

Economic evaluation of resistant major depressive disorder treatment in Iranian population: a comparison between repetitive Transcranial Magnetic Stimulation with electroconvulsive

Hesam Ghasvand¹, Mohammad Moradi- Joo², Nazanin Abolhassani³
Hamid Ravaghi^{*4}, Seyed Mansoor Raygani⁵, Sahar Mohabbat-Bahar⁶

Received: 9 September 2015

Accepted: 11 November 2015

Published: 17 February 2016

Abstract

Background: It is estimated that major depression disorders constitute 8.2% of years lived with disability (YLDs) globally. The repetitive Transcranial Magnetic Stimulation (rTMS) and Electroconvulsive Therapy (ECT) are two relative common interventions to treat major depressive disorders, especially for treatment resistant depression. In this study the cost- effectiveness and cost-utility of rTMS were compared with ECT in Iranian population suffering from major depressive disorder using a decision tree model.

Methods: A decision tree model conducted to compare the cost-effectiveness ratio of rTMS with ECT in a health system prospective and 7 months' time horizon. The outcome variables were: response rate, remission rate and quality-adjusted life-years (QALYs) of the rTMS and ECT as primary and secondary outcomes extracted from systematic reviews and randomized control trials. The costs were also calculated through a field study in one clinic and one hospital; the direct costs have only been considered.

Results: The total cost for rTMS and ECT strategies were 11015000 Rials (373 US\$) and 11742700 Rials (397.7 US\$), respectively. Also the rTMS/ECT ratio of costs per improved patients was 1194410 Rials (40.5 US\$); the ratio for costs per QALYs utility was 21017139 Rials (711.72 US\$). The incremental cost- effectiveness ratio of rTMS versus ECT was 1194410 Rials (40.44 US\$) after treatment and maintenance courses.

Conclusion: Given the current prevalence of depressive disorders in Iranian population, the ECT is more cost-effective than TMS. The sensitivity analysis showed that if the prevalence of major depressive disorders declines to below 5% or the costs of rTMS decrease (rTMS provided by public sector), then the rTMS becomes more cost-effective compared with ECT. However, efficacy of rTMS depends on the frequency of pulsed magnetic field, the location of rTMS on the head, the number of therapeutic sessions and the length of each session.

Keywords: Major Depressive disorders, Electroconvulsive Therapy, repetitive Transcranial Magnetic Stimulation, Decision tree.

Cite this article as: Ghasvand H, Moradi- Joo M, Abolhassani N, Ravaghi H, Raygani SM, Mohabbat-Bahar S. Economic evaluation of resistant major depressive disorder treatment in Iranian population: a comparison between repetitive Transcranial Magnetic Stimulation with electroconvulsive. *Med J Islam Repub Iran* 2016 (17 February). Vol. 30:330.

Introduction

Changing pattern of diseases and out-

stripping the prevalence of chronic diseases requiring long-term care, have led to

¹. PhD of Health Economics, Health Services Management Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. hesams82@gmail.com.

². MSc in Health Technology Assessment, Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. moradijoo@gmail.com

³. PhD of Health Policy and Management, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. na_abolhassani@yahoo.com

⁴. (**Corresponding author**) PhD of Health Policy, Assistant Professor, Department of Health Services Management, School of Health Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran. ravaghi.h@iums.ac.ir

⁵. Physical Medicine and Rehabilitation Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. rayegani@sbmu.ac.ir.

⁶. PhD student in Psychology, Ferdowsi University of Mashhad, Faculty of Psychology and Educational Sciences, Mashhad, Iran. sahar_mohabbatbahar@yahoo.com.

changes in policy approaches and plans of health systems particularly in developing countries. These changes have had adverse consequences, especially in developing countries that have less potential and are less prepared to manage them. Mental disorders and illness are chronic health problems that have adverse effects on the quality of life in households and the social and economic development on a national scale (1).

Major depression's prevalence, morbidity, mortality and disability rates are growing now and it is predicted that they will be ranked as the first worldwide burden of diseases in developed countries in 2030 (2). Studies on the Global Burden of Diseases conducted in 1990 and 2000 have had a main role in shifting international attraction and emphasis from the physical disorders to mental disorders, especially the depression (3-5). According to Ferrari A.J.et.al., the depressive disorders have been the second leading cause of years lived with disability (YLDs and the major depressive disorders are accounted for 8.2% (5.9%- 10.8%) of global YLDs. Also, they found that even though no mortality is attributed to depressive disorders, it is the leading cause of DALYs and the MMD is accounted for 2.5% (1.9%- 3.2%) of global DALYs (6).

