Coupé, V.M.H., Veenhof, C., Tulder, M.W. van, Dekker, J. Bijlsma, J.W.J., Ende, C.H.M. van den
The cost-effectiveness of a behavioral graded activity in patients with osteoarthritis of hip and/or knee.
Annals of the Rheumatic Diseases: 66, 2006, nr. 2, p.215-221

Postprint Version	1.0
Journal website	http://ard.bmj.com/
Pubmed link	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=16880195&dopt=Abstract
DOI	10.1136/ard.2006.054478

The cost-effectiveness of behavioural graded activity in patients with osteoarthritis of hip and/or knee.

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ABSTRACT

Objectives: To evaluate whether exercise therapy based on behavioural graded activity comprising booster sessions is a cost-effective treatment for patients with osteoarthritis of the hip and/or knee compared to usual care.

Methods: An economic evaluation from a societal perspective was carried out alongside a randomised trial involving 200 patients with osteoarthritis of the hip and/or knee. Outcome measures were pain, physical functioning, self perceived change, and quality of life, assessed at baseline, 13, 39 and 65 weeks. Costs were measured using cost diaries for the entire follow-up period of 65 weeks. Cost and effect differences were estimated using multilevel analysis. Uncertainty around the cost-effectiveness ratios was estimated by bootstrapping and graphically represented on cost-effectiveness planes.

Results: 97 patients received behavioural graded activity and 103 usual care. At 65 weeks, no differences between the two groups in improvement with respect to baseline were found on any of the outcome measures. The mean (95% CI) difference in total costs between the groups was -€773 (-€2360 ; €772), that is, behavioural graded activity resulted in less costs but this difference was non-significant. Since effect differences were small, a large incremental cost-effectiveness ratio of € 51385 per QALY was found for graded activity versus usual care.

Conclusions: This study provides no evidence that behavioural graded activity is either more effective or less costly than usual care. Yielding similar results to usual care, behavioural graded activity seems an acceptable method to treat patients with osteoarthritis of the hip and/or knee.

INTRODUCTION

Osteoarthritits of the hip and/or knee is a common joint disorder. The incidence in general practices in the Netherlands is 2.1/1000 per year for osteoarthritis of the hip and 3.6/1000 for the knee.[1] Treatment is directed at pain relief and prevention of disability. A systematic review of several randomised trials showed that exercise therapy for irrecoverable chronic diseases such as osteoarthritis has a short term positive effect on pain and daily functioning.[2] However, this effect seems to decline over time and finally disappear, resulting in a recurring need for treatment, increased disability, work absenteeism and health care utilization.[2, 3] Maintaining the short-term benefits of exercise therapy is therefore important.

The current study is a cluster randomised controlled trial that investigates whether behavioural graded activity, that is a behavioural treatment integrating the concepts of operant conditioning with exercise therapy comprising booster sessions, consolidates the positive short term effects of usual exercise therapy. The clinical paper shows a positive long term effect of behavioural graded activity.[4] Contrary to previous findings, however, this positive effect is also found for usual exercise therapy, leading to insignificant effect differences between the treatment groups.

As osteoarthritis may lead to considerable costs, it is important that the clinical evaluation of a new treatment programme is accompanied by an economic evaluation. In this paper, we present a cost-effectiveness analysis of the behavioural graded activity programme in comparison to usual exercise therapy.

METHODS

Study design

An economic evaluation was conducted alongside a cluster randomised controlled trial comparing behavioural graded activity and usual care according to the Dutch Osteoarthritis guideline of the Royal Dutch College for Physiotherapy (KNGF). Effectiveness and cost-effectiveness over 65 weeks were investigated. The study was approved by the Medical Ethical Committee of the VU University Medical Center, Amsterdam, The Netherlands.

