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Research report

Cost-effectiveness of transcranial magnetic stimulation vs. electroconvulsive therapy for severe depression: A multi-centre randomised controlled trial

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Abstract

Background: Electroconvulsive therapy (ECT) has a long history of use in treating depression. Repetitive transcranial magnetic stimulation (rTMS) has been introduced more recently to the treatment spectrum. Its cost-effectiveness has not been explored.
Method: Forty-six right-handed people with severe depressive episodes referred for ECT were randomised to receive either ECT twice weekly or rTMS on consecutive weekdays. Health and other service use were recorded for retrospective periods of 3 months prior to initiation of treatment and during the 6 months following the end of allocated treatment. Costs were calculated for the treatment period and the subsequent 6 months, and comparisons made between groups after adjustment for any baseline differences. Cost-effectiveness analysis was conducted with incremental change on the 17-item Hamilton Rating Scale for Depression (HRSD) as the primary outcome measure, and quality-adjusted life years (based on SF6D-generated utility scores with societal weights) as secondary outcome, cost-effectiveness acceptability curves plotted.
Results: Based on the HRSD scores and other outcome measures, rTMS was not as effective as ECT. The cost of a single session of rTMS was lower than the cost of a session of ECT, but overall there were no treatment cost differences. In the treatment and 6-month follow-up periods combined, health and other service costs were not significantly different between the two groups. Informal care costs were higher for the rTMS group. Total treatment, service and informal care costs were also higher for the rTMS group. The cost-effectiveness acceptability curves indicated a very small probability that decision-makers would view rTMS as more cost-effective than ECT.

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Limitations: Small sample size, some sample attrition and a relatively short follow-up period of 6 months for a chronic illness. Productivity losses could not be calculated.
Conclusions: ECT is more cost-effective than rTMS in the treatment of severe depression.

Keywords: Cost-effectiveness; Quality of life; Depression; Electroconvulsive therapy; Repetitive transcranial magnetic stimulation

1. Introduction

Patients with severe depression who do not respond to treatment with antidepressant medication or psychological therapies may be offered treatment with electroconvulsive therapy (ECT). The use of ECT remains controversial because of the need to anaesthetise the patient, the induction of a seizure and risk of cognitive side-effects (UK ECT Review Group, 2003; Rose et al., 2003). Recently, repetitive transcranial magnetic stimulation (rTMS) – which does not need anaesthesia, is non-convulsive and has no apparent cognitive side-effects – has been introduced to the range of available treatments (George et al., 1999).

Although there have been studies of the comparative effectiveness of ECT and rTMS (e.g. Grunhaus et al., 2003), there have been no economic evaluations based on prospective designs. A modelling study suggested that rTMS would cost less than ECT and that effectiveness would be equivalent (Kozel et al., 2004), but the model was built more on assumptions than observational data. Based on a pragmatic randomised controlled trial, the present study sought to examine whether rTMS represents a more cost-effective intervention than ECT for people with severe depression.

2. Method

2.1. Design

2.1.1. Research settings

The study involved inpatients and outpatients from the South London and Maudsley NHS Trust and Pembury Hospital in the Invicta Community Care Trust, Kent, UK (Eranti et al., 2007). Ethical approval was obtained from both Trusts and written informed consent was obtained from the patients following a complete description of the study.

2.1.2. Selection of participants

All right-handed patients referred for ECT with a severe depressive episode (unipolar or bipolar) between January 2002 and August 2004 were considered eligible. Exclusion criteria were: aged under 18 years; evidence of dementia; history of substance misuse in the previous 6 months; diagnosis of schizophrenia or other functional psychosis; history of epilepsy or recent CVA/MI/cardiac failure; any condition rendering the patient medically unfit to receive a general anaesthetic; raised intracranial pressure; electronic and metallic implants or foreign bodies; inability to provide informed consent.

2.1.3. Randomisation

An independent third party performed randomisation following baseline assessment. Randomisation software was used to aid concealment. Patients who consented to participate in the study were randomly allocated to ECT or rTMS, stratified by Trust, and the treatment allocation passed on to the trial coordinator who assigned patients to their groups and updated the relevant clinical team. Patients were not blind to treatment allocation.

2.2. Intervention

Treatments were as previously described (Eranti et al., 2007) and had different staffing level requirements. Briefly, ECT was administered twice weekly for up to 5 weeks by a senior psychiatrist and according to the Royal College of Psychiatrists' guidelines. The number of treatments depended upon response as determined by each patient's referring psychiatrist. In contrast, rTMS was given once daily on consecutive weekdays for up to 15 sessions, starting on a Monday.

ECT was administered using a Thymatron DGx device (Somatics, Lake Bluff, Ill, USA) in the South London and Maudsley Trust sites and a Mecta SR2 device (Mecta Corp., Lake Osewego, Ore., USA) was used at the Pembury site. Methohexitone (0.75–1.0 mg/kg) was used as an anaesthetic and suxamethonium (0.5–1.0 mg/kg) as muscle relaxant. To ensure that the patient was given the minimum effective stimulus, seizure thresholds (ST) were established in the first ECT session using a method of limits (Sackheim et al., 1993). After this, patients were treated with 2.5 × seizure threshold for bilateral ECT and 2.5 × seizure threshold for unilateral ECT; if necessary, the charge dose was titrated upwards following standard stimulus dosing protocols (Royal College of Psychiatrists, 1995). For both in- and

outpatients, a ward nurse would accompany patients from the ward to the treatment suite, remain with them during treatment and recovery and then escort them back to their ward. Anaesthesia was administered by a consultant anaesthetist and an operating departmental assistant (ODA). An ECT nurse coordinator was also present during treatment.

Research physicians trained in rTMS techniques administered rTMS to the left dorsolateral prefrontal cortex as previously described (Eranti et al., 2007). A Magstim Super Rapid stimulator (Magstim Co., Whitland, UK) was used at all treatments sites. In addition to actual treatment the first session also required determination of the motor threshold of the abductor pollicis brevis (APB) site in the left motor cortex. Treatments were then administered at a stimulus intensity of 110% of the motor threshold and involved 20 trains at 10 Hz for 5 s with 55-second inter-train intervals. A full course of 15 sessions of rTMS thus entailed a total of 15,000 magnetic pulses. Inpatients were accompanied by a ward nurse during treatment sessions whereas outpatients had no nursing escort but attended with a friend or relative.