This situation may become worse, if we consider the sexual and demographic distribution of the major depression. According to studies, the prevalence of major depression is more in female and also in young and productive population groups (6,7). So the major depression may lead to serious social and economic challenges in both developing and developed countries. There is no accurate estimation about the major depression in Iranian population, but according to the results of a systematic review conducted in Iran, the MMD prevalence was 4.1% (95% CI: 3.1-5.1) and women were 1.95 times more likely to have the MDD (8). Also, in a national survey conducted in 2003, the major depressive disorders (MMD) ranked in the high four burden in all ages and both sexes. It is

also the second cause of DALYs between Iranian female (9).

Another study reported the MMD as the top cause of YLDs and the third cause of DALYs among 20 countries in MENA (the Middle East and North Africa countries including Iran) in 2010 (10).

The considerable prevalence and burden of major depressive disorders made them as a high priority health challenge that requires adopting and implementing effective policies to solve it. The appropriate treatment strategy is the heart of solving this challenge. Nowadays, there are some therapeutic interventions to treat the major depressive disorders. The pharmacological interventions (11) and non-pharmacological Neuromodulation Therapies (NMTs) include electroconvulsive therapy (ECT) and the transcranial magnetic stimulation (TMS) (12). But in major depressive disorders (MMDs) treatment, what makes the situation worse is the inefficacy of pharmacological interventions; Berlim et al (2008) concluded that up to 20–30% of subjects suffering from MMD remain significantly ill despite the use of multiple therapeutic interventions (13). These cases are called the treatment resistant depression. So, each therapeutic intervention has its advantages and disadvantages.

The electroconvulsive therapy has been used to treat the patients who do not respond to antidepressant medication or psychological therapy. The ECT has been criticized as a therapeutic intervention because of the need to anesthesia, the risk of seizure and cognitive side effects (15,16).

The transcranial magnetic stimulation (TMS) and subsequent repetitive Transcranial Magnetic Stimulation (rTMS) have been developed in order to achieve effective and safe interventions for the treatment of the treatment-resistant depression over the last three decades. The TMS was first used in 1985 by Barker et al (16).

Considering the above-mentioned findings, the choice of appropriate intervention should be selected based on appropriate criteria including: safety, clinical efficacy

and economic considerations. The economic considerations imply the economic evaluation that is conducted through cost-effectiveness and cost-utility analyses based on the current modeling approaches including the decision tree and Markov model.

This study aimed to calculate and compare the cost-effectiveness and cost-utility of the repetitive Transcranial Magnetic Simulation (rTMS) with electroconvulsive strategy through conducting a decision tree approach in the treatment of Iranian population suffering from the major depressive disorder.

Methods

Study Design: This economic evaluation study was conducted using a decision tree model. The cost-effectiveness and cost-utility analyses were used to compare the rTMS with ECT as two therapeutic interventions for Iranian population suffering from major depression disorders (MMDs). According to clinical guidelines, treatment of major depressive disorders requires a one year intervention and follow up (17); but there are many studies recommended a 7 month time horizon (15-18). So, we selected a 7 month time horizon including 3-4 weeks for intervention and about 6 months for the follow-up phase.

Data and Setting: Data related to the costs of resource evaluated in each therapeutic strategy. The direct costs were collected from the clinics and hospitals providing the ECT and rTMS to the patients suffering from major depressive disorder. The hospitalization and anesthesia are needed for the ECT, so the data regarding its cost were collected from a hospital. Hospitalization and anesthesia are not needed for the rTMS and it can be provided within outpatient settings and facilities. All those related costs were collected from the clinics of a public hospital and a private medical center both located in Tehran, Iran.