Study population

Eighty-seven physiotherapists, willing and able to participate in the study, were recruited. Participating physiotherapeutic practices were randomly assigned to one of the two treatment programmes. Because recruitment of patients through participating physiotherapists was slow, a second recruitment strategy was used, i.e. patients responded to articles in local newspapers about the benefit of exercise therapy and the performed study. Thus recruited patients were referred to a participating physiotherapist. An description of the recruitment strategies and the influence on the study population is published elsewhere.[5] Patients were included if they fulfilled the clinical criteria for osteoarthritis of the hip or knee of the American College of Rheumatology.[6, 7] All patients willing and eligible to participate gave their informed consent. In total, 200 patients were included. For more details on the trial, we refer to the clinical paper.[4]

Interventions

The behavioural graded activity group received a treatment integrating the concepts of operant conditioning with exercise therapy comprising booster sessions. Graded activity was directed at increasing the level of activities in a time-contingent way, with the goal to integrate these activities in the daily living of patients.[8, 9, 4] Treatment consisted of a 12- week period with a maximum of 18 sessions, followed by five pre-set booster moments with a maximum of seven sessions (in week 18, 25, 34, 42, and 55, respectively).

The usual care group received treatment according to the Dutch physiotherapy guideline for patients with OA of hip and/or knee.[10] This guideline consists of general recommendations, emphasizing provision of information and advice, exercise therapy, and encouragement of a positive coping with the complaints. Treatment consisted of a 12-week period with a maximum of 18 sessions and could be discontinued within this 12-week period if, according to the physiotherapist, all treatment goals had been achieved.

Clinical outcome measures

Patients completed health questionnaires at baseline, 13, 39 and 65 weeks. Primary outcome measures were pain (VAS and WOMAC), physical function (WOMAC) and self perceived change (Patient Global Assessment) according to the core set of outcome measures of clinical trials with patients with osteoarthritis defined by OMERACT III.[11, 12, 13] For the cost-effectiveness analysis also health related quality of life (EuroQol-5D) was measured. [14]

Assessment of resource utilization

Patients provided data on the direct costs of osteoarthritis within and outside the health care sector and on the indirect costs of productivity loss. To this end, patients recorded resource utilization per week in cost diaries, covering the periods 1-12, 13-24, 25-36, 37-38, 39-50, 51- 62, 63-65 weeks. Important resources used within the health care sector were physiotherapeutic treatment and osteoarthritis related hospitalisation. Resource utilization outside the health care sector included alternative therapies and informal care by friends or family members. Indirect costs of productivity loss were estimated by measuring absenteeism from paid and unpaid work.

Valuation of health care consumption; unit costs

The economic evaluation was conducted from a societal perspective. As the study was carried out between 2002 and 2004, 2003 prices were used. Because of the short follow-up period, no discounting was applied. Standard prices were used to value most resources considered (Table 1).[15, 16] Prices of medication were obtained from the Royal Dutch Society for Pharmacy.[17] Absenteeism from paid work was valued with the friction cost method, i.e only absenteeism during a friction period needed to replace a person is taken into account.[18] Production loss was valued using mean age- and sex-specific incomes of the Dutch population.[15] Using the shadow price method, unpaid work was valued at the cost of the professional required if the unpaid workers were unavailable.[19, 15]. The shadow price of voluntary work and informal care was assumed to be equal to the tariff for cleaning work.

[TABLE 1]

Statistical analysis

Statistical analyses were carried out on an intention-to-treat principle. We imputed missing data for patients with an incomplete set of cost diaries using the Expectation Maximization (EM) Algorithm in SPSS 12.0.1.[20] This is an iterative optimisation method to estimate missing data given available data.

Patients treated by the same physiotherapist formed clusters within the trial. Such clustered data requires multilevel analysis, which we performed using MlwiN.[21, 22] The resulting cost and effect differences between treatment groups are corrected for dependence between patients treated by the same physiotherapist.

As cost data is typically skewed, confidence intervals for cost differences cannot be estimated with conventional methods that assume normality. We therefore applied the non-parametric bootstrap, i.e. 1000 samples of the same size as the original dataset were sampled with replacement from the data.[23, 24, 25] These resamples were used to estimate confidence intervals.

