ORIGINAL ARTICLE

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A Basic Approach to Select the Appropriate Method in case of Extended Dominance

ABSTRACT

Objective: In cost-effectiveness analysis, treatment methods are ranked by cost and effectiveness, and a method more costly but less effective, is dominated. In models that none of the methods is absolutely dominated but one of them is extendedly dominated, selecting cost-effective method is complicated. Aim of this study was to propose a classification for magnitude of incremental cost-effectiveness ratio of extendedly dominated method, which can use for deciding about cost-effectiveness of this treatment.

Methods: Simulated data based on actual data, and simulated hypothetical data in accordance with actual data were used. All possibilities were tried to consider by generating different costs, effectiveness and response rates. Proportional magnitudes of incremental cost-effectiveness ratios of treatments extendedly dominated were investigated. Descriptive statistics for each model, and weighted means by response rates were calculated and change in percentage of extended dominance were compared.

Results: Magnitude of incremental cost-effectiveness ratio of the method extendedly dominated is a quite important factor to decide about it, when response rates of alternative methods are similar or same. Slight changes were observed as the response rates differ from each other, but there was not an extreme impact on proportions of extended dominance.

Conclusions: A very simple and practical classification which can be used to assess the proportional magnitude of the incremental cost-effectiveness ratio of extendedly dominated treatment method and be valid regardless of whether response rates of treatments in model are same or different was suggested.

Keywords: Cost-Effectiveness Analysis, Incremental Cost-Effectiveness Ratio, Dominance, Extended Dominance.

Genişletilmiş Baskınlık Durumunda Uygun Yöntem Seçimi için Temel Bir Yaklaşım

ÖZET

Amaç: Maliyet etkililik analizinde, tedavi yöntemleri maliyet ve etkinliğe göre sıralanır ve daha maliyetli fakat daha az etkin olan yöntem baskılanır. Yöntemlerden hiçbirinin kesin olarak baskılanmadığı, ancak bunlardan birinin genişletilmiş baskınlıkta kaldığı modellerde, maliyet-etkin yöntemin seçilmesi karmaşıktır. Bu çalışmanın amacı, genişletilmiş baskınlıkta kalan yöntemin artan maliyet-etkinlik oranı büyüklüğü için, bu tedavinin maliyet etkinliğine karar vermekte kullanılabilecek bir sınıflandırma önermektir.

Gereç ve Yöntem: Gerçek verilere dayanan simüle edilmiş veriler ve gerçek verilerle uyumlu varsayımsal veriler kullanılmıştır. Farklı maliyet, etkinlik ve yanıt oranları oluşturularak tüm olasılıklar değerlendirilmeye çalışılmıştır. Genişletilmiş baskınlıkta olan tedavilerin artan maliyet etkinlik oranlarının oransal büyüklükleri incelenmiştir. Her bir model için tanımlayıcı istatistikler ve yanıt oranlarına göre ağırlıklı ortalamalar hesaplanmış ve genişletilmiş baskınlık yüzdesindeki değişim karşılaştırılmıştır.

Bulgular: Genişletilmiş baskınlıkta kalan yöntemin artan maliyet-etkinlik oranının büyüklüğü, alternatif yöntemlerin yanıt oranları benzer veya aynı olduğunda karar vermek için oldukça önemli bir faktördür. Yanıt oranları birbirinden farklılaştıkça küçük değişiklikler gözlemlenmiş, ancak genişletilmiş baskınlık oranlarında aşırı bir etkilenme görülmemiştir.

Sonuç: Genişletilmiş baskınlıkta kalan tedavi yönteminin artan maliyet-etkinlik oranının oransal büyüklüğünü değerlendirmek ve modeldeki tedavilerin yanıt oranlarının aynı ya da farklı olduğuna bakmaksızın kullanılabilecek çok basit ve pratik bir sınıflandırma önerilmiştir.

Anahtar Kelimeler: Maliyet-Etkinlik Analizi, Artan Maliyet-Etkinlik Oranı, Baskınlık, Genişletilmiş Baskınlık.