2.3. Effectiveness measures

For the purposes of the evaluation the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) was identified prior to the recruitment of any patients as the primary measure of effectiveness. Quality-adjusted life years (QALYs) were used as a secondary measure of effectiveness, estimated by combining the time each patient spends in each health state with the estimated utility value of that health states. These utility values were derived using data generated by the SF-36, revised into a six-dimensional health state classification (the SF-6D) and societal weights attached (Brazier et al., 2002). All ratings were performed by researchers blind to treatment allocation. Data on measures of effectiveness were collected before randomisation, at the end of treatment (2–3 days after final session) and at 6-month follow-up.

2.4. Service utilisation measure

The Client Service Recipient Inventory (CSRI; Beecham and Knapp, 1992) was adapted for the study to collect data on service utilisation and other dimensions relevant to the measurement of costs (Beecham and Knapp, 2000). The CSRI collects information about each patient's background, accommodation, health care and other services used, and (in some adaptations) informal care provided by family and others. Through a patient interview, data on service use and informal care support were collected at baseline for the 3-month period prior to entering the study and at follow-up interviews for the 6 months following the completion of the allocated treatment course. The CSRI provides a standardised way of recording service use that is commensurate with accurate cost estimation. During the treatment period (on average 3 weeks) we collected information on place of accommodation (inpatient/outpatient) and frequency of treatment (ECT or rTMS). Other service use and informal care support during this short period was interpolated from baseline and follow-up data, distinguishing inpatient and outpatients in the interpolations.

2.5. Unit costs of services

For each service used we sought the best approximation to long-run marginal opportunity cost. For most services nationally applicable unit costs at 2003/04 prices were employed (the period during which most patients were treated), taken from the annual PSSRU compendium (Curtis and Netten, 2004). National Health Service reference costs (Department of Health, 2004) were used to estimate the cost of inpatient and outpatient attendances. Details of the unit costs used are shown in Appendix A.

2.6. Costing ECT and rTMS

The unit costs of ECT and rTMS treatment administration were estimated using local data on capital costs (including the treatment suite and machines used during treatment) and cost of professionals' time related to treatment.

Data on contacts with all professionals and resources used in administering the treatment were used to estimate these unit costs after combination with data collected on capital (such as the treatment suite, machinery used in treatment and maintenance costs associated with the machinery). For the estimation of costs associated with the treatment suite, the size of the suite was obtained from floor plans and valued using estimates of a new-build NHS treatment room. This amount was annuitised at a rate of 3.5% over 60 years. The costs of machinery used in treatment were obtained from suppliers, and the market value of the equipment annuitised at 3.5% over 10 years plus any associated maintenance costs. The annual costs of the treatment suite and machinery were then divided by the number of administrations of treatments for the year (there were 362 for ECT and 348 for rTMS; data obtained from ECT administrator at the Trust).

To measure staff time we recorded: the profession and grade of the staff involved in the treatment; the duration of time spent in treatment; the percentage of time spent in face-to-face contact and percentage of time spent on administrative tasks (that is patient-specific activities that did not involve contact with the patient) associated with treatment. Staff included the physician administering the treatment, anaesthetist, nurse coordinator, operating departmental assistant and ward nurse. The amount of professional time varied between patients; mean time consumptions are shown in Table 1. Included in the valuation of time associated with treatment administration of professionals were salaries and salary on-costs, direct overheads (such as travel, stationery and clerical support), indirect overheads (such as finance, maintenance and electricity) and capital overheads (such as physical land and premises).

These calculations produced the following figures. ECT costs the NHS £211 per treatment administration, and rTMS between £106 per treatment administration for outpatients and £115 per treatment administration for inpatients. We used the lower cost for rTMS throughout the analyses, although using the higher figure would not change the findings. These amounts cover capital and professional time. For ECT the average number of treatments was six, which means a course of ECT will usually cost the NHS on average £1308. Actual treatment costs ranged from £422 to £2110. Patients using rTMS received on average fourteen sessions, at an average cost per course of treatment of £1444 (with a range of costs from £530 to £1590). Though the unit cost per treatment session is lower for rTMS the cost of a course of treatment is higher compared to ECT because of the number of treatment sessions required.

Table 1
Resources and cost associated with ECT and rTMS treatment

Resource use	ECT	rTMS
Average time spent in treatment	60 min	25–30 min
Mean number of treatment administrations (SD)	*N*=22 6.2 (2.5)	*N*=24 13.7 (2.7)
Professionals	Mean time in treatment administration (min)	Mean time in treatment administration (min)
Psychiatrist	45	25
Anaesthetist	45	–
Operating departmental assistant	60	–
ECT nurse coordinator	60	–
Ward nurse	60	35
Mean cost per treatment administration (£)		
Capital	64	71
Professionals	147	44
Total cost per treatment administration	211	115

2.7. Service costs

Direct costs of services in each of the treatment groups were derived by multiplying the frequency and duration of health and social care resources used during the study with the unit cost of each resource.

2.8. Informal care costs

Unpaid child care, personal care, and care within or outside the home by family and other carers was costed under a replacement assumption using the average hourly rate for a local authority home care worker (Curtis and Netten, 2004) as the assumed cost for each hour of unpaid informal care.

2.9. Economic evaluation

The economic evaluation was conducted from two perspectives: (a) from the perspective of the health and personal social services system; and (b) from a societal perspective. A cost-effectiveness analysis was conducted comparing the comprehensively measured service costs between rTMS and ECT with, first, the difference between the treatments in change in the primary outcome measure (depressive symptoms as measured by the HRSD), and then with the difference between the treatments in QALYs gained. In each case an incremental cost-effectiveness ratio (ICER) was computed as the mean cost difference between rTMS and ECT divided by the mean difference in change in primary and secondary outcome respectively.