For the cost-effectiveness analysis, the difference in total cost between the two treatment groups was compared to the difference at 65 weeks in improvement in VAS and WOMAC scores, in percentage improved according to Patient Global Assessment, and in percentage responders obtained form applying the OMERACT-OARSI response criteria to the outcome measures of this trial.[26] The ratings of Patient Global Assessment were assessed by patients on an 8-point scale (1=vastly worsened; 8=completely recovered) and dichotomised as improved (“completely recovered” to “much improved”) versus not improved (“slightly improved” to “vastly worsened”). To compare the difference in total cost with the difference in quality of life years gained over 65 weeks, the scores on the EuroQol-5D were translated into a utility using preferences of the UK general population.[27] The utilities of patients at baseline, 13, 39 and 65 weeks were used as weights for the periods 0-13, 13-39, and 39-65 weeks in the trial, giving the total Quality Adjusted Life Years (QALYs).[28, 29]

Uncertainty around the cost-effectiveness ratios was estimated using the bias corrected and accelerated bootstrapping method (5000 replications) and presented in a cost-effectiveness plane. [24, 30]

Sensitivity analyses were carried out to study the effect of different imputation strategies. Firstly, we imputed zero costs if data were missing for the last half of the follow-up period. Secondly, we imputed mean costs for missing data. Also, a complete case analysis was carried out, considering only the patients who completed all cost diaries. To investigate the effect of outliers, we performed an analysis in which 5% of patients with total costs more than €11000 were excluded. The threshold of €11000 was chosen after inspection of the data of patients with extremely high costs of absenteeism from either paid or unpaid work.

Both for the complete cases as for the dataset completed by EM imputation, per-protocol analyses were performed, in which all patients with deviations from the treatment protocol were excluded. Deviations were defined as less than 6 sessions physiotherapy within the first 12 weeks (both groups), or less than 2 booster sessions (graded activity group) after the first 12 weeks, or a total hip / knee replacement during the whole study period (both groups).

RESULTS

Clinical outcomes

At baseline, no differences in clinical characteristics and in paid/unpaid work were found between the behavioural graded activity and the usual care group. Both groups showed beneficial effects in the long term. However, no differences in improvement between the two groups were found on any of the outcome measures (Table 4b). Full details on the clinical outcomes are presented in the clinical paper. [4]

[TABLE 4B]

Resource use

Ten patients never returned any cost diary and were excluded from the evaluation. These patients did not differ from the remaining 190 patients with respect to baseline characteristics and effect of treatment on primary outcome measures, The 190 remaining patients returned 84% of the cost diaries. Only 64% of the patients completed all diaries. For these patients, Table 2 lists the utilization of health care resources and absenteeism from paid and unpaid work. Note that the remainder of the paper focuses on the EM imputed data.

[TABLE 2]

Behavioural graded activity was associated with less medical-specialist care, hospitalisation, hip replacements, and absenteeism from paid work compared to usual care, but with more informal care and help in housekeeping. The differences were small and not statistically significant. One interesting detail in Table 2 is the small number of patients with work absenteeism in the behavioural graded activity group.

Costs

Table 3 shows the mean (standard deviation) costs for the two groups. Compared to the usual care group, we observed lower direct health care costs and higher costs outside the health care sector in the behavioural graded activity group. Total direct costs were similar. From the direct health care costs, a substantial part was attributable to hospitalisation. In the usual care group these costs doubled those in the graded activity group, but this difference was not significant. Indirect costs in the graded activity group were approximately half those in the usual care group. This difference, caused by differences in work absenteeism, was not significant. The difference in total costs was -€773 (95% CI: -€2360 to €772), €2530 (SD €4888) for behavioural graded activity and €3341 (SD €5055) for usual care. This difference was not significant.

[TABLE 3]

Cost-effectiveness

Table 4a shows the total costs and effects at 65 weeks for the different outcome measures. Table 4b shows the differences in total costs and effects, the incremental cost-effectiveness ratios, and their 95% confidence intervals.