INTRODUCTION

Cost-effectiveness analysis (CEA) is a method comparing two or more treatment methods proportionally in terms of difference between health benefits and costs of treatments (1-11). The aim of CEA is to determine the cost-effective treatment method by comparing different treatment methods providing same health benefit in terms of costs and gains. Treatment methods being compared are sorted according to their costs, and cost and effectiveness differences of each treatment from the treatment ranking previously in term of cost are calculated. Incremental cost-effectiveness ratio (ICER) for each treatment is calculated based on the ratio of these differences called incremental cost and incremental effectiveness. ICER is calculated by incremental cost divided by incremental effectiveness, and represents incremental cost associated with per additional unit of effectiveness. If there are more than two alternative treatments, ICER of each treatment is calculated subsequently two-by-two. ICERs increase as moving to more costly options, as a usual result. Basic result and decision criterion of a CEA is ICER which shows cost per unit of effectiveness and provides comparison of treatments (1-5,7,12-16). If the ICER is lower than incremental effectiveness, the second-rank treatment in terms of cost is considered to be more cost-effective than the first-rank treatment (1-8,17-23).

Two types of dominance assessment is made based on the ICERs, in CEAs: absolute dominance and extended dominance. Absolute dominance is determined by the fact that one of the treatments has a negative ICER when compared with the treatment ranking previously in term of cost. That is, the treatment method absolutely dominated is less effective but more costly than the treatment ranking previously in term of cost. Reason for negative ICER is negative incremental effectiveness of that treatment. If there is an absolutely dominated treatment method, final results are calculated and interpreted by removing that method from model (2-8,20). If there is an absolute dominance in CEA, it will be easy and clear to identify; with a negative ICER. There may be models in which none of the treatment methods is absolutely dominant, but has a greater ICER than the subsequent treatment in term of cost ranking; extended dominance (2-5,24,25). In these cases, ICER of second-rank treatment is positive, since both incremental effectiveness and incremental cost are positive, but increase in cost and effectiveness are not linear, and ICER of third-rank treatment is very important to decide. If effectiveness of third-rank treatment method increases linearly with cost, then ICER of this treatment method will be lower than ICER of second-rank treatment method. Thus, although a treatment method has a positive ICER compared to previous treatment method if the ICER is greater than subsequent treatment method, extended dominance emerges for this treatment, and it is extendedly dominated (2-5,24,25). Reason of greater ICER depends on effectiveness and may occur in two ways: a) cost of extendedly dominated second-rank treatment method by cost ranking is higher than first-rank treatment method but its effectiveness is not high enough, and/or b) effectiveness of third-rank treatment method by cost ranking is higher than second-rank treatment method while its cost increases in a less manner. In case of extended dominance, model indicates both effectiveness and cost of extendedly dominated treatment increase while incremental effectiveness is lower than incremental cost, but not point out a clear decision. Extendedly dominated treatment method remains in the model (2-8). Therefore, researchers have difficulty deciding which treatment method in model is more cost-effective, whether to continue using extendedly dominated treatment as an alternative method or not recommend it.

The aim of this study was to propose a classification for magnitude of ICER of extendedly dominated treatment method in case of extended dominance, which can use for deciding about cost-effectiveness of this treatment. In this respect, studies were done with both a data set based on actual data and eleven different hypothetical data sets in accordance with actual data. All the possibilities that could be encountered in practice were tried to consider by forming various combinations modelled treatment methods with different cost, different effectiveness and different response rate. All these combinations were reproduced by simulation studies to determine which of these criteria effect the extended dominance and how this effect emerged.

MATERIAL AND METHODS

The CEAs in this study carried out in two parts; one with simulated data based on actual data and the other with simulated hypothetical data in accordance with actual data. In calculation of treatment costs, all needed methods and procedures were taken into account.

In first part of this study, a model which shown extended dominance in CEA is examined detailed and replicated with simulation studies. This real model with extended dominance was appeared in data from Medical Oncology Department, School of Medicine, Mersin University. This model was consisted of three alternative second order treatments for metastatic renal cell carcinoma progressing after the first order treatment; Sorafenib, Everolimus, and Best Supportive Care (Figure 1) (26). Response rates for these arms were 0.73, 0.75 and 0.67 respectively. Median costs were 79825, 65565 and 48648 Turkish Lira for arms