In the event that one treatment was both more effective and more costly than the other, a decision-maker would need to consider whether it is worth incurring the higher costs in order to achieve the improved outcomes. The approach employed to reveal the nature of these trade-offs – and to represent the inherent uncertainty in any evaluation – was to plot a cost-effectiveness acceptability curve (CEAC) for each cost–outcome combination (van Hout et al., 1994; Fenwick et al., 2004). The CEAC reveals the nature of the trade-off faced by the decision-maker. It shows the likelihood of rTMS being seen as cost-effective relative to ECT given different (implicit monetary) values placed on incremental outcome improvements. In the

present study, for each different monetary value that might be attached to a one-point improvement in the HRSD or to each QALY gained we calculated the probability that rTMS would be viewed as more cost-effective than ECT.

The CEAC also represents uncertainty in the estimation of the ICER, including in circumstances where statistical power limits significance testing (Briggs, 2000) and helps in understanding the sensitivity of the results to key assumptions in the analysis, particularly where lack of statistical power is a problem, as is often the case in mental health studies (Sturm et al., 1999). Bootstrap analyses were used to draw 1000 repeat samples from the data, and the CEAC generated by plotting the proportion of ICERs that were cost-effective for a range of assumed willingness-to-pay values. The bootstrap approach also allows for possible skewness in the cost variable (Dunn et al., 2003).

We also compared costs between the groups at 6-month follow-up. Regression analysis included covariates for baseline values of total cost excluding costs associated with care giving, depression at baseline (using baseline HRSD score) and caregiver hours.

2.10. Analyses

An 'intention to treat' analysis was conducted to preserve the unbiased distribution of factors (on average) in the groups produced by randomisation. A received-treatment analysis was performed as a sensitivity analysis. Missing costs were not imputed because of small sample sizes. All follow-up costs were adjusted for baseline HRSD score, pre-randomisation service costs and pre-randomisation informal care hours. All costs reported below are therefore adjusted for any differences in baseline characteristics. Mean costs were compared using Student's *t*-test and the robustness of the results confirmed using non-parametric bootstrapping techniques to account for any non-normality in their distribution. Data were analysed using SPSS v10 and STATA v8.0 (StataCorp, Texas, USA).

3. Results

3.1. Characteristics of participants

The socio-demographic and clinical characteristics of the sample of patients are summarised in Table 2. There were no statistically significant differences in demographic and clinical characteristics between the treatment groups at baseline. There were more females in both groups than males (73% for ECT; 67% of rTMS) and the great majority of participants lived in ordinary (non-care) accommodation (80% for ECT; 95% for rTMS).

Table 2
Descriptive characteristic of participants at baseline

Characteristics	ECT	rTMS
	N=22	*N*=24
Age: mean (SD)	68 (13)	64 (17)
Gender		
Female (%)	16 (67)	16 (73)
Type of accommodation		
Owner occupied home (%)	11 (55)	11 (55)
Privately rented home (%)	–	2 (10)
Housing association/local authority rented (%)	5 (25)	6 (30)
Residential home (%)	2 (10)	–
Sheltered housing (%)	1 (5)	1 (5)
Other (%)	1 (5)	–
Employment		
Managerial and professional occupations	2 (10)	–
Administrative and secretarial	1 (5)	1 (5)
Personal service occupation	1 (5)	1 (5)
Retired	11 (55)	10 (50)
Routine occupations	–	4 (20)
Unemployed	4 (20)	4 (20)
Patients with psychosis	3 (13.6%)	4 (16.7%)
HRSD score [a]	24.8 (5.0)	23.9 (7.0)
SF-36 MCS score [b]	42.7 (7.5)	48.9 (12.6)

[a] HRSD — Hamilton Rating Scale in Depression.
[b] MCS score — mental health component score.

3.2. Treatment rates

The mean number of treatment administrations for the ECT group was 6.3 (SD 2.5; range 2 to 10), with 68% of patients having 6 or more administrations. For the rTMS group the mean number of administrations was 13.7 (SD 2.7; range 5 to 15). Treatment course durations were very similar for rTMS (mean 19.5, SD 6.3) and ECT (mean 22.4, SD 12.7).

3.3. Outcomes

The clinical outcome results have been reported in detail in Eranti et al. (2007). In summary, at end of treatment HRSD scores were significantly lower for the ECT group than the rTMS group with thirteen (59%) ECT patients meeting the criterion for remission (HRSD ≤ 8) and only four (17%) of the rTMS group in remission. During follow-up, 5 of the rTMS patients crossed over to have ECT, and none of the ECT patients

had RTMS. At the end of 6-month follow-up, HRSD scores for both groups did not differ significantly between the groups ($p=0.93$). Scores on the Beck Depression Inventory, Visual Analogue Mood Scale and the Brief Psychiatric Rating Scale were lower for the ECT group than the rTMS group at the end of treatment, and remained lower at 6 months. There were no major differences on side-effects or cognition (Eranti et al., 2007).

3.4. Formal and informal service use

At baseline 15/24 in the rTMS group and 15/22 in the ECT group were inpatients. The sample is too small to allow us to test for cost differences between inpatients and outpatients. At the 6-month follow-up point, none of the 18 rTMS sample and none of 10 ECT sample were inpatients.

Table 3 gives the proportion of patients in each of the groups using health and community-based services 6 months after treatment. At 6-month follow-up, service use data were collected on 28 patients (10 in the ECT group, 18 in the rTMS group). A wide range of services was used, delivered by a range of local authority, NHS and voluntary sector organisations.

Table 3
Services used 6 months after treatment

	ECT		RTMS	
	$n=10$		$n=18$	
	No. using	Mean [a]	No. using	Mean [a]
Hospital based care				
Inpatient (bed day)	1	25	5	21
Outpatient (attendance) [b]	3	1	7	6
Accident and emergency (attendance)	1	1	2	1
Day hospital (contact)	1	1	–	–
Community-based care				
Day services (day)	1	1	1	0.17
Lunch club (visit)	1	7	–	–
Social club (visit)	1	25	–	–
District nurse (contact)	1	2	2	4
GP (contact)	5	2	12	6
Practice nurse (contact)	1	1	2	1
Community psychiatrist (contact)	1	1	7	4
CPN (contact)	2	5	6	11
Social worker (contact)	2	7	3	7
Psychologist (contact)	1	6	3	6
Other community-based professional (contact) [c]	7	2	6	2

Resources used over a 3-month period.
– No use made of service.
[a] Mean calculation based on users of relevant service only, not across full sample.
[b] Includes outpatient contact for specialist services (diabetic clinic, X-ray, urine test, psychiatry).
[c] Includes dentist, optician and home treatment team.

