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The Cost-Effectiveness of Cognitive-Behavioral Group Training for Patients with Unexplained Physical Symptoms

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ABSTRACT

Objective: The aim of the study was to evaluate the cost-effectiveness of a cognitive-behavioral group training compared with a wait-list control for patients with unexplained physical symptoms (UPS). **Methods:** A probabilistic decision-analytic Markov model was developed with three health states (poor health, average health, and death) based on a cutoff score of the Physical Component Summary of the short-form 36 health survey. To assess the cost-effectiveness in terms of cost per quality-adjusted life-year (QALY), a societal perspective was adopted. The model consisted of cycles of 3 months and a time horizon of 4 years. Data for the model were derived from a randomized controlled trial, in which 162 patients with UPS were randomized either to cognitive-behavioral group training or to the wait-list control. Data were assessed at baseline and after the training of 3 months or after a wait-list period of 3 months. In addition, the training group was followed in an uncontrolled phase and assessed at 3 months and 1 year after the training. **Results:** After 4 years, the group training was in terms of cost-effectiveness "dominant" compared with the wait-list control; there was a positive effect of 0.06 QALYs and a €828 reduction in costs. The cost-effectiveness improved with a longer time horizon. A threshold of €30,000/QALY was passed after 18 months. The group training was cost saving after 33 months. **Conclusions:** Cognitive-behavioral group training is a cost-effective treatment compared with the wait-list control for patients with UPS.

Keywords: cost-effectiveness, Unexplained physical symptoms, quality-adjusted life-year.

Background

Unexplained physical symptoms (UPS) are physical symptoms that cannot be fully explained on the basis of a known medical condition. These symptoms can be classified as a *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*) somatoform disorder if they 1) are not intentionally produced or feigned, 2) cause clinically significant distress or impairment in functioning, 3) persist for at least 6 months, and 4) are not better accounted for by other *DSM-IV* classifications. Somatoform disorders are common in primary care [1,2]. Their prevalence ranges from 4% (without the prevalence of undifferentiated somatoform disorder and body dysmorphic disorder in a 18–80-year old population) [3] to 16% (without the prevalence of somatoform disorder not otherwise specified in a 25–80-year old population) [4]. By definition, somatoform disorders are accompanied by high levels of psychosocial distress and/or impairment, resulting in lost labor-force and household productivity [5] and in a high use of health care services [6,7]. The high prevalence rate of UPS combined with its high costs make it not only a considerable burden for patients but also an economic burden for society [5,6,8].

Research indicates that cognitive-behavioral therapy is the most effective therapy for UPS [9,10], but research into the cost-effectiveness of this therapy is scarce and has methodological limitations. A recent systematic literature review [11] identified eight economic evaluations of treatments for UPS, of which only two investigated the cost-effectiveness by explicitly combining differences in costs with differences in effects into incremental cost-effectiveness ratios (ICERs) (the ratio of additional costs and additional effects). Even these studies, however, did not use a state-of-the-art cost-effectiveness research design, which makes meta-syntheses difficult, because they did not include costs due to work-related productivity losses, applied a time horizon limited to 1 year [12] or to 3 months [13], and mainly used disease-specific measures of effectiveness such as "cost per unit reduction in Health Anxiety Inventory score" [12] and "cost per additional successfully treated patient" rather than quality-adjusted life-years (QALYs) [13]. The use of such specific effect measures complicates comparisons of cost-effectiveness ratios of

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different treatments not only within the same disease but also between different diseases, such as comparing the cost-effectiveness ratios of treatments for UPS with those of treatments for diabetes. When these comparisons of cost-effectiveness ratios are favorable to treatments for UPS, one would have a strong argument to reimburse treatment of UPS similar to diseases with a known medical diagnosis. Such comparisons require the use of generic effect variables such as costs per QALY, which is the preferred outcome in health economics [14].

In health economics, one tries to incorporate all costs and effects, even if the costs and effects occur in the future [14], complemented with implementation costs. Future costs and effects are, for instance, important if one claims that the initial investment in the treatment is offset by future saving in health care costs elsewhere and can be modeled with a Markov model [13]. Uncertainty in the parameter values can be modeled with probabilistic sensitivity analysis [15].