[TABLE 4A]

Considering the scale of the outcome measures, the effect differences were close to zero. Therefore, large cost-effectiveness ratios with large confidence intervals were found. The incremental cost-effectiveness ratio for quality of life years gained was €51385 per QALY. The difference in QALY over 65 weeks being negative, this incremental cost-effectiveness ratio means that implementing graded behavioural activity yields €51385 per QALY that is lost by not giving usual care. Figure 1a shows the cost-effectiveness plane for QALYs gained. Ninety-two percent of the cost-effect pairs lie below the x-axis, the area where behavioural graded activity is associated with lower costs.

[FIGURE 1A]

The cost-effectiveness ratio for responders according to the OMERACT-OARSI criteria was -€11886 per responder, meaning that implementing behavioural graded acticity yields €11886 per additional treatment responder due to behavioural graded activity. Figure 1b shows the corresponding cost-effectiveness plane. For ninety percent of the cost-effect pairs, the costs of behavioural graded activity are lower.

[FIGURE 1B]

Sensitivity analysis

Uncorrected cost differences were similar to cost differences corrected for clustering of patient data.. The uncorrected difference in total costs was –€811 (95% CI: -€2106 to €946). When excluding from the analysis eleven patients with total costs exceeding €11000, we found a difference in total cost of -€740 (95% CI: -€1447 to €72). Considering only patients with complete follow-up resulted in a difference in total costs of -€1096 (95% CI: -€3105 to € 819). When zero costs were imputed for missing cost diaries in the last half of the follow-up period, the difference in total costs was -€889 (95% CI: -€2601 to €857). Imputation of mean costs for missing cost diaries resulted in a difference of -€627 (95% CI: (-€1846 to €824).

Per-protocol analysis

Twenty patients from the graded activity group and ten from the usual care group were excluded from the per-protocol analysis. Mean difference in total costs between the groups was -€987 (95% CI: -€2777 to €786). For patient with complete follow-up on cost data, this difference was -€1057 (95% CI: -€3308 to €834) (n=45/60).

DISCUSSION

Differences in direct and indirect costs between the behavioural graded activity and usual care group were not statistically significant. However, with the exception of direct costs outside the health care sector, costs in the behavioural graded activity group were consistently lower than in the usual care group. This was particularly true for the indirect costs of absenteeism. This cannot be explained by a difference in the number of patients with paid work at baseline in both groups (28% versus 29%), nor by the higher hospitalisation rate in the usual care group (i.e. no significant relation between hospitalisation and work absenteeism was found). Possibly, the behavioural component of the graded activity program leads to less avoidance behaviour, so that patients are less inclined to refrain from working.

In the usual care group, a higher hospitalisation rate was observed. This cannot be explained by baseline differences between the groups. Although this rises the question whether behavioural graded activity reduces the need for surgery, we feel that the observed difference is most likely due to chance. Interestingly, both groups are associated with similar costs for allied health care. Apparently, the graded activity protocol, prescribing more treatment sessions than the usual care program, did not result in more treatment sessions.

Total costs were lower in the behavioural graded activity group. However, the difference in total costs (-€773) was surrounded by large confidence bounds (-€2360 to €772) and may thus be coincidental. The effect differences between the two treatment groups on any of the outcome measures were extremely small and the sign of these differences seem of no importance. As such, it is hard to interpret the cost-effectiveness ratios and it seems more reasonable to base conclusions on cost differences rather than on cost-effectiveness.

The results of this cost-effectiveness study are possibly confounded by the two different strategies that were used to recruit patients. In Veenhof et al. (2005), it was concluded that the different strategies lead to different baseline characteristics, but that the treatment effect after adjustment for these characteristics was similar for all outcome measures. In addition, in Veenhof et al. (2006), it was shown that baseline characteristics in both treatment groups were similar and that the difference in treatment effect did not change after adjusting for baseline characteristics. As such, we conclude that it is unlikely that our cost-effectiveness results are confounded by having used two different recruitment strategies.

