screenshot of TES, in which two antidepressant treatments are evaluated against a hypothetical patient profile.

Next, Fig. 9 shows approximated values for each treatment profile.

Finally, Fig. 10 shows the evaluation results, after entering the patient profile.

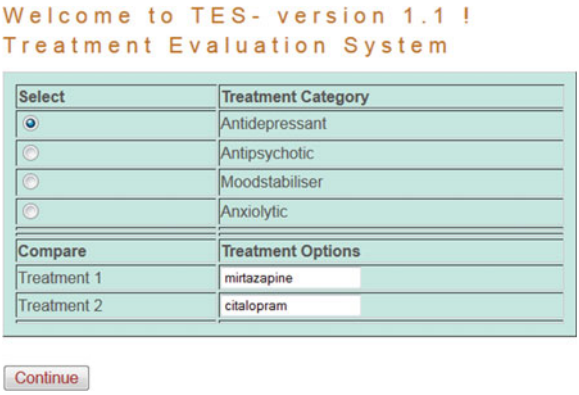

Fig. 8 Implementation of the model as treatment evaluation system in psychiatry

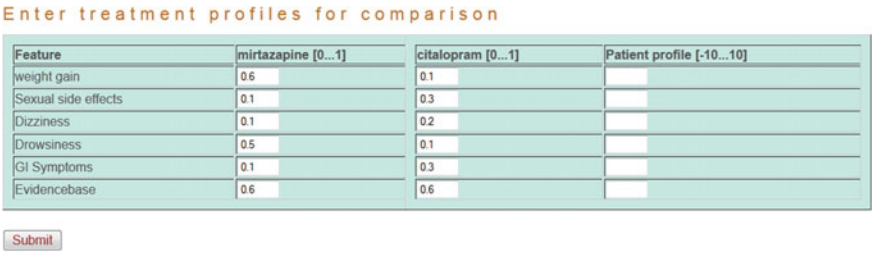

Fig. 9 Treatment profiles and the patient profile

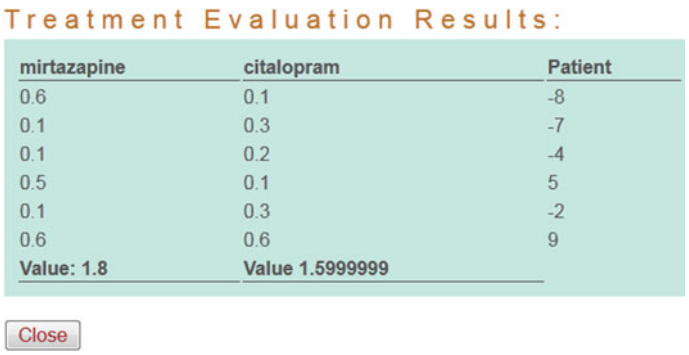

Fig. 10 Outcome of the treatment evaluation

8 Conclusion

This paper presents a new model that can be used for effectively evaluating competing treatment options. The model has been described at a relatively abstract level, and encapsulates the essence of treatment decision making across different branches of clinical medicine. Therefore, the model can be implemented as a decision support tool in any branch of clinical medicine irrespective of the nature of the involved treatment options. The proposed model was originally formulated to prescribe psychotropic medications for complex patients in psychiatric practice, and its implementation, TES, is currently being evaluated with the view to introduce further enhancements.

References

1. Charles, C., Gafni, A., Whelan, T.: Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango). Soc. Sci. Med. **44**, 681–692 (1997)
2. Fernando, I., Henskens, F.A.: A web-based flatform for collaborative development of a knowledgebase for psychiatric case formulation and treatment decision support. In: IADIS e-Health 2012 International Conference. Lisban, Portugal (2012)
3. Fernando, I., Henskens, F.A., Cohen, M.: A collaborative and layered approach (CLAP) for medical expert systems development: a software process model. In: Proceedings, SERA (2012)
4. Fernando, I., Henskens, F.A., Cohen, M.: An expert system model in psychiatry for case formulation and treatment decision support. In: Proceedings, HealthInf-12, pp. 329–336 INSTICC (2012)
5. Fernando, I., Henskens, F.A., Cohen, M.: Software Engineering, Artificial Intelligence, Networking and Parallel/Distributed Computing, Studies in Computational Intelligence, vol. 492, chap. An Approximate Reasoning Model for Medical Diagnosis, pp. 11–24, Springer, Heidelberg (2013)
6. Goldberg, D.E.: Genetic Algorithms in Search, Optimization, and Machine Learning. Addison-Wesley Professional, New York (1989)
7. Liberatore, M.J., Nydick, R.L.: The analytic hierarchy process in medical and health care decision making: a literature review. Eur. J. Oper. Res. **189**, 194–207 (2008)

8. Saaty, T.L.: How to make a decision: the analytic hierarchy process. Eur. J. Oper. Res. **48**, 9–26 (1990)
9. Singh, S., Dolan, J., Centor, R.: Optimal management of adults with pharyngitis - a multi-criteria decision analysis. BMC Med. Inform. Decis. Mak. **6**(1), 14 (2006)
10. Singpurwalla, N., Forman, E., Zalkind, D.: Promoting shared health care decision making using the analytic hierarchy process. Socio-Econ. Plann. Sci. **33**, 277–299 (1999)