The efficacy data were collected through searching the reviews available in the literatures. The literature review conducted

using a predefined search strategy in PubMed/Medline, Scopus, INAHTA, CRD, Trip, PsycInfo, Google Scholar, and Cochrane Library databases. The search strategy did not contain any time limitation and the appropriate terminology checked according to Mesh. We used the terms rTMS/TMS and ECT therapeutic efficacy and major depressive disorders, rTMS/TMS and ECT response rate and major depressive disorders, rTMS/TMS and ECT remission rate and major depressive disorders, rTMS/TMS and ECT relapse rate and major depressive disorders, and rTMS/TMS and ECT recurrence rate and major depressive disorders. A large number of primary outcomes are available as the clinical efficacy (therapeutic) for TMS and ECT methods. Among these indicators, response rate to the treatment, remission and relapse rates, number of patients requiring treatment and the risk difference were considered. Each of these indicators are based on Hamilton Scale, 17 or 24 (HDRS 17 or 24) and the Montgomery-Asberg Depression Rating Scale (MADRS), BDI scores and AUSSI. In this study, the primary outcomes included the response, remission and relapse rates among the target population. The secondary outcome includes the rate of the change in the quality of life which is based on the overall index (Based on the overall quality of life).

Costing Approach: Costing was evaluated according to the resources utilized to provide the therapeutic services in each of ECT and TMS strategies. Each of these strategies have specific processes and activities including the manpower, machines and equipment, physical environment, materials, supplies and medication. These costs include both phases of the treatment (3-4 weeks) and follow-up (26-week maintenance phase) and also their weighted sum. After identification of these resources, an appropriate measure was used to measure the amount of initiatives done by each method. Finally, the total cost of each strategy was derived by multiplying the market price by the units of used resources. Before

computing the total cost, the process and activities constituting each therapeutic strategy were identified. The abovementioned processes are explained as below (14,17,18):

- *The treatment process in (r) TMS:* People suffering from resistant major depressive disorders undergo rTMS under supervision of a psychiatric. Usually the therapeutic plan includes one session (the first session) for examination the patient, 10 sessions for the therapeutic intervention (using rTMS) and 3 sessions for assessing the therapeutic trend and following up the patients. The first eleven sessions are done in 3 to 4 weeks and called the initial/primary phase. Each session lasts about 20 to 30 minutes and a psychiatric performs related activities and practices. In cases with no response to the treatment, the psychiatric performs the therapeutic plan again. Patients with proper response to the treatment will enter the follow up (maintenance) phase. The second three sessions constitute the maintenance (follow up) phase and the patients will be visited every two months by a psychiatric or clinical psychologist. During the maintenance period, a certain dose and number of antidepressant (usually Fluoxetine) is prescribed for patients.

- *Treatment process in ECT:* In the ECT strategy, patients are hospitalized and they are taken to the ECT room after primary preparation for the therapeutic intervention. Initially, an IV line is taken, and then a rapid-action intravenous anesthetic medication (e.g. Thiopental) and a muscle relaxant medication (e.g. Esculin) are injected by an anesthesiologist. Under the supervision of a psychiatrist and by a trained nurse, patients receive shock using two electrodes that are placed on their temporal sides and are connected to the ECT device. The patients' seizure times are recorded. After finishing the shocking process, anesthetic technician gives patients nasal oxygen, removes pharyngeal secretions by suction and then patients are transferred to the recovery room. After their recovery, IV line is removed

and the patient will be transferred to the waiting room.

At the end of the intervention and total consciousness, patients will be referred to their wards. Here, several issues must be considered: First, the time length of the ECT procedure in each session is not exactly fixed and may vary between 20 seconds to 1 minute. Second, the number of sessions depends on the patient's condition and his/her response to the treatment. Totally, between 8 to 17 sessions is needed; and in each session the patient is often hospitalized for 2 to 3 weeks. The maintenance or follow-up period lasts between 5 to 6 months and repeated visits will be done by a psychiatrist once a month. In addition, during the maintenance period, patients are taken anti-depressants each day and a sleeping medication every two days (type, dose and use of medications depend on the psychiatrist's prescription).

Modeling and description: A decision tree model was conducted to calculate the cost-effectiveness and cost-utility ratios of rTMS and ECT strategies. This model includes two strategies, rTMS and ECT. Considering major depressive disorders prevalence in Iran (about 0.127 that is equal to 169 people per 100000 Iranian population), a total of 9544008 patients were included in each strategy. The therapeutic intervention in each strategy had two phases: The first phase was the intervention period which lasted three weeks. During this period, patients were treated with both of these strategies. After the intervention period, patients entered the second phase in which they were monitored by a psychiatrist and a clinical psychologist. Medications were prescribed in this period on a regular basis. It was considered that patients may be improved after the first phase to be eligible to enter to the second phase or they may show no response to the treatment and should be re-treated. In fact, the first phase is intervention and the second phase is the maintenance (follow up) phase. Table 1 presents the parameters used in the study.