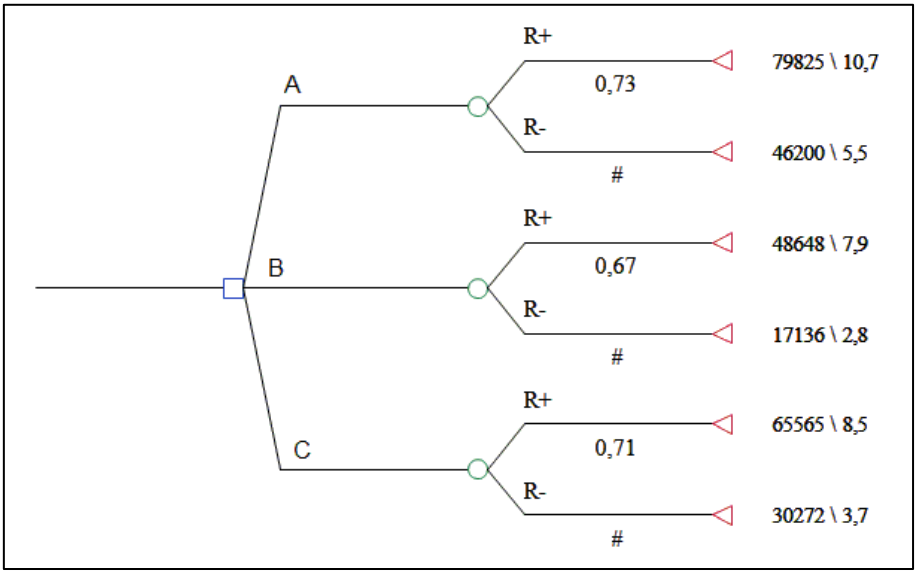

Figure 1. Initial model constructed with real data (A:Sorafenib, B:Best Supportive Care, C:Everolimus)

which patients treated, and 46200, 30272 and 17136 Turkish Lira for arms consist of patients not responded the treatment. The costs determined by the reference study based on the prices declared annually by the Turkish Ministry of Health for the year 2012 in which the study was done. Outcome values (quality-adjusted life years, QALY) were 10.7, 8.5 and 7.9 months for treated arms, and 5.5, 3.7 and 2.8 months for unresponsive arms, respectively. After determining median, minimum and maximum values of costs (Turkish Lira) and effectiveness (month) of each branch, simulations were done based on these values. This model (called Model 1) simulated 10000 times based on initial values and these models were analyzed and extended dominance was examined. Since the main goal is not to do CEA of Sorafenib and/or Everolimus but examine the extended dominance, cost of these treatments were not updated according to current prices and they were coded with A, B, and C. In simulation study, values for costs and effectiveness were generated randomly between minimum and maximum values of real model (Table 1). In addition, response rates to treatment were varied between 0.50 and 0.90 and all alternatives were generated by modelling the treatment alternatives with same and different rates, for examining effect of it on extended dominance. In term of response rate, firstly effect of 0.05 change was examined in 1000 models for each combination (0.50 to 0.95 by 0.05) and it was seen that there is no considerable differences for 0.05 change according to 0.10 change. Therefore, 11 different combinations (called Model 2 to 12) of response rates 0.50 to 0.90 by 0.10 were generated (Table 2).

Table 1. Cost and effectiveness values considered in simulations

Treatment	Response	Value	Min	Max
(A)	Yes	Cost (TL)	63860	95790
		Effectiveness (month)	8.6	12.8
	No	Cost (TL)	36960	55440
		Effectiveness (month)	4.4	6.6
(B)	Yes	Cost (TL)	52452	78678
		Effectiveness (month)	6.8	10.2
	No	Cost (TL)	24218	36326
		Effectiveness (month)	3.0	4.4
(C)	Yes	Cost (TL)	38918	58378
		Effectiveness (month)	6.3	9.5
	No	Cost (TL)	13709	20563
		Effectiveness (month)	2.2	3.4

Incremental Cost-Effectiveness Ratio (ICER): Proportional magnitude between ICER of treatment extendedly dominated and ICER of following treatment in term of cost were evaluated for each model. In this way, a value showing that the ICER of treatment extendedly dominated is how many times bigger than the ICER of following treatment in term of cost were calculated. Median, quartiles and percentages of these values were calculated for each model. Descriptive statistics for these quartiles and percentages were calculated for each 12 model combinations in Table 2. Finally, weighted means were calculated with response rates considered and percentages of extended dominance in that model.

Software: MedCalc ® v.12.2.1 (27) was used for simulation studies and TreeAge Pro Suite 2012 (28) for cost-effectiveness analyses.