Earlier publications on the cost-effectiveness of different types of exercise therapy for osteoarthritis of the hip and/or knee are not available. In a study by Van Baar et al., exercise therapy in combination with advice and medication was compared to advice and medication only.[3] As this study focuses on other treatment modules than our study, it is hard to compare the results.

In conclusion, this study provides no evidence that behavioural graded activity for patients with osteoarthritis of the hip and/or knee is either more effective or less costly than usual care. Yielding similar results, behavioural graded activity seems an acceptable method to treat patients with osteoarthritis of the hip and/or knee.

ACKNOWLEDGEMENTS

The authors thank the physiotherapists and patients for participating in this study. The study was supported by a grant from the Dutch Health Care Insurance Board.

TABLES AND FIGURES

Table 1. Costs per unit health care resource used in the economic evaluation of behavioural graded activity (year 2003)

Healthcare resource [Unit]	Cost per unit (€)
General practice consultation	
General practitioner [visit]	20.20
Physiotherapist [Session]	22.75
Manual therapist [Session]	31.46
Outpatient attendance	
Policlinic care [visit]	56.00
Specialist care [visit]	98.00
Diagnostic procedures	
X-ray	39.00
MRI	255.29
CT-scan	98.00
Hospital inpatient stay	
Hospital admission [day]	337.00
Replacement knee	1962.42
Replacement hip	2061.68
Other	
Absenteeism paid labour [hour]	34.98*
Absenteeism unpaid labour [hour]	8.30[†]
Professional home care [hour]	21.70
Informal care [hour]	8.30[†]

* *Average cost per hour according to the friction cost method. In the analysis gender and age dependent costs are used.*
[†] *Shadow price, being equal to the hour price for cleaning work.*

Table 4a. Mean costs (€) and effects by treatment group for all patients (missing data imputed).

	Behavioural graded activity		Usual care	
Effect measure	*Costs*	*Effects*	*Costs*	*Effects*
QALYs (EuroQol) (n=87/92)	2375	0.71	3440	0.73
WOMAC pain (scale 0-20)(n=83/91)	2418	3.67*	3400	3.14*
WOMAC physical (scale 0-68) (n=77/89)	2284	7.03*	3169	7.29*
VAS pain now (scale 0-10) (n=84/91)	2410	0.85*	3400	0.57*
VAS pain past week (scale 0-10) (n=84/89)	2410	1.92*	3458	1.79*
PGA (% improved) (n=83/87) **	2435	54	3483	48
Responders OARSI criteria (%) (n=90/100)	2530	46	3341	42

* A positive sign indicates improvement compared to baseline.
** Patient Global Assessment

Table 4b. Mean cost (€) and effect differences between treatment groups and cost-effectiveness ratios for all patients (missing data imputed).

	Behavioural graded activity – Usual care		
Effect measure	*Cost difference**	*Effect difference**	*ICER † + 95% CI*
QALYs (EuroQol) (n=87/92)	-1028	-0.02	51385 (-104674;1663872)
WOMAC pain (scale 0-20)(n=83/91)	-942	0.60	-1575 (-103391;3854)
WOMAC physical (scale 0-68) (n=77/89)	-813	-0.17	4701 (484;299159
VAS pain now (scale 0-10) (n=84/91)	-952	0.27	-3476 (-652950;869)
VAS pain past week (scale 0-10) (n=84/89)	-1016	0.13	-7699 (-8101771;-1865)
PGA (% improved) (n=83/87) **	-1005	6.5	-15462 (-4732743;9039)‡
Responders OARSI criteria (%) (n=90/100)	-773	6.5	-11886 (-1484690;697)‡

* Cost and effect difference corrected for clustering within the factor physiotherapist
** Patient Global Assessment
† Incremental Cost-Effectiveness Ratio
‡ Incremental cost per patient improved/responder.

Table 2. Reported mean (SD) healthcare utilisation for patients with complete cost data over 65 weeks by treatment group. The last column (N) indicates the number of patients with resource utilisation.