Table 1. The parameters used in economic evaluation model

Parameters	Rate	Reference
Iran population	75149669	(19)
The prevalence of major depression in Iran.	0.127 (169 people per 100000 Iranian population), 0.041	(20) and (8)
Response Rate to the rTMS in the first phase.	0.167, 0.17 and 0.4	(21), (22) & (23)
Remission Rate with the rTMS in the second phase (maintenance phase).	0.5, 0.5 and 0.36	(21), (22) & (23)
Response Rate to the ECT in the first phase.	0.303, 0.467 and 0.59	(15) & (24)
Remission Rate with ECT in the second phase (maintenance phase).	0.03 and 0.234	(18) & (24)
Rate of the change in the quality of life in the first phase of the rTMS.	0.023	(18)
Rate of the change in the quality of life in the second phase of the rTMS.	0.053	(18)
Rate of the change in the quality of life in the first phase of the ECT.	0.0263	(18)
Rate of the change in the quality of life in the second phase of the ECT.	0.053	(18)

Here, some required explanations are presented:

1. There are no comprehensive statistics on the prevalence of major depressive disorders in Iran. A set of data has been announced by the Mental Health Office of Iran’s Health Ministry. However, these data have been revised using the major depressive disorders statistics collected from a systematic review conducted in 2010(8) as well as expert opinions. So, three possible prevalence rates were considered including 4.1%, 8% and 10% in the analysis section.

2. The economic evaluation was conducted in two phases: At three to four weeks for the therapeutic phase and from 6 months to one year (49 weeks) for the maintenance (follow up) phase.

3. The incremental cost- effectiveness ratio, was calculated as below:

$$ICER = \frac{Cost_{rTMS} - Cost_{ECT}}{RemissionRate_{rTMS} - RemissionRate_{ECT}}$$

4. Robustness of the model: A sensitivity analysis was conducted to assess the validity and reliability of the model. The sensitivity analysis was performed on the response rate, remission rate and costs variations for each of the TMS and the ECT methods based on the prevalence of major depression in the general population.

Results

Total costs for the rTMS and the ECT as therapeutic strategies for major depressive disorder are presented in Table 2. This table shows the costs for the primary phase and maintenance (follow up) phase and total costs of both phases for rTMS and ECT, separately.

The costs were calculated using a resource based valuing scale, in which all payments for the utilized resources for providing services had been computed. These costs included payments for psychiatrics, clinical psychologists, purchase of rTMS and cots for establishing, running and repairing of instruments, physical space and its furnishing, as well as costs of the rTMS consumption energy and supplies and consumable materials. Payments for drugs and psychiatric visits during the follow up phase were also calculated. Similar payments were also calculated for the ECT strategy with some differences. As the ECT required the hospitalization and anesthesia, these costs were also included. These included costs for hospital beds, ICU (if needed), recovery and ward charges, nursing services, food and other hospital accommodation charges. Therefore, the ECT strategy is a little more expensive than the rTMS strategy. Complete profiles of both rTMS and ECT strategies have been pre-

Table 2. The costs of therapeutic phases of major depressive disorders*

Therapeutic Strategy	Costs of primary phase	Costs of follow up phase	Total Costs after finishing the therapeutic course
rTMS strategy	9757500Rials (330.4 US\$)	1257500Rials (45.6US\$)	11015000Rials (376US\$)
ECT strategy	9880000Rials (334.6US\$)	1862700Rials (63US\$)	11742700Rials (397.7US\$)

* All costs have been calculated since the January to March 2014 when the 1US\$=29530 I.R.I Rial