Table 4 summarises the number of hours of carer inputs in the 6-month follow-up period, distinguishing personal care, child care, help in and around the home, and help outside the home. Total caregiver input was lower after treatment (2 h/week for ECT patients; 11 h/week for rTMS patients) than at baseline (8 h/week for ECT patients and 9 h/week for rTMS patients).

3.5. Cost of treatment and services

Patients receiving ECT received a wider range of professional input than those managed by rTMS. The cost calculations were summarised in Table 1. The cost per session of rTMS was lower than the session cost of ECT. Nevertheless, over the study period the mean cost of rTMS treatment of £1444 (SD £286) was significantly higher than the mean cost of ECT (£1314; SD £525) because of differences in the number of treatment sessions.

Frequency of use (Table 3) was weighted by each service's unit cost to give the total cost of service-based inputs at 6-month follow-up. The costs of all services and support (both formal and informal) used after treatment are shown in Table 5. These are all adjusted for baseline HRSD scores, service costs and informal care hours. Other service costs were not different between ECT and rTMS groups during the treatment or follow-up periods. Service and treatment costs aggregated over the treatment and follow-up periods were not different between the groups.

Informal care costs were higher for the rTMS group (a difference of £2964; $p=0.02$) and contributed substantially to the total cost for this group.

Total costs – summing treatment, other services and informal care – were lower for the ECT group than for the rTMS group ($p=0.04$). These costs are adjusted for baseline HRSD and pre-randomisation service costs and informal care hours.

3.5.1. Sensitivity analysis

Sensitivity analyses were performed to examine the responsiveness of costs to changes in different variables. The effects of two key scenarios on total mean NHS costs and total costs are given towards the base of Table 5. The scenarios were: (a) varying the unit cost of informal care from a replacement to an opportunity cost basis by substituting the average gross hourly wage for an adult

Table 4
Caregiver input by treatment group

	Baseline				6-month follow-up			
	ECT		rTMS		ECT		rTMS	
	N=22		*N*=24		*N*=10		*N*=18	
Number receiving support with child care	0		2		0		2	
Hours per week of child care [a]	–	–	2.67	(12.24)	–	–	1.8	(6.6)
Number receiving support with personal care			1		2		3	
Hours per week of personal care [a]	–	–	0.29	(1.43)	0.9	(2.2)	0.6	(1.4)
Number receiving help in and around home	9		8		1		8	
Hours per week of help in and around home [a]	4.95	(9.30)	4.42	(8.52)	0.8	(2.5)	6.0	(7.9)
Number receiving help outside the home	8		7		2		10	
Hours per week of help outside the home [a]	3.45	(6.50)	2.00	(3.96)	0.5	(0.9)	2.4	(3.6)
Total caregiver input (hours per week) [a]	8.40	(15.16)	9.38	(15.91)	2.2	(4.6)	10.8	(13.3)

[a] Data are shown as mean hours (SD) across full sample.

(£11.47); and (b) varying the unit cost of informal care to costs based on the minimum wage (£4.85).

Under both scenarios, there were marginal changes in mean total costs (Table 5). In our study sample the average length of time spent in at least one category of caregiving was 16 h/week. When the gross hourly wage for an adult was used as an estimate of the unit cost of informal care, the mean difference in total costs became £4023. Under a more conservative estimate of the hourly cost of informal care of £4.85, the difference in the total costs became £3990. These differences are significant.

3.6. Cost-effectiveness

The primary measure of cost-effectiveness was the incremental cost per change in HRSD over the full study period (29 weeks). The secondary analysis was the incremental cost per QALY gain over that same period.

The lack of statistically significant differences in (some measures of) cost and effects is a common finding in cost-effectiveness studies. In such a scenario the decision-maker needs to assess the likelihood of a treatment being cost-effective, which can be assisted by plotting the cost-effectiveness acceptability curve (CEAC) based on an underlying net-benefit approach. The approach illustrates for a range of willingness-to-pay values (λ) for an incremental improvement in an outcome measure (such as change in depressive symptoms) the proportion of cases where rTMS would be seen as more cost-effective than ECT. The CEAC for rTMS compared to ECT for the primary outcome (HRSD) and for costs measured so as to cover treatment and all services, but not to include informal care, is

Table 5
Mean total costs at 6-month follow-up [a]

Cost category	Mean cost £ (SD)				Mean difference	95% CI
	ECT		rTMS		ECT−rTMS	
Treatment cost [b]	1314	(525)	1444	(286)	−130	−387 to +127
Other service cost during the treatment period	2584	(1793)	2310	(1897)	274	−116 to +376
Treatment and other service cost during the treatment period	3898	(1846)	3754	(1789)	144	−1174 to +909
Service costs during the 6-month follow-up period	1695	(3002)	2987	(4425)	−1292	−1614 to +4074
Service costs during the 6-month follow-up period *plus* treatment and other service cost during the treatment period	5469	(3016)	6829	(4420)	−1360	−1565 to +4049
Informal care during the treatment period *plus* follow-up period	834	(1481)	3803	(4507)	−2969	+676 to +5600
Total cost during treatment and follow-up period	6303	(3513)	10,632	(7234)	−4329	+278 to +8370
Sensitivity analysis 1: informal care cost based on average gross hourly earning (£11.47)	6197	(3443)	10,220	(6834)	−4023	+164 to +7869
Sensitivity analysis 2: informal care cost based on minimum wage (£4.85)	6147	(3462)	10,137	(6832)	−3990	+123 to +7846

[a] Adjusted for baseline HRSD, service costs and informal care hours
[b] Treatment costs and other service costs are estimated based on a sample of 22 patients in the ECT group and 24 patients in the rTMS group. All other costs are based on sample sizes of 10 and 18 for the ECT and rTMS groups respectively.

shown in Fig. 1. If society were willing to pay nothing for an improvement in depressive symptoms, there is a 24% probability that rTMS would be seen as a cost-effective alternative to ECT. If, however, society is willing to pay £500 for each unit improvement in depressive symptoms for each person (as measured by the HRSD), there is a 98% probability that rTMS would be viewed as more cost-effective. If informal care costs are also included, the CEAC is as in Fig. 2, and the probability that rTMS is more cost-effective than ECT is lower at each assumed value for the willingness to pay for an incremental improvement in symptoms as measured by the HRSD.