RESULTS

Model 1 (Response Rates with A=0.73, B=0.75 and C=0.67): Extended dominance was seen in the vast majority of models, while absolute dominance was less than it according to results of CEAs for 10000 trials performed for the model based on the response rates from actual data. And in some models all three treatments were considered as cost-effective. Extended dominance was seen 5176 times, while absolute dominance was 2426. All three treatments were considered as cost-effective 2398 times (Table 3).

Table 2. Response rates considered in simulations

Model	A	B	C
1	0.73	0.75	0.67
2	0.90	0.90	0.90
3	0.80	0.80	0.80
4	0.70	0.70	0.70
5	0.60	0.60	0.60
6	0.50	0.50	0.50
7	0.90	0.50	0.70
8	0.90	0.70	0.50
9	0.70	0.50	0.90
10	0.70	0.90	0.50
11	0.50	0.70	0.90
12	0.50	0.90	0.70

In 5176 models with extended dominance, treatment B was extendedly dominated 5157 times while A was only 19 times. A total of 2426 models in which one of the treatments being dominated absolutely, B was dominated 2027 times by A and C treatments, and A was dominated by B and C treatments remaining 399 times.

Out of 2027 model, treatment B was most costly treatment 629 times and absolutely dominated while it was second order in term of cost 1398 times and absolutely dominated. Treatment A was most costly treatment in all 399 models in which treatment A was absolutely dominated.

Table 3. Frequencies of absolute and extended dominance in study 1

Treatment	Dominance (2^{nd} cost)	Dominance (3^{th} cost)	Extended Dominance	No Dominance
A	0	399	19	9582
	399			
B	1398	629	5157	2816
	2027			
C	0	0	0	10000
	0			
Model	1398	1028	5176	2398
	2426			

There were 2398 models in which all three treatments being considered as cost-effective in same model. Number of each treatment being considered as cost-effective was changing depend on whether dominant or dominated in models emerging absolute dominance or extended dominance. Treatment A was considered as a cost-effective method 9582 times, while treatment B was considered only 2816 times because of it was the mostly treatment absolutely and/or extendedly dominated. Treatment C was not absolutely and/or extendedly dominated in any model, it was considered as a cost-effective method for all 10000 trials.

Overview of All Models: Frequencies of absolute dominance by cost order and extended dominance for all models were summarized in Table 4, and frequencies of total absolute dominance and extended dominance were summarized in Table 5. Results of CEAs for trials performed for the models constructed with same response rates for all three treatments (Model 2 to 6) were shown similarity to results of CEAs for the first model (Model 1) based on response rates from actual data.

Table 4. Frequencies of dominance by cost order and extended dominance in all models

		Model											
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
A	**D-2**	0	12	4	0	0	0	0	0	0	0	367	159
	D-3	399	684	449	238	134	56	0	2	778	1518	2939	2597
	ED	19	36	20	7	1	0	0	0	0	252	79	1340
	No	9582	9268	9527	9755	9865	9944	10000	9998	9222	8230	6615	5904
B	**D-2**	1398	2782	2620	2383	2056	1646	5966	164	6525	0	4796	397
	D-3	629	977	683	405	185	66	0	50	0	1853	1438	2461
	ED	5157	3614	4158	4803	5501	6149	2860	7168	559	3944	1323	1633
	No	2816	2627	2539	2409	2258	2139	1174	2618	2916	4203	2443	5509
C	**D-2**	0	18	1	0	0	0	116	0	282	0	245	0
	D-3	0	0	0	0	0	0	0	0	0	0	0	0
	ED	0	0	0	0	0	0	29	0	321	0	41	0
	No	10000	9982	9999	10000	10000	10000	9855	10000	9397	10000	9714	10000
Model	**D-2**	1398	2812	2625	2383	2056	1646	6082	164	6807	0	5408	556
	D-3	1028	1661	1132	643	319	122	0	52	778	3371	4377	5058
	ED	5176	3650	4178	4810	5502	6149	2889	7168	880	4196	1443	2973
	No	2398	1965	2085	2165	2123	2083	1029	2616	2105	2433	1105	1491

* **D-2:** Dominance (2^{nd} cost), **D-3:** Dominance (3^{th} cost), **ED:** Extended Dominance, **No:** No Dominance

Treatment B was absolutely and/or extendedly dominated in the vast majority of models in these trials. Treatment A and C were considered as cost-effective with a considerable majority, even if absolutely and/or extendedly dominated in a few models. Treatment B was extendedly dominated 3614 to 6149 times, and absolutely dominated 1712 to 3759 times in general, for these five models.