The purpose of this study was to evaluate the cost-effectiveness of a cognitive-behavioral group training compared with a wait-list control for patients with UPS using a probabilistic Markov model.

Methods

Design

The data for the study emerged from a 3-month randomized controlled trial combined with an uncontrolled 1-year follow-up investigating the effectiveness of cognitive-behavioral group training for patients with UPS [16]. In the trial, after completing the baseline measurement (T0), patients were randomized either to the group training (training group 1) or to a wait-list control group. The treatment effect was measured 3 months later, corresponding with the length of the training (T1).

After T1, patients on the wait-list control also attended the training (training group 2). In training group 2, the T1 was the baseline score (T0) and the training group 2 followed the same procedure as did training group 1. In the uncontrolled follow-up, the outcome for both training groups was measured at 3 months after the end of the training (T2) and once again at 1 year after the end of the training (T3). The study was approved by the Erasmus Medical Research Ethics Committee, and registered in the Dutch Trial Register (NTR 1609) [17]. A detailed description of the study protocol has been published elsewhere [18].

Participants

Participants were recruited in outpatient clinics at general hospitals, and by Riagg Rijnmond, a secondary community mental health service in the Rotterdam area in The Netherlands. General practitioners and specialists were asked to refer patients aged between 18 and 65 years whose physical symptoms, according to their clinical judgment, could not be explained on the basis of a known medical condition. Patients were included if they signed the informed consent and if their UPS fulfilled the *DSM-IV* criteria for an undifferentiated somatoform disorder or a chronic pain disorder using the *Structured Clinical Interview for DSM-IV Axis I Disorders/Patient edition* [19]. Patients were excluded if poor language skills or handicaps, such as cognitive impairment, prevented them from understanding the cognitive-behavioral group training. Table 1 presents the patients' baseline characteristics.

Table 1 – Baseline characteristics.

Characteristic	Group training (n = 84)	Wait-list control (n = 78)
Age (y), mean	46	44
Sex: female (%)	80	82
Physical Component Summary (PCS) score, mean	29.34	29.05
Mental Component Summary (MCS) score, mean	43.68	46.72
Duration of UPS (y), median	8	9.5
Classification of comorbid *DSM-IV* axis I disorders measured by *SCID-I/P*		
Mood disorder (lifetime)	13 (40)	11 (30)
Anxiety disorder (lifetime)	20 (36)	27 (41)
Substance-related disorder (lifetime)	1 (12)	0 (6)
Eating disorder (lifetime)	1 (4)	0 (2)
Psychotic disorder (lifetime)	0 (0)	0 (1)
Somatization disorder	14	10
Hypochondriasis	1	1
Adjustment disorder	2	2

DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); *SCID-I/P*, *Structured Clinical Interview for DSM-IV Axis I Disorders/Patient edition*.

Cognitive-Behavioral Group Training

The cognitive-behavioral group training is called "Coping with the consequences of unexplained physical symptoms." This weekly 2-hour manual-based [20] training was held over a 3-month period. The group training started with a minimum of 5 and a maximum of 10 patients. Patients assigned to the group training attended, on average, 11 of the 13 sessions, with a minimum of 6. The aim of the group training was to improve health-related quality of life. Corresponding to this aim, the primary outcome measures in the randomized controlled trial were the two component summaries of the 36-item Medical Outcomes Study short-form health survey (SF-36) [21,22]: Physical Component Summary (PCS) and Mental Component Summary. More details of the group training [18,23,24] as well as its effectiveness [16] have been published elsewhere.

Cost-Effectiveness

The randomized controlled trial provided empirical data of the costs and effects of the group training and the wait-list control. The uncontrolled follow-up extended the empirical data by 1 year by following both training groups 1 and 2. It is to be expected, however, that the effect will sustain longer than these periods. We therefore developed a Markov cohort model [15] in which we simulated a cohort of patients that moved through health states over time.

PCS was used as the primary outcome measure [16]. Patients reported the quality of life in the physical domain as most burdensome, compared with that in the mental domain, and PCS had been shown to be a sensitive parameter for the effects of the group training. The Markov cohort model defined three fixed mutually exclusive health states: average health (AH), poor health (PH), and death (Fig. 1). To define AH and PH, a cutoff score of 40 on the PCS was used because the score of 40 was in the middle between the scores of the general population (mean 50 ± 10) and the scores of the patients included in this study (mean = 29 ± 9). AH represented patients with scores higher than 40 on the PCS, and PH represented patients with scores lower than 40 on the PCS.