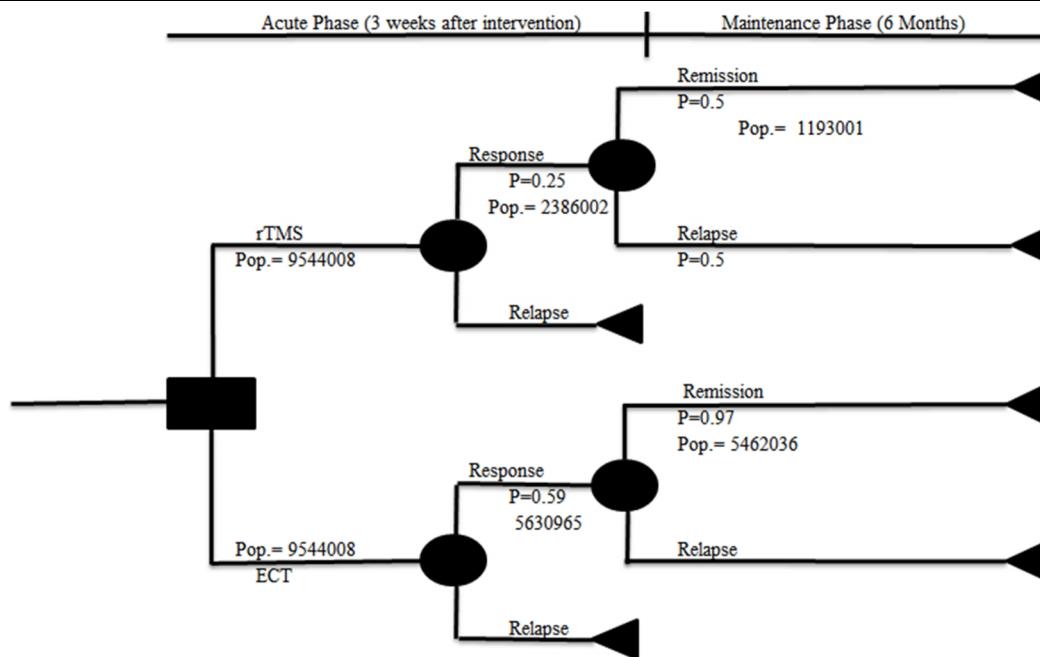


Fig. 1. The decision tree model of rTMS versus ECT in treatment of major depressive disorder

sented in Appendices 1 and 2.

After calculating the costs of rTMS and ECT strategies, the cost- effectiveness and cost- utility ratios have computed through a decision tree model. The decision model has been presented in Fig. 1.

There was no comprehensive and accurate data on major depressive disorder in Iran and the I.R.I Ministry of Health Mental Health Office has been considered as a referral for the estimation of MMD prevalence in Iranian population. According to this issue, it was estimated that 9544008 Iranian people suffer from MMD. This fig-

ure has been calculated considering the Iranian Statistics Centre estimation of the country population which was about 75149669 people in 2011. So, the cost- effectiveness and cost- utility ratios were computed based on the response, remission and relapse probabilities extracted from the literature. Calculations presented in Table 3.

The sensitivity analysis has been conducted to assess the robustness of the results. Here, one-way linear sensitivity analysis was conducted for the MMD prevalence, the remission rate and the costs of

Table 3. The ICER results for the rTMS and ECT among Iranian population suffering from MMD

Effectiveness variable	Amount of Effectiveness	Costs per improved patients the rTMS to ECT Rials (US\$)
Number of patients who improved by the rTMS in the intervention phase (the first 3 weeks)	2368002	996890.1(33.75)
Number of patients who improved by the ECT in the intervention phase (the first 3 weeks)	5630965	
Number of patients who improved by the rTMS in both intervention and maintenance phases	1184001	1194410(40.44)
Number of patients who improved by the ECT in both intervention and maintenance phases	5462036	
The change in the Quality of life in patients who improved by the rTMS in the first 3 weeks	54878.05	36641760(1240.8)
The change in the Quality of life in patients who improved by ECT in the first 3 weeks	143651.5	
The change in the Quality of life in patients who improved by rTMS in both intervention and maintenance phases	62752.05	21017139(711.72)
The change in the Quality of life in patients who improved by rTMS in both intervention and maintenance phases	305874	

each strategy.

1. If the MMDs prevalence is 4.1%, the ICER is:

At the end of the initial treatment phase (the first 3 weeks): 62327641000 Rials (2110654.961 US\$) the ICER of the rTMS to the ECT. At the end of the follow up phase (including the first and maintenance phases): 252516000000 Rials (8551168.303 US\$) the ICER of the rTMS to the ECT.