Models constructed with different response rates for each three treatments (Model 7 to 12) were shown different results depending on response rates. Increasing response rate for each treatment affected its own results positively for selecting cost-effective while decreasing ones affected negatively. And varying response rates of other two treatments affected the results in a different way when the response rate of a treatment is constant. Number of considering as a cost-effective method was increased when response rate of treatment B was the greatest, especially response rate of treatment A was lowest. But treatment B had never been considered more cost-effective than treatment A, even in the worst case for A (Model 12). The least affected treatment from varying response rates was the treatment C.

Table 5. Frequencies of dominance and extended dominance in all models

		Model											
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
A	**D**	399	696	453	238	134	56	0	2	778	1518	3306	2756
	ED	19	36	20	7	1	0	0	0	0	252	79	1340
	No	9582	9268	9527	9755	9865	9944	10000	9998	9222	8230	6615	5904
B	**D**	2027	3759	3303	2788	2241	1712	5966	214	6525	1853	6234	2858
	ED	5157	3614	4158	4803	5501	6149	2860	7168	559	3944	1323	1633
	No	2816	2627	2539	2409	2258	2139	1174	2618	2916	4203	2443	5509
C	**D**	0	18	1	0	0	0	116	0	282	0	245	0
	ED	0	0	0	0	0	0	29	0	321	0	41	0
	No	10000	9982	9999	10000	10000	10000	9855	10000	9397	10000	9714	10000
Model	**D**	2426	4385	3737	3025	2375	1768	6082	216	7015	3371	7542	5536
	ED	5176	3650	4178	4810	5502	6149	2889	7168	880	4196	1443	2973
	No	2398	1965	2085	2165	2123	2083	1029	2616	2105	2433	1105	1491

* **D:** Dominance, **ED:** Extended Dominance, **No:** No Dominance

Extended Dominance and ICERs: Firstly, since number of extended dominance for each model and relationships between ICERs in these models were different, each model evaluated separately. Median, quartiles and percentages of ICERs were calculated for each model, and mean of them in general (Table 6).

Table 6. Magnitude of ICERs

Model	Q_1	Q_2	Q_3
1	2.00	4.09	10.62
2	2.05	4.40	12.88
3	2.11	4.36	11.99
4	2.04	4.16	10.90
5	1.95	3.83	9.66
6	1.86	3.53	8.41
7	2.02	3.83	9.54
8	1.75	3.10	6.64
9	2.01	4.08	11.49
10	1.77	3.31	7.59
11	2.14	4.78	15.02
12	2.12	4.67	13.24
General	1.99	4.01	10.67

Afterwards, proportional relationships between ICERs were evaluated for examining how effects of response rates and percentage of extended dominance are occurred, weighting ICERs with response rates for each treatment and percentage of extended by dominance for each model. Again, median, quartiles and percentages of ICERs calculated in this way were compared in general (Table 7). Dot-plot and box-plot graphs of ICERs for the treatment extendedly dominated in general were shown in Figure 2.

Table 7. Weighted magnitude of ICERs

	Q_1	Q_2	Q_3
Direct	1.99	4.01	10.67
Weighted by response rates	1.99	4.04	10.79
Weighted by percentage of ED	1.95	3.85	9.84
General	1.97	3.97	10.43