Over the study period ECT patients had a mean QALY gain of 0.0297 (SD 0.056) and rTMS patients had a mean QALY gain of 0.0300 (SD 0.053). The incremental QALY gain of treatment with rTMS over ECT was just 0.0003 ($p=0.987$). Treatment by rTMS does not provide any additional gains in quality of life over ECT over a 6-month period. In terms of cost-effectiveness, at values of willingness-to-pay up to £30,000 per additional QALY, the probability of cost-effectiveness is still less than 20% (Fig. 3). Thus, the findings suggests that rTMS has a very low probability of being seen as a cost-effective alternative to ECT for treatment-resistant depression.

4. Discussion

Resources for health care are almost always scarce relative to needs or wants, and the purpose of an economic evaluation is to inform the choices that decision-makers face in these circumstances. This study investigated the resource implications and cost-effectiveness of repetitive transcranial magnetic stimulation compared to electroconvulsive therapy, and so offers information that may help choice of treatment for people with severe depression.

The study has limitations, including a small sample size, and a relatively short follow-up period of 6 months for an illness that often is chronic. There was also some sample attrition, but there was no difference between the intention-to-treat and per-protocol analyses with respect to the primary outcome (HRSD) and so no reason to suspect biased findings as a result (Eranti et al., 2007). Inpatients and outpatients could not be separately analysed because of the small sample size.

A further limitation was that we did not measure indirect costs associated with lost employment or productivity, which can be quite large for people with depression. We can only speculate as to whether there would have been a difference between the groups: the difference in informal care support might suggest that

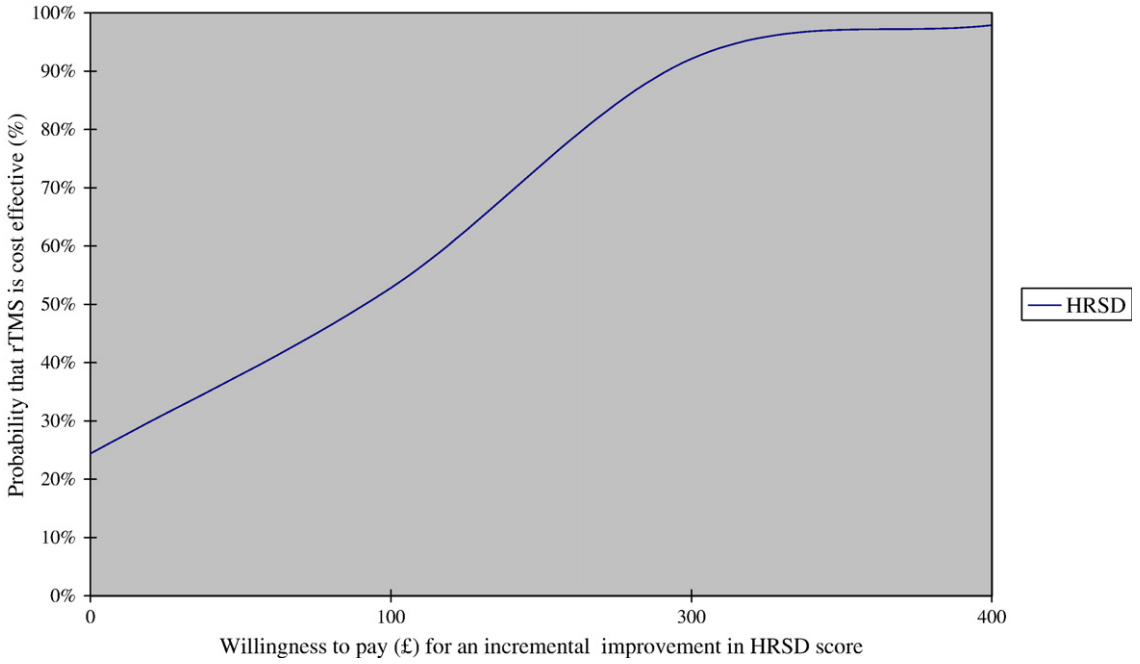

Fig. 1. Cost-effectiveness acceptability curve — probability that rTMS is cost-effective as a function of the decision-makers' willingness to pay for incremental improvements in HRSD score. Costs measure treatment and services over treatment and follow-up periods.