The variation over time in the effects and in the costs within the health states AH and PH was nonsignificant and assumed to be constant over time. The length of the Markov cycles was chosen to be 3 months, so that the 3 months of the training could

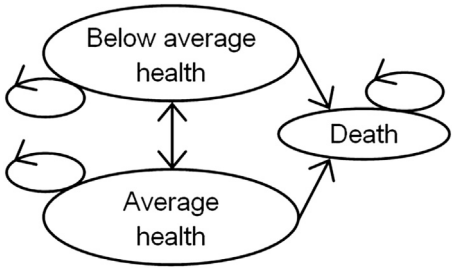

Fig. 1 – State transition diagram of the Markov model for unexplained physical symptoms.

be accommodated in just one cycle. To acknowledge the uncertainty of the long-term effects, we used a time horizon of 4 years and not an infinite time horizon as baseline scenario. Although an infinite time horizon would align with health-economic guidelines [14], it would also assume that the effects will sustain well beyond 4 years. This was considered an unrealistic assumption, given that we had only 3-month data to compare the effects of the group training with those of the wait-list control. Because we did not know how long effects might sustain, we were also interested in the minimal duration of sustained effect needed to show acceptable cost-effectiveness. If the time horizon would be short, the assumption of sustaining the effect would be less influential in considering the validity of the cost-effectiveness estimated. Both the mean age of the simulated patient cohort in the model (45 years) and the distribution of patients over health states (AH = 11%; PH = 89%) at the start of the model were derived from the trial data at baseline (T0). Costs per patient will depend on the number of participants per training: more participants would mean lower cost per patient, under the assumption of similar effects. The average number of participants per training in the model was six patients.

Transition Probabilities

To allow transitions between health states (improve or relapse), transition probabilities were computed on the basis of study data (Table 2). For patients on the wait-list control, data from only T0 and T1 were available. After T1, the transition probabilities for the wait-list control condition had to be assumed. In the wait-list control group, nine patients were in health state AH at T0, and none of them deteriorated (relapsed) to the health state PH in the first cycle. Other patients on the wait-list control were in health state PH at T0, and two patients improved from PH to AH. Given the chronic character of UPS (in our sample, the median duration of UPS was 9 years), a zero relapse chance for patients on the wait-list control in the health state AH did not seem to be a reasonable assumption. In fact, given the median duration, it might be more likely that relapse and improvement in the wait-list control condition were in balance. We therefore assumed "transition balance" after the first cycle of 3 months, in which the probabilities were estimated in such a way that the number of transitions between the health states in the wait-list control condition was equal. The relapse in the first cycle was in line with the data, so no patients deteriorated in this cycle.

For the training group, the transition probabilities for the first cycle were estimated using the T0-T1 data of the training group 1 (the original "experimental" training group) combined with the T0-T1 data of training group 2 (the original wait-list control group). The transition probabilities after attending the training were determined using data T1 through T3, and assumed to be constant after T3.

Mortality figures were derived from the Dutch standard life tables in 2010 provided by Statistics Netherlands CBS [25]. It included an average death risk depending on age for both men and women but not for patients with UPS specifically. We assumed the same mortality for patients with AH and PH.

Costs

The costs of the group training were calculated on the basis of a local cost study (see Table 3), and included the estimation of the volume and cost prices of personnel [26], overhead, material, housing, training and retraining of personnel, recruitment, and travel. Productivity cost related to the time patients needed to follow the group training was not measured because only 45% of the patients were working, of whom 48% worked 24 hours or less. Furthermore, patients had the opportunity to follow the training outside working hours. Note that we did measure the productivity cost related to the illness but, as explained above, not the productivity costs associated with the training.

To estimate all medical costs other than the group training, with the exclusion of the trial costs, we used the 2002 version of the *Trimbos/iMTA Questionnaire for Costs associated with Psychiatric Illness* (TiC-P), a self-report questionnaire for assessing health care–related and work-related costs of illness. The TiC-P has 29 questions and semi-fixed-response alternatives [27,28]. The first part of the TiC-P measures health care–related costs incurred through the use of health care services and medications over the past 4 weeks. The second part of the TiC-P, which is based on the short form of the Health and Labour Questionnaire, measures work-related costs over the past 2 weeks caused by absenteeism (the absence from work), presenteeism (a reduced efficiency at work), and substitution of domestic tasks.