2. If the response rate in initial treatment phase is 0.4 after rTMS, the ICER is: At the end of the initial treatment phase (the first 3 weeks): 556339000000 Rials (188397900.4 US\$) the ICER of the rTMS to the ECT. At the end of the follow up phase (including the first and maintenance phases): 641393000000 Rials (217200474.1 US\$) the ICER of the rTMS to the ECT.

3. If the remission rate in the maintenance phase is 0.5 percent after TMS, the ICER is: At the end of the initial treatment phase (the first 3 weeks): 586339000000 Rials (198557060.6 US\$). At the end of the follow up phase (including the first and maintenance phases): 6620962300000 Rials (224211388.4 US\$)

4. If the response rate in the initial treatment phase is 0.234 percent after ECT, the ICER is: at the end of the initial treatment phase (the first 3 weeks): 556339000000 Rials (188397900.4 US\$). At the end of the follow up phase (including the first and maintenance phases): 893580000000 Rials (302600745 US\$).

5. If costs of the rTMS strategy are based on a public-sector -regardless of profit and depreciation costs for equipment and buildings, the ICER is: at the end of the initial treatment phase (the first 3 weeks): 263008260 Rials (8906.476803). At the end of the follow up phase (including the first and maintenance phases): 630719860 Rials (21358.61361 US\$).

Discussion

Economic evaluation is a technique to allocate resources for the each health ser-

vices. Mental health disorders especially the major depression is a growing problem that involves the female more than male and also the young population more than elders. The WHO has reported the major depression as a manageable health system challenge that can be controlled by reasonable and bearable costs if it is diagnosed in the primary phase and the initial stage. The prevalence and subsequent burden of MMD have an increasing pattern and trend. Treatment-resistant depression makes double problems for health systems and requires serious action. In Iran, the prevalence of major depression and especially the treatment resistant depression are not clear and the need of a comprehensive survey to monitor major depression is of great importance. Nevertheless, in this study major depression disorder therapeutic regimens including rTMs and ECT were analyzed in terms of cost-effectiveness and cost- utility ratios using a decision tree model. The total cost for treating major depression disorder by rTMS was 11015000 Rials (373 US\$) and by the ECT was 11742700 Rials (397.7 US\$). So, there is little difference in the calculated costs for the two strategies. The ECT strategy requires patients' hospitalization and anesthesia and also nursing care, therefore the ECT is more expensive than the rTMS. The main cost resource of the rTMS is associated with the purchase of the rTMS and also related human resources but the ECT's main costs are related to human resources and the physical space needed to establish the ECT. Knapp et al. concluded that "The cost of a single session of rTMS was lower than the cost of an ECT session, but overall there is no treatment cost differences" (15). Kozel et al. mentioned "The total costs, incurred during the 52-week period were \$57,845,347 for rTMS and \$186,359,571 for ECT" (23).

If we consider informal costs including loss of productivity and transportation costs, it may be no difference between both rTMS and ECT strategies. McLoughlin et al. concluded that although the individual

treatment session costs were lower for rTMS than ECT, the cost for a course of rTMS was not significantly different from that for a course of ECT as more rTMS sessions were given per course (18).

If the MMD prevalence is supposed to be 0.127 in Iranian population, the ICER results show that the ECT is more cost-effective than the rTMS. The ECT response rate, especially in the initial or intervention phase, is more than rTMS. The costs of both strategies are also not very different; and the ECT is more cost-effective than the rTMS. In addition, in the follow up (maintenance) phase, the remission rate for rTMS is supposed to be more than the ECT but in the total therapeutic phase the ECT is more effective.

Furthermore, the incremental cost-utility analysis showed that, the patients' quality of life has been changed after the ECT strategy more than the rTMS. So, the rTMS has greater cost-utility than the ECT. Although the ECT requires anesthesia and shock, more efficacy was resulted from the ECT in long term; and greater improvements in patients' living status may compensate these disadvantages. Generally, the ECT seems preferable to the rTMS.