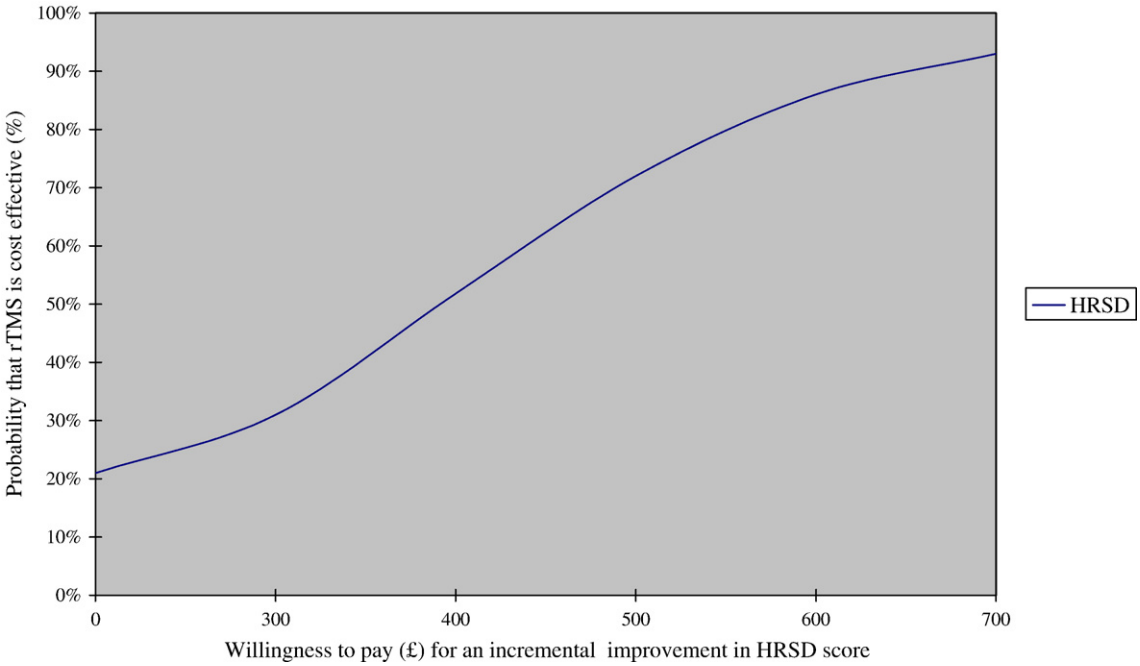

Fig. 2. Cost-effectiveness acceptability curve — probability that rTMS is cost-effective as a function of the decision-makers' willingness to pay for incremental improvements in HRSD score. Costs measure treatment and services over treatment and follow-up periods, plus informal care costs.

the ECT group, which had less informal care, might have been more likely to have secured employment, but this remains to be tested. Medication use did not change during the treatment phase of the study but we did not collect this information for the follow-up period. The results apply to the health care context within which the

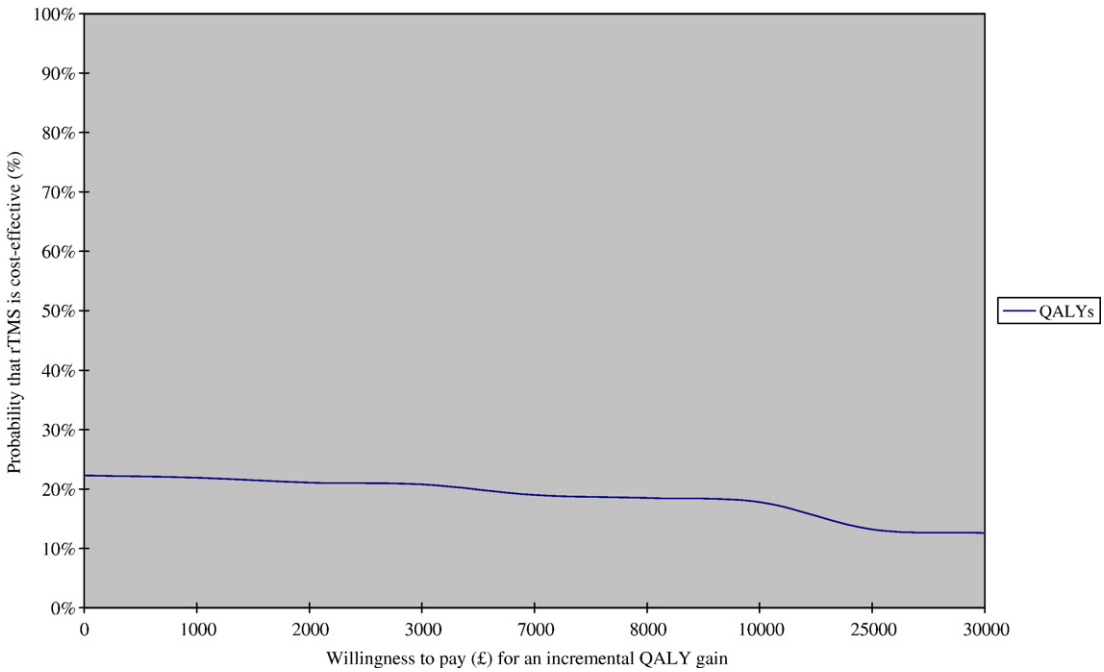

Fig. 3. Cost-effectiveness acceptability curve — probability that rTMS is cost-effective as a function of the decision-makers' willingness to pay for each additional QALY. Costs measure treatment and services over treatment and follow-up periods.

trail was conducted and generalisation to other contexts would need to be made carefully; however, even markedly different costs in another health care system would be unlikely to alter the core findings of this study, such are the probabilities demonstrated by the cost-effectiveness acceptability curves.

Although the cost of a single session of rTMS was lower than the cost of a session of ECT, patients receiving rTMS had more treatment sessions and direct treatment costs turned out to be higher. Total health and social care service costs were not significantly different between the groups, but the costs associated with the unpaid inputs of family and other carers were much higher for the rTMS group. Overall, the sum of formal and informal care costs during the treatment and 6-month follow-up periods was £10,220 for the rTMS group and £6303 for the ECT group, which was a significant difference.

There have been no previous prospective economic evaluations of ECT and rTMS, but these cost estimates are broadly consistent with previous cost-of-illness research suggesting that depression is associated with high use of health services (Thomas and Morris, 2003).

Using the widely employed Hamilton Rating Scale for Depression (HRSD) measure, we found that scores did not differ between the groups at 6-month follow-up. However, at end of treatment HRSD scores were substantially lower for the ECT group ($p=0.002$) than for the rTMS group and similar results were found in other self-rated mood scales (Eranti et al., 2007). Thus, short-term treatment for severe depression was much better with ECT than rTMS.

Health-related quality of life was measured using the SF-36, from which it is possible to calculate measures of quality-adjusted life years (using the SF-6D approach of Brazier et al., 2002). ECT has been reported to be associated with improved quality of life that is evident within the first month post-treatment and that can be maintained for up to one year (McCall et al., 2001, 2004). This contrasts with the present research, which found no relative QALY gains for either treatment over the other. Whether the SF-6D is sufficiently sensitive to measure changes in health-related quality of life for people with severe depression is unclear; mental health-specific QALY measures have still to be developed.