The health states were fixed and assumed to be constant over time. Therefore, an average of the cost scores was used per cycle for the health states. This assumption was supported by the constant flat distribution of total costs over time, which can be observed in Table 4. Costs were discounted at 4%, consistent with Dutch guidelines of pharmacoeconomical evaluations, and represented 2011 cost prices [29].

QALYs

The effects were expressed in terms of QALYs. The quality-of-life weights needed to estimate the QALYs (the so-called utilities) were extracted from the SF-36 [21]. Eleven of the 36 items of this self-report questionnaire are converted into six dimensions (six-dimensional health state short form [derived from SF-36]): physical functioning, role limitations, social functioning, pain, mental health, and vitality [30]. Like costs, utilities were assumed to be constant over time and therefore an average of the utility scores was used per cycle for the health states. This assumption was supported by the constant distribution over time, which can be observed in Table 5. Effects were discounted at a rate of 1.5% per year, consistent with Dutch guidelines of pharmacoeconomical evaluations [29].

Analysis

Because this study involved synthesizing data from a number of sources with different forms of sampling errors and with different assumptions, it is important to assess the uncertainties in the model in a multivariable way and under varying assumptions. Probabilistic sensitivity analysis of the uncertainty of parameters (i.e., the uncertainty that relates to sampling error) was undertaken with second-order Monte Carlo simulation. The parameters included transition probabilities, QALYs, and costs. Because the costs were skewed, gamma distributions were used for the costs in the model. For the transition probabilities and QALYs, beta distributions were used. Ten thousand simulations were

Table 2 – Transition probabilities extracted from the trial.

Transition	T0->T1			T1->T2			T2->T3		
	Mean	SE	N	Mean	SE	N	Mean	SE	N
Group training*									
Improve (from PH to AH)	0.18	0.041	16	0.11	0.037	8	0.04	0.023	7
Stay in PH	0.82†		71	0.89†		64	0.96†		60
Relapse (from AH to PH)	0.17	0.103	2	0.32	0.091	8	0.14	0.066	10
Stay in AH	0.83†		10	0.68†		17	0.86†		17
Wait-list control									
Improve (from PH to AH)‡	0.04	0.024	2						
Stay in PH‡	0.96†		55						
Relapse (from AH to PH)	0.0	0.0	0	0.29§	0.132				
Stay in AH	1.0		9	0.71†,§					

AH, average health; PH, poor health.
* In the calculations, training groups 1 and 2 were used.
† This is the inverse of a transition and has the same standard error.
‡ Transitions were measured only in the first cycle and extrapolated to the subsequent cycles.
§ The mean was based on "transition balance" and extrapolated to the subsequent cycles.

conducted, in which parameter values for transition probabilities, costs, and QALYs were randomly sampled from their distribution. This resulted in 10,000 unique sets of parameters, which were used in the model to calculate the expected costs and QALYs of a cohort of 1000 patients in the training condition and a cohort of 1000 patients on a "4-year wait-list control" condition. The resulting costs and effects were combined to calculate the ICER. If a trade-off needs to be made between costs and effects, a threshold is needed; that is, how much is society willing to pay for additional health? The societal willingness-to-pay (WTP) level was set at €30,000 per gained QALY, which roughly reflects an accepted WTP level in The Netherlands [31].

Furthermore, a cost-effectiveness acceptability curve (CEAC) was created. A CEAC indicates the probability that the intervention under evaluation will be cost-effective at different values of WTP for a QALY. By definition, a CEAC crosses the y-axis at the probability that the intervention is cost neutral: the WTP is then zero [32].

Sensitivity Analysis

The societal perspective adopted in this article is consistent with the methods guidelines for economic evaluations in The Netherlands. In many countries, however, the advised perspective is more restrictive, focusing on health care costs. To allow for international comparisons, we also presented an analysis considering health care costs only, and thus excluding productivity costs.