	Behavioural graded activity (n=56)			**Usual care** (n=66)		
	mean	*(SD)*	*N*	*mean*	*(SD)*	*N*
HEALTH CARE SECTOR						
General practice consultation						
General practitioner [visits]	1.4	(2.2)	*27*	1.5	(2.7)	*35*
Physiotherapist [sessions]	18.0	(16.7)	*53*	20.2	(14.6)	*66*
Other allied health care [sessions]	0.5	(1.8)	*12*	0.2	(1.1)	*10*
Outpatient attendance						
Policlinic care [visits]	0.2	(1.6)	*2*	0.2	(0.9)	*4*
Specialist care [visits]	0.6	(1.6)	*12*	1.4	(2.6)	*28*
Diagnostic procedures						
X-ray [number]	0.6	(1.3)	*22*	0.9	(1.4)	*33*
MRI [number]	0.1	(0.3)	*4*	0.1	(0.4)	*6*
Other [number]	0.1	(0.4)	*5*	0.2	(0.6)	*11*
Hospital inpatient stay						
Hospital admissions [days]	0.1	(0.9)	*2*	1.1	(3.0)	*12*
Replacement knee [number]	0.02	(0.1)	*1*	----	----	*0*
Replacement hip [number]	----	----	*0*	0.2	(0.4)	*9*
OUTSIDE HEALTH CARE SECTOR						
Complementary or alternative therapist [sessions]	0.5	(3.0)	*4*	0.3	(1.6)	*4*
Absenteeism paid labour [hours]	2.6	(17.4)	*3*	5.4	(19.9)	*11*
Absenteeism unpaid labour [hours]	59.1	(156.1)	*15*	49.5	(112.0)	*32*
Informal care [hours]	32.7	(79.0)	*13*	18.9	(45.7)	*20*
Housekeeper [hours]	19.4	(57.3)	*10*	15.2	(60.3)	*10*

Table 3. Mean (SD) costs (€) over 65 weeks by treatment group for all patients (missing data imputed).

	Behavioural graded activity * (n=90)		**Usual care*** (n=100)		**Difference** (95% CI) †
	mean	*(SD)*	*mean*	*(SD)*	
HEALTH CARE SECTOR					
Primary care costs	462	(354)	519	(327)	-57 (-142 ; 35)
General practitioner	28	(41)	33	(50)	-5 (-18 ; 9)
Allied health care	433	(341)	486	(318)	-53 (-144; 36)
Secondary care costs	463	(1095)	813	(1761)	- 350 (-742; 83)
Policlinic care	13	(144)	8	(41)	5 (-13; 24)
Specialist care	71	(82)	127	(244)	-55 (-114 ; 3)
Diagnostic procedures	73	(138)	76	(141)	-3 (-36; 31)
Hospitalisation	306	(999)	603	(1522)	-297 (-666 ; 74)
Medication costs	41	(92)	57	(128)	-16 (-50 ; 18)
Professional home care costs	67	(314)	178	(650)	-110 (-254 ; 34)
Direct health care costs	**1033**	**(1334)**	**1567**	**(2160)**	**-534 (-2261 ; 672)**
OUTSIDE HEALTH CARE SECTOR					
Complementary or alternative therapy	48	(174)	30	(136)	18 (-27 ; 63)
Informal care	212	(542)	135	(318)	77 (-51 ; 200)
Housekeeper	524	(1416)	290	(1133)	230 (-130 ; 598)
Direct costs outside health care sector	**783**	**(1641)**	**455**	**(1282)**	**330 (-80 ; 723)**
Total direct costs	**1816**	**(2628)**	**2022**	**(2671)**	**-205 (-958 ; 516)**
Absenteeism paid labour	462	(2991)	1041	(3705)	-578 (-1596 ; 334)
Absenteeism unpaid labour	251	(873)	278	(734)	-15 (-442 ; 447)
Indirect costs	**714**	**(3208)**	**1319**	**(4888)**	**-600 (-1763 ; 493)**
Total costs	**2530**	**(4888)**	**3341**	**(5055)**	**-773 (-2360 ; 772)**

* Raw estimates
† Difference corrected for clustering within the factor physiotherapist with 95 % confidence intervals obtained from a non-parametric bootstrap with 1000 replications.