There are now numerous economic evaluations of depression treatment, although not of the specific treatments studied here (Barrett et al., 2005). A recent attempt to generate a model proved inconclusive mainly due to a lack of suitable randomised controlled trial data and uncertainty around the optimal treatment parameters for ECT (Greenhalgh et al., 2005). A published decision analytical model of the cost-effectiveness of rTMS suggested that it would be cost-effective compared to ECT alone (Kozel et al., 2004). In contrast, the randomised controlled trial described in this paper has found that rTMS has a very low probability of being more cost-effective than ECT. Indeed, when considering the cost of achieving an additional quality-adjusted life year, the cost-effectiveness of rTMS does not look at all attractive by reference to the threshold revealed by a review and econometric analysis of recommendations made by the National Institute for Health and Clinical Excellence (NICE) (Devlin and Parkin., 2004).

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Conflict of interest

None of the authors has any conflict of interest.

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Appendix A. Unit costs and sources of information

All unit cost are based on 2003/2004 prices.

Table A1
ECT treatment administration

ECT treatment administration		
Cost component	Unit cost (£)	Source/notes
a) Capital		
Treatment suite per administration	60	Using BCIS cost per metres square estimates of treatment suite discounted at 3.5% over 60 years weighted by 362 ECT administrations for the year
Machine per administration	4	Cost of machine (£12,342) annuitised at 3.5% over 10 years weighted by the number of ECT administrations for the year were 362

Table A1 (*continued*)

ECT treatment administration		
Cost component	Unit cost (£)	Source/notes
Total capital cost per treatment administration	64	
b) Staffing		
Anaesthetists	52/h 0.87/min	The midpoint salary of consultant MC 21. The estimate includes national insurance and superannuation contributions, and direct and indirect overheads. The cost per hour was based on someone working 41 weeks per annum and 48.2 h/week £52/h
Consultant psychiatrist	69/h 1.15/min	Curtis and Netten (2004)
Operating departmental assistant (ODA)	19/h 0.32/min	The midpoint of a Medical technical officer (MTO) of MT03 (in advance letters (PBT) 1/2003, annex A (I)). The estimate includes national insurance and superannuation contributions, and direct and indirect overheads. The cost per hour was based on someone working 42 weeks per annum and 37.5 h/week £19/h
Nurse coordinator	21/h 0.35/min	Curtis and Netten (2004). Nurse ward manager used as a proxy
Ward nurse	16/h 0.27/min	Curtis and Netten (2004)

Table A2
rTMS treatment administration

rTMS treatment administration		
a) Capital		
Treatment suite per administration	63	Using BCIS cost per metres square estimates of treatment suite discounted at 3.5% over 60 years weighted by 348 rTMS administrations for the year
Machine per administration	8	Cost of machine (£22,325) annuitised at 3.5% over 10 years weighted by the number of ECT administrations for the year were 348
Total capital cost per treatment administration	71	
b) Staffing		
Consultant psychiatrist	69/h 1.15/min	Curtis and Netten (2004)
Ward nurse	16/h 0.27/min	Curtis and Netten (2004)

Table A3
Unit cost of services

Service	Unit cost	Source
Assessment/rehabilitation ward; per bed day	204	Department of Health National Schedule of Reference Costs, 2004
Continuing care/respite ward; per bed day	188	Department of Health National Schedule of Reference Costs, 2004
Medical ward; per bed day	289	Medical ward cost for 2001/2002 inflated using Hospital and community health service pay and price inflator
Other hospital ward; per bed day	111	Generic inpatient ward per bed day uprated using Hospital and community health service pay and price inflator
Diabetic outpatient ward; per bed day	92	Department of Health National Schedule of Reference Costs, 2004
Psychiatric outpatient ward; per bed day	105	Department of Health National Schedule of Reference Costs, 2004
Radiotherapy outpatient; per attendance	88	Department of Health National Schedule of Reference Costs, 2004
Urine test	41	Cost per test. Department of Health National Schedule of Reference Costs, 2004
Accident and emergency; per attendance	83	Curtis and Netten (2004)
Day hospital	77	Cost per day hospital attendance for people with mental health problems in Netten, Rees and Harrison 2001 uprated using Hospital and community health service pay and price inflator

(continued on next page)

Table A3 (*continued*)

Service	Unit cost	Source
Community-based care		
Day care — local authority provision; per session	18	Curtis and Netten (2004)
Day care — voluntary organisation provision; per session	18	Curtis and Netten (2004)
Day care — NHS provision; per session	28	Curtis and Netten (2004)
Lunch club — voluntary sector provision; per session	6.10	http://www.cash-online.org.uk/content/1/6/3/#wrapper [accessed December 2004]. Based on the cost per meal
Social club per session	18	Cost of day centre used as a proxy. Curtis and Netten (2004)
District nurse per hour clinic visit	36	Curtis and Netten (2004)
District nurse per hour home visit	50	Curtis and Netten (2004)
GP per surgery or clinic minute	2.03	Curtis and Netten (2004)
GP per home visit minute	3.18	Curtis and Netten (2004)
Practice nurse per hour home visit	31	Curtis and Netten (2004)
Practice nurse per hour clinic visit	24	Curtis and Netten (2004)
Community psychiatrist per hour	95	Curtis and Netten (2004)
CPN per hour clinic visit	36	Used unit cost of district nurse as proxy. Curtis and Netten (2004)
CPN per hour clinic visit	50	Used unit cost of district nurse as proxy. Curtis and Netten (2004)
Social worker cost per hour	21	Curtis and Netten (2004)
Psychologist cost per hour	30	Curtis and Netten (2004)
Home treatment team per hour	27	Community mental health team used as a proxy. Curtis and Netten (2004)

The unit costs not included in this table are described below.