In addition, to get more insight into the development of cost-effectiveness over time, we plotted the ICER after each cycle. As described before, the effects of the training on training group 2 (the original wait-list control group) were combined with those on training group 1. One could argue that the new T0-T1 data may not represent the effect on which the randomized controlled trial was based (for instance, because the waiting time also had an effect). Therefore, we tested the accuracy of combining the data in a sensitivity analysis by using data only from training group 1, and plotted the ICER of training group 1. Furthermore, an analysis was done for a 10-year time horizon, to look beyond the 4-year time horizon.

Results

The mean 4-year costs and health outcomes are presented in Table 6. The table shows that the training group had lower mean costs than did the wait-list control group, suggesting that costs of training were offset with savings elsewhere. The training group had a higher number of mean QALYs than did the wait-list control group, suggesting better outcome for patients after the training. Thus, after 4 years, the training showed better effects against lower costs in comparison to the wait-list control, making it a dominant strategy.

The impact of parameters' uncertainty on the ICER is shown in Figure 2, in which results of 10,000 probabilistic simulations are plotted in a scatterplot. The scatterplot shows the differences in costs and QALYs per simulation per patient between the group training and the wait-list control. When ICERs are in the bottom right quarter of the scatterplot, the training is dominant, that is, cost saving with QALY improvement. When ICERs are in the top left quarter, the training costs more, and does not improve health. For the top right quarter, a trade-off should be made between costs and effects. Around 64% of the simulations ended up in the bottom right quarter, which means cost saving and QALY improvement. Approximately 86% of the simulations were below the threshold of €30,000 per gained QALY, which means that costs for improvement were within the borders that society is willing to pay for additional health (WTP). The increase in QALYs seemed to be modest, smaller than 0.18 over 4 years. Because almost all simulations ended up at the right side of the y-axis, however, improvement appeared with high certainty.

Figure 3 indicates the probability that the cognitive-behavioral group training will be cost-effective at different values of WTP for a QALY. The CEAC for the group training crossed the y-axis at the probability of 0.65, which means that the group training was cost saving (WTP = 0) in approximately 65% of the simulations. This

Table 3 – Costs per training.

Category	Cost (€)
Personnel	7,048
Overhead	2,502
Material	131
Housing	1,050
Training and retraining*	20
Recruitment	15
Travel	775
Total cost	11,541
Total cost per patient	1,924

* Average per training.

Table 4 – Health care–related and work-related costs per cycle.

Costs (€)	T1*		T2		T3		Average†,‡	
	PH (N = 133)	AH (N = 35)	PH (N = 78)	AH (N = 28)	PH (N = 72)	AH (N = 27)	PH (N = 283)	AH (N = 90)
Health care–related costs								
Medication costs	56	17	65	18	58	26	59	20
Other medical costs	1,181	677	1709	640	1827	571	1491	634
General practitioner	130	89	112	51	109	56	120 (4.13)	67 (2.31)
Therapist (Riagg)	256	296	258	206	144	43	228 (1.29)	192 (1.08)
Medical specialist	159	90	143	35	205	153	166 (2.23)	92 (1.23)
Paramedic	193	66	201	108	221	108	202 (5.42)	92 (2.46)
Hospitalization days	194	0	745	69	934	0	534 (1.02)	22 (0.04)
Work-related costs								
Absenteeism	343	18	184	104	341	–	298 (10.26)	40 (1.37)
Presenteeism	188	23	97	–	50	9	128 (9.26)	11 (8.10)
Substitution of domestic tasks	498	102	492	43	586	12	519 (35.23)	57 (4.19)
Total costs	2266	837	2547	805	2861	619	2495	762

AH, average health; PH, poor health.
* In the calculations, the T1 of training group 1, "new T1" of training group 2, and T1 of wait-list control group were used.
† For the model, the average values were used because differences between measurements were nonsignificant.
‡ Average volumes of service use and lost to work time is placed within parentheses.

indicated a high certainty that costs will reduce over time after the group training. If society is willing to pay €30,000/QALY, the chance that the group training will be a more cost-effective option than a wait-list control was 80%. Stated differently, if society is willing to pay €30,000/QALY, the chance that the wait-list control will be the most cost-effective option was only 20%.

Sensitivity analysis concerning adoption to the health care perspective resulted in higher incremental costs after 4 years (Table 6), resulting in a low positive ICER.