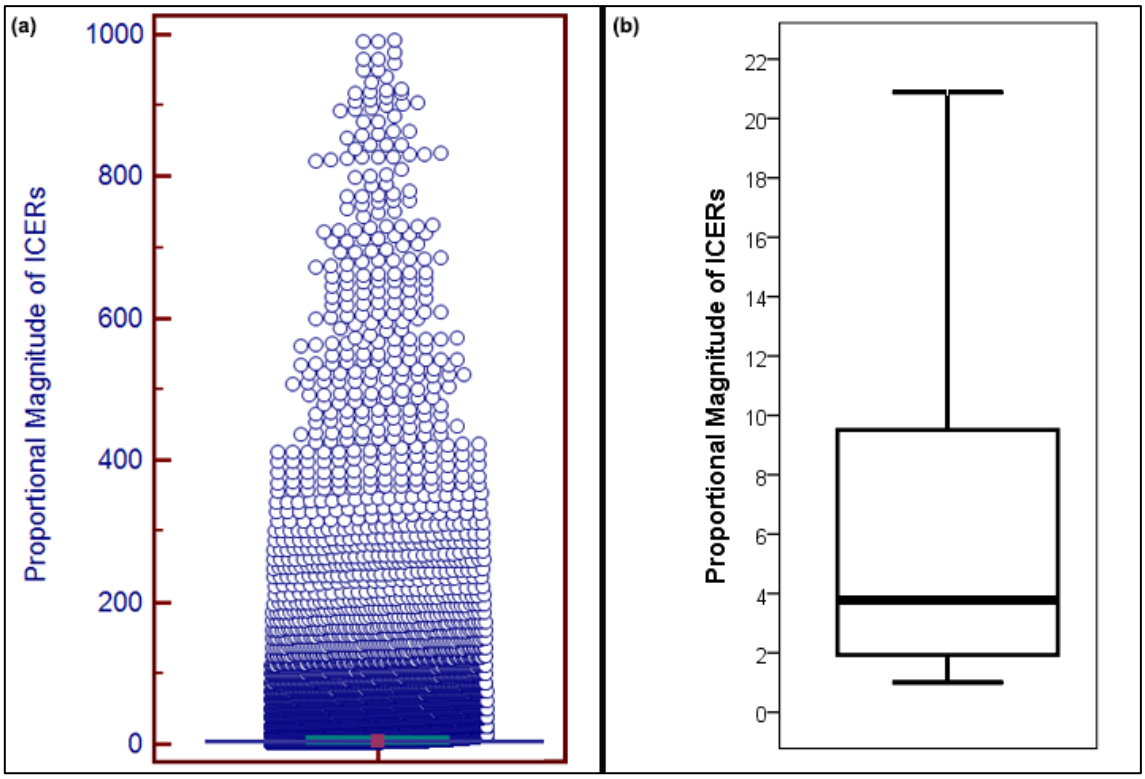

Figure 2. (a) Dot plot and (b) box plot for proportional magnitude of ICERs

DISCUSSION

Interpretation and use of CEA results sometimes may have problems since the concept of extended dominance is often not understood exactly. There is no difficulty in understanding the concept of absolute dominance, everyone can understood it clearly. The concept of extended dominance is a little more complex concept. It is necessary to investigate in detail causes of extended dominance and to examine whether the treatment method extendedly dominated is cost-effective or not. Advantages and disadvantages of the treatment method extendedly dominated should be assessed carefully evaluating the health benefits that the treatment method provide and required cost.

In this study, in the case of extended dominance in CEA, the following results were obtained regarding the treatment method extendedly dominated:

1. When response rates of the treatment methods compared were identical or similar to each other, if there was a treatment method extendedly dominated;

a. This treatment method had also absolutely dominated in the vast majority of models (between 44.46% and 58.58% for this study) in which it had not been extendedly dominated.

b. Increase or decrease in response rate of the treatment did not cause a crucial change in this respect. Since the change in response rate effects both number of extended dominance and absolute dominance, there was no significant difference in overall results. Number of extended dominance varied inversely proportional with response rate, while absolute dominance was directly proportional. Therefore, number of models in which this treatment being considered as cost-effective did not change significantly, as the number of absolute dominance and extended dominance were shifted inversely proportional each other.

c. If this treatment method is used as an alternative method, it will not be a significant contribution in terms of both cost and effectiveness, and will often (between 73.73% and 78.61% for this study) fail to provide expected result.

d. This treatment method which is relatively much less likely (between 21.39% and 26.27% for this study) to provide expected effectiveness with expected cost will be inadequate, since there are two alternative treatments that are more likely (between 92.68% and 100% for this study) to provide expected effectiveness with expected costs.

2. When response rates of the treatment methods compared were different from each other, if there was a treatment method extendedly dominated;

a. This treatment method had also absolutely dominated in the vast majority of models (between 30.60% and 83.56% for this study) in which it had not been extendedly dominated.

b. Increase in response rate of this treatment did not cause a crucial change in this respect. Number of models in which this treatment being considered as cost-effective increased only if response rate of this treatment method increased and response rates of other treatment methods decreased excessively. Of course, decreased otherwise. Therefore, overall number of models in which this treatment being considered as cost-effective did not change significantly, and remained less likely to provide expected results.

c. If this treatment method is used as an alternative method, it will not be a significant contribution in terms of both cost and effectiveness, and will often (between 57.97% and 88.26% for this study) fail to provide expected result.

d. This treatment method which is relatively much less likely (between 11.74% and 42.03% for this study) to provide expected effectiveness with expected cost will be inadequate, since there are two alternative treatments that are more likely (between 93.97% and 100% for this study) to provide expected effectiveness with expected costs.