FIGURE LEGENDS

Figure 1a: Cost-effectiveness plane for qaly's gained at 65 weeks for behavioral graded activity versus usual care.

Figure 1b: Cost-effectiveness plane for the difference, at 65 weeks, in the proportion responders according to the OMERACT-OARSI response criteria, for behavioral graded activity versus usual care.

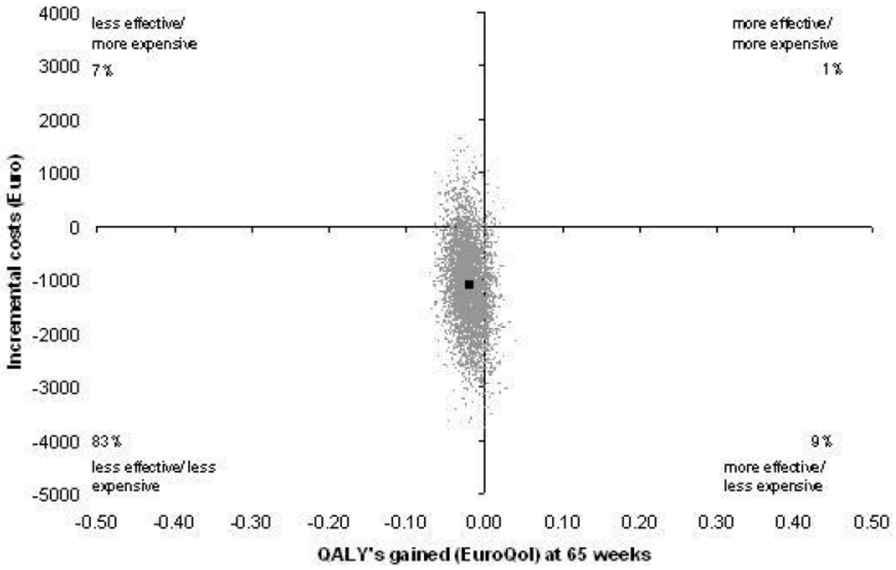

Figure 1a

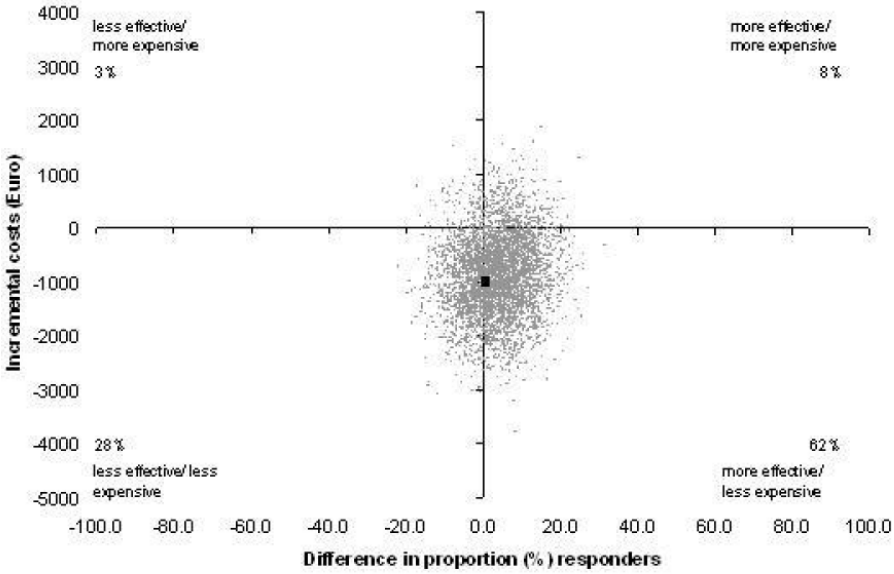

Figure 1b

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