Figure 4 reflects the uncertainty of the ICERs over time, and also includes the ICERs when excluding the effect data of training group 2. After 18 months (six cycles), the cost of a gained QALY because of the group training was less than €30,000. After 30 months (10 cycles), the cost of a gained QALY because of the group training was zero. When using data only from training group 1, comparable results were found. When increasing the time horizon to a period of 10 years (not shown in figure), the group training was in terms of cost-effectiveness "dominant" compared with the wait-list control and there was a positive effect of 0.13 QALYs and a €3777 reduction in costs.

Discussion

Principal Findings

We estimated the cost-effectiveness of cognitive-behavioral group training for patients with UPS over a 4-year time horizon using a multivariable probabilistic model. After 4 years, the group training had a better effect on health-related quality of life and lower costs from a societal perspective than did the wait-list control. The group training was a dominant strategy: it was both more effective and cost saving compared with the wait-list control. After 30 months, the effect of the cognitive-behavioral group training was cost saving. If society is willing to pay €30,000 per gained QALY, then the group training was cost-effective after 18 months. This corresponds more or less with the end of the study period (15 months), which indicates that only a small amount of extrapolation of costs, effects, and transition data was needed in the group training before a reasonable cost-effectiveness was reached. Using a time horizon of 4 years and assuming no WTP for gained QALYs, the chance that the training will be cost-effective compared with the wait-list control was 65%.

Our Principal Findings in Relation to the Existing Literature

Our study is one of the few cost-effectiveness studies in patients with UPS, and the first to use a state-of-the-art health economic model and the preferred outcome in health economics: QALYs. To our knowledge, only two studies investigated the cost-effectiveness of treatment for patients with UPS using cost-effectiveness ratios [11]. Because these studies used a specific outcome "cost per unit reduction in Health Anxiety Inventory score" [12] and "cost per additional successfully treated patient"

Table 5 – Utilities.

Health state	Baseline	T1*	T2	T3	Average†
Poor health					
Mean (SE)	0.57 (0.007)	0.58 (0.007)	0.58 (0.011)	0.58 (0.012)	0.58 (0.004)
Average health					
Mean (SE)	0.69 (0.027)	0.71 (0.015)	0.74 (0.019)	0.73 (0.021)	0.72 (0.010)

SE, standard error.
* In the calculations, the "new T1" of training group 2 was also used.
† For the model, average values were used because differences between measurements were nonsignificant.

Table 6 – Deterministic discounted costs and health outcomes over 4 y.

Group	Costs (€)	QALYs	ICER (€)	Proportion in average health (%)*	From a health care perspective	
					Costs (€)	ICER (€)
Group training	32,929	2.35	Dominant	14.0	21.757	8.165/QALY
Wait-list control	33,757	2.29	–	10.8	21.278	–

ICER, incremental cost-effectiveness ratio.
* Percentage of participants in the average health state at 4 y.

[13], the cost-effectiveness of different treatments within UPS is difficult to compare.

Limitations

In the model, several assumptions were made, of which some might be considered as in favor of the cost-effectiveness of the group training, whereas others might be considered as conservative. First, where most common comparators used in economic evaluations are categorized as current standard of care or all relevant treatment alternatives, this economic evaluation is based on a randomized controlled trial comparing cognitive-behavioral group training with a wait-list control. For patients with UPS, several treatments are available in mental health centers. Patients, however, typically refuse to be referred to these mental health services [33,34]. For this reason, most patients with UPS have contacts only within the medical health services. Therefore, when looking at alternative treatments for this group of patients with UPS, it is believed that regular GP and other medical care services are the most relevant comparison because these patients were not (did not want to be) referred to regular mental health care services. Second, assuming "transition balance" in the wait-list control condition after the first cycle might be considered as enhancing cost-effectiveness because then "spontaneous improvement" was balanced with relapse. The idea of transition balance comes from the observation that the UPS of this patient group was chronic: the minimum duration of UPS was 6 months, and its median duration was 9 years. In addition, any favorable effect of the "transition balance assumption" was limited by the time horizon of 4 years and by the finding that a satisfying ICER was already reached after 18 months. Another possible alternative for estimating the relapse rate of the wait list after the first cycle was using the relapse rate found in the group training. This might result, however, in an overestimation of the relapse rate because the group training has a higher relapse in time due to the effectiveness in the first period. The latter strategy will provide a too optimistic perspective and is therefore not used.