In CEA, it can be said that extended dominance based on ICERs between alternative treatment methods, is not completely different from absolute dominance. The ICER is negative in case of absolute dominance, while the reason for not being negative in case of extended dominance is sometimes a very small effectiveness difference. When cost ranking is performed, a treatment method is absolutely dominated when its effectiveness is lower than the treatment method ranking previously, but is not absolutely dominated when its effectiveness is higher than the previous treatment method, even if there is only a slight difference. In such a case, this treatment method is controlled for extended dominance by comparing its ICER with ICER of the subsequent treatment method, and if its ICER is greater, than extended dominance decision is made (2-8,24,25). Greatest ICER is the only criterion for extended dominance decision, and this criterion is very general and susceptible to interpretation. The question “How big?” is very important at this point. In terms of magnitude only, 2 is greater than 1, 2000 is greater than 1, so there is no difference between them. Therefore, a cost-effective treatment may excluded due to only a negligible amount, if the decision is made based solely on magnitude of ICER. On the contrary, an ineffective treatment method almost being absolutely dominated may be extendedly dominated.

The most important criterion for comparison of treatment methods in CEA should be numerical value of ICER, not only magnitude. When interpreting results of CEA, it is necessary to consider how large or small this number is, and average cost-effectiveness ratio should not be ignored. It cannot be said that any treatment method that is not absolutely dominated is cost-effective. A treatment method being not absolutely dominated but has a great ICER can be controlled for whether cost-effective or not, by comparing the ICER of subsequent treatment method. Therefore, examination of numerical value of ICERs in CEA, and determining a cut-off value or a classification for it will facilitate interpretation of results. Effective use of ICER will allow to identify treatment method indeed need to be extendedly dominated even if it does not appear in model and being considered as a cost-effective method in some models. It will also become easier and clearer to decide about all alternative treatment methods by comparing ICERs whether being extendedly dominated or not, by means of a cut-off value or classification being determined for ICER. A classification method that would provide this and help to clinicians to decide on cost-effectiveness of a treatment method extendedly dominated was tried to obtain, in this study. In addition, a criteria about when extended dominance decision should be made distinctly was developed, by calculating how many times greater is ICER of a treatment than ICER of subsequent treatment. Quartiles for all studies reflected the actual situation fairly well. A very simple and practical classification which can be used to assess the proportional magnitude of ICERs were suggested by making a detailed analysis, and had been interpreted for its use in practice.

If ICER of a treatment method extendedly dominated in model

- ≤2.00 times greater than ICER of the subsequent treatment method; extended dominance is emerged due to only a slight difference to be neglected in practice. Therefore, the treatment method appears to be extendedly dominated should remain as an alternative treatment method.
- 2.01 to 10.00 times greater than ICER of the subsequent treatment method; extended dominance is emerged clearly. Therefore, decision about the treatment method extendedly dominated should made considering economic conditions, willingness to pay and ethical principles.
- ≥10.01 times greater than ICER of the subsequent treatment method; the treatment method extendedly dominated is an ineffective treatment method almost being absolutely dominated. Therefore, the treatment method extendedly dominated should be excluded from alternative treatment methods.

This recommended classification is valid regardless of whether response rates of treatments in model are same or different. Furthermore, this classification does not change even if response rates of treatments different from each other. Because, when response rate of the treatment method extendedly dominated is low, number of extended dominance decreases, while number of absolute dominance increases. Thus, response rate of the treatment success effects numbers of extended and

absolutely dominance, but and there is no impact on proportional magnitude of ICERs. Similarly, this recommended classification is not effected by percentage of extended dominance in the model.

It is 50% easier to decide about treatment method if an extended dominance occurs in a study, with this proposed classification. For the treatment method has been still decided that it extendedly dominated (when ICER of the treatment method extendedly dominated is 2.01 to 10.00 times greater than ICER of the subsequent treatment method) with remaining 50% probability, studying on its cost may make some solutions. From this point of view, changing the effectiveness of a treatment method is very difficult and perhaps impossible, so working about how to reduce the cost is suggested. If the cost can be reduced, perhaps this treatment method may not be extendedly dominated and can be regarded as one of the alternative treatment methods.

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