Dentist

Dental practices can take either private or NHS patients and most practices are a mixture of both. Other dentists work in the Community Dental Service (CDS), in hospitals, universities, industries or the armed forces. Dentists in mixed practice could earn in the region of £58,000. The average income for a dentist doing purely NHS work was used and includes National Insurance contributions and 15% management and administrative overheads. Hours worked by dentists vary according to where the work. Dentists who work in general practice will work a five-day week from 9:00 am–5:00 pm. The cost per hour was estimated based on 42 weeks per annum and 37 h/week.
(£39/h)

Optician

There is a recommended fee payable to for ophthalmic medical practitioners who administer sight tests, however Optometrists undertake the majority of tests. The salaries of Optometrists can vary depending on the setting in which they practice (private or hospital or combination of the two). The range of typical salaries in private practice based on salary data collected Jan 2003 (www.prospects.ac.uk/links/occupations) was £25,000–£35,000 while in hospital the range was £16,000–£20,000. Senior optometrists in private practice can earn up to £55,00, while in the senior optometrist in hospital typical salaries at age 40 can earn from £38,000 to £55,000. Working hours are usually nine to five thirty, Monday to Saturday. Hours worked can vary but Optometrist generally work 38 h/week. The average salary for private practice was used. The cost per hour was estimated based on 41 weeks per annum, 38 h/week.
(£29/h)

References

Barrett, B., Byford, S., Knapp, M., 2005. Evidence of cost-effective treatments for depression: a systematic review. Journal of Affective Disorders 84, 1–13.

Beecham, J., Knapp, M., 1992. Costing psychiatric interventions. In: Thornicroft, G., Brewin, C., Wing, J. (Eds.), Measuring Mental Health Needs. Gaskell, London, pp. 163–183.

Beecham, J., Knapp, M., 2000. Costing psychiatric Interventions, In: Thornicroft, G. (Ed.), Measuring Mental Health Needs, Second edition. Gaskell, London.

Brazier, J.E., Roberts, J., Deverill, M., 2002. The estimation of a preference based measure of health from the SF-36. Journal of Health Economics 21, 271–292.

Briggs, A., 2000. Economic evaluation and clinical trials: size matters (editorial). British Medical Journal 321, 1362–1363.

Curtis, L., Netten, A., 2004. Unit Costs of Health and Social Care. PSSRU, University of Kent.

Department of Health, 2004. National Health Service Schedule of Reference Costs 2004. . http://www.doh.gov.uk/nhsexec/refcosts.htm. [accessed May 2005].

Devlin, N., Parkin, D., 2004. Does NICE have a cost effectiveness threshold, and what other factors influence its decisions? A binary choice model. Health Economics, 13, pp. 437–452.

Dunn, G., Mirandola, M., Amaddeo, F., Tansella, M., 2003. Describing, explaining or predicting mental health care costs: a guide to regression models. British Journal of Psychiatry 183, 398–404.

Eranti, S., Mogg, A., Pluck, G., Landau, S., Purvis, R., Brown, R.G., Howard, R., Knapp, M., Philpot, M., Rabe-Hesketh, S., Romeo, R., Rothwell, J., Edwards, D., McLoughlin, D.M., 2007. A randomized controlled trial with 6-month follow-up of repetitive transcranial magnetic stimulation and electroconvulsive therapy for severe depression. American Journal of Psychiatry 164, 73–81.

Fenwick, E., O'Brien, B., Briggs, A., 2004. Cost-effectiveness acceptability curves — facts, fallacies and frequently asked questions. Health Economics 13, 405–415.

George, M.S., Lisanby, S.H., Sackheim, H.A., 1999. Transcranial magnetic stimulation — applications in neuropsychiatry. Archives of General Psychiatry 56, 300–311.

Greenhalgh, J., Knight, C., Hind, D., Beverley, C., Walters, S., 2005. Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: Systematic reviews and economic modelling studies. Health Technology Assessment 9, 9.

Grunhaus, L., Schreiber, S., Dolberg Plack, D., Dannon, P.N., 2003. A randomized controlled comparison of electroconvulsive therapy and repetitive transcranial magnetic stimulation on severe and resistant nonpsychotic major depression. Biological Psychiatry 15:53 (4), 324–331.

Hamilton, M., 1960. A rating scale for depression. Journal of Neurology Neurosurgery and Psychiatry 2356–2362.

Kozel, F.A., George, M.S., Simpson, K.N., 2004. Decision analysis of the cost-effectiveness of repetitive transcranial magnetic stimulation versus electroconvulsive therapy for treatment of nonpsychotic severe depression. CNS Spectrums 9 (6), 476–482.

McCall, W.V., Reboussin, B.A., Cohen, W., Lawton, P., 2001. Electroconvulsive therapy is associated with superior symptomatic and functional change in depressed patients after psychiatric hospitalization. Journal of Affective Disorders 63, 17–25.

McCall, W., Dunn, A., Rosenquist, P.B., 2004. Quality of life and function after ECT. British Journal of Psychiatry 185, 405–409.

Rose, D., Wykes, T., Leese, M., Bindman, J., Fleischmann, P., 2003. Patients' perspectives on electroconvulsive therapy: systematic review. British Medical Journal 326, 1363–1365.

Royal College of Psychiatrists, 1995. The ECT Handbook: The Second Report of the Royal College of Psychiatrists' Special Committee on ECT. Royal College of Psychiatrists, London. [Council Report CR39].

Sackeim, H.A., Prudic, J., Devanand, D.P., Kiersky, J.E., Fitzsimons, L., Moody, B.J., Mcelhiney, M.C., Coleman, E.A., Settembrino, J.M., 1993. Effects of stimulus-intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive-therapy. New England Journal of Medicine 328, 839–846.

Sturm, R., Unutzer, J., Katon, W., 1999. Effectiveness research for study design: sample size and statistical power. General Hospital Psychiatry 21, 274–283.

Thomas, C., Morris, S., 2003. Cost of depression among adults in England in 2000. British Journal of Psychiatry 183, 514–519.

UK ECT Review Group, 2003. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 361, 799–808.

van Hout, B., Al, M., Gordon, G., Rutten, F., 1994. Costs, effects and cost-effective ratios alongside a clinical trial. Health Economics 3, 309–319.