Furthermore, merging training groups 1 and 2 might have a favorable effect on cost-effectiveness. We tested the effect of this merging in a sensitivity analysis, however, and did not find such a favorable effect.

Moreover, the assumption that none or only a limited amount of productivity losses occurred as a result of attending the training might be considered as enhancing cost-effectiveness. The assumption, however, was supported by the fact that most patients in our study group had only limited working obligations and they could attend the training after working hours.

A conservative assumption was the assumption that there were no differences in terms of mortality. Because the physical quality of life improved as a result of the training, the life expectancy might have been increased too.

Finally, the choice of a cutoff score of 40 on the PCS of the SF-36 might have had an effect on the results. From a clinical point of view, the use of change scores to define the health states might be more appropriate than the use of a cutoff score

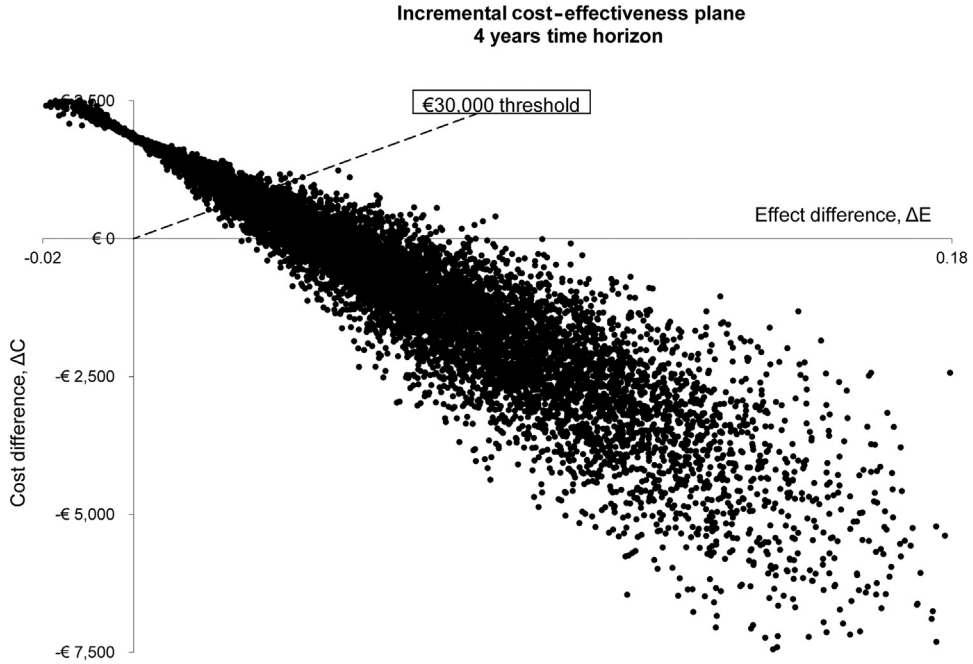

Fig. 2 – Incremental cost-effectiveness ratio scatte rplot.

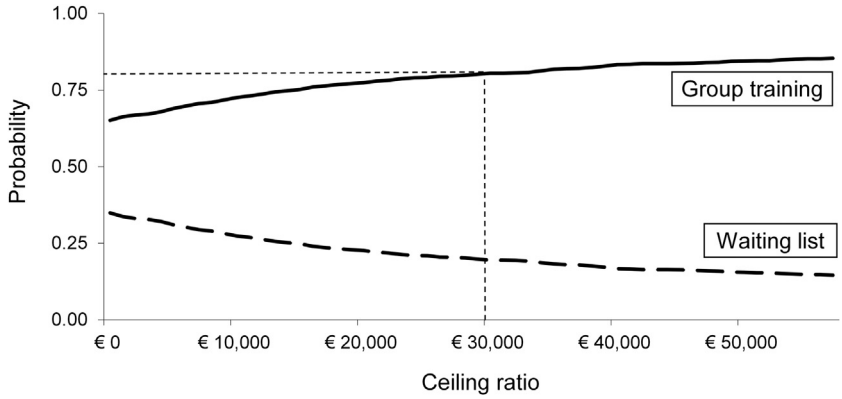

Fig. 3 – Cost-effectiveness acceptability curve.

because change scores would most likely show more transitions in health states than a cutoff score at a fixed quality-of-life level would do.

Theoretical Implications

The aim of the cognitive-behavioral group training is to improve health-related quality of life of patients with UPS. Because patients' quality of life is also negatively related to being older, being female, having a low level of education, living without a partner, having one or more comorbid medical conditions [35], and having one or more comorbid mental disorders [4,36] and given the fact that patients with UPS seem to run a high risk on these conditions [4,6,37–42], only a modest increase in quality of life should be expected. This modest ambition is often accompanied by the claim that treatment will reduce health care consumption [11], which would be beneficial for both patients, because it might avoid unnecessary medical interventions and perhaps even iatrogenesis, and society, because it might reduce health care costs. There is hardly any data to support this claim, but results of the present study indeed suggested that this hypothesis might be true: the increase in QALYs was modest, but the decrease in costs was substantial, which made the treatment cost saving and preferable over the wait-list control condition.

Clinical and Policy Implication

The clinical and policy implication of this study is that the favorable results of the cost-effectiveness analysis are an additional and strong argument to implement and reimburse cognitive-behavioral therapy for patients with UPS. Such an implementation will give patients the opportunity to increase their quality of life and support health care services to provide the appropriate and most cost-effective treatment for this patient group. The results are also useful for the payers of health care services because the results show strong evidence of cost saving after treatment.

Further Research

It is tempting to advice that further research should be a randomized controlled trial with a longer follow-up in the control wait-list control condition. In that way, we could test the assumption of transition balance between health states in the wait-list control condition. Given that we have already established the effectiveness of this treatment, it will be unlikely that such a design will be approved by any medical ethical research committee. Instead, it might be more realistic to advise to conduct a cost-effectiveness study in which different therapies for patients with UPS are compared head-to-head. Another

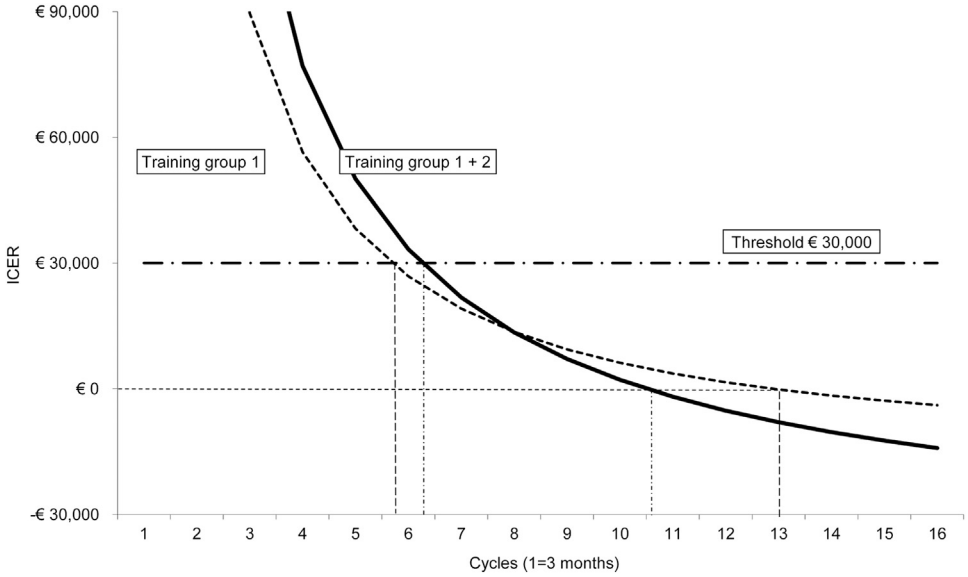

Fig. 4 – Incremental cost-effectiveness ratio (ICER) over time.

advisable investigation might be "implementation research" because it is likely that treatment compliance of both patients and health care providers will influence the cost-effectiveness of the treatment [42].

Conclusions

Our study is one of the few cost-effectiveness studies in patients with UPS, and the first to use a state-of-the-art health economic model and the preferred outcome in health economics: QALYs. We showed that the cognitive-behavioral group training is a cost-effective treatment in patients with UPS compared with a wait-list control condition.

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