Knapp et al. found that rTMS has a very low probability of being more cost-effective than ECT. Indeed, considering the cost of achieving an additional quality-adjusted life year, the cost-effectiveness of rTMS does not look 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) (15). On the other hand, McLoghlin et al. presented a more conservative conclusion and expressed that ECT is a more effective and potentially cost-effective antidepressant treatment than a 3 week rTMS. Optimal treatment parameters for rTMS need to be established for treatment of depression. More research is required to refine further administration of ECT in order to reduce associated cognitive side-effects while maintaining its effectiveness. There is a

need for large scale, adequately powered RCTs comparing different forms of ECT (18).

The sensitivity analysis shows that, if the MMD prevalence in Iranian population is 4.1%, the rTMS is more cost-effective than the ECT. Considering low prevalence of MMD, rTMS' lower costs compared with ECT have a more prominent role than the ECT with greater remission rate. In fact, it seems that the rTMS' lower cost compensates the ECT's greater remission rate.

Moreover, if the rTMS is provided by a public medical facility (such as public hospitals) the rTMS is more cost-effective than the ECT. As mentioned previously, the rTMS has lower costs than the ECT; if the rTMS is provided by a public medical facility, the costs will be reduced considerably and cover its lower response and remission rates.

According to the results of the sensitivity analysis on the key parameters, the response rate in the initial and follow up therapeutic phases showed that our results were adequately robust across a range of parameter values for both comparisons. If the costs of the rTMS reduces, the results will be change in favor of the rTMS. This is a common result that may occur in economic evaluation studies and it is related to natural uncertainty of the circumstances. Kozel et al. concluded that "If repetitive Transcranial Magnetic Stimulation (rTMS) were to be made widely available in the USA, it would offer a substantial economic benefit over electroconvulsive therapy (ECT) in treating resistant depression" (23).

Conclusion

Considering a low prevalence of MMD between Iranian populations, the rTMS is more cost-effective than ECT. If the costs of rTMS decrease through providing this service by a public medical facility, the rTMS is more cost-effective than the ECT.

Limitations

There are no accurate and comprehensive statistics about the MMD prevalence

among the Iranian population and the authors used the prevalence ratio that extracted from a systematic review in 2010 and expert's opinions. Also, in the costing process, the direct costs have been considered and the indirect cost including the productive loss costs have not been taken into account in this study.

Conflict of interest

The authors declared there is no conflict of interest.

Source of funding

This study was supported by the I.R. Iran's National Institute of Health Research, Tehran University of Medical Sciences as a part of The Health Technology Assessment of repetitive Transcranial Magnetic Stimulation versus Electroconvulsive Therapy in Major Depressive Disorder, Contract No: 241/M/91279.

References

1. Ebmeier KP, Donaghey C, Steele JD. Recent developments and current controversies in depression. *Lancet* 2006;367:153–167.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine* 2006;3:e442.
3. Murray CJL, Lopez AD, editors. 1996. The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge (Massachusetts): Harvard School of Public Health on behalf of the World Health Organization & the World Bank.
4. World Health Organization. 2008. The Global Burden of Disease: 2004 update. Switzerland. Available: http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en.
5. Mathers CD, Stein C, Fat D MA, Rao C, Inoue M, Tomijima N, et al. Global Burden of Disease 2000: version 2 methods and results. Geneva: World Health Organization. Available: <http://www.who.int/healthinfo/paper50.pdf>. 2002.
6. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJL, et al. Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease Study 2010. *PLoS Med* 2013;10(11):e1001547.
7. World Health Organization. Atlas: Mental health resources in the world 2005. World Health Organization, Geneva. Available at http://www.who.int/mental_health. 2005.
8. Sadeghirad B, Haghdoost AA, Amin-Esmacili M, Shahsavand Ananloo E, Ghaeli P, Rahimi-Movaghar A, et al. Epidemiology of Major Depressive Disorder in Iran: a Systematic Review and Meta-Analysis, *Int J Prev Med* 2010;1(2):81–91.
9. Naghavi M, Abolhassani F, Pourmalek F, MoradiLakeh M, Jafari N, Vaseghi S, et al. *opul Health Metr* 2009;7:9.
10. Shahrzad S, Forouzanfar MH, Sepanlou SG, Dicker D, Naghavi P, Pourmalek F, et al. Population health and burden of disease profile of Iran among 20 countries in the region: from Afghanistan to Qatar and Lebanon. *Arch Iran Med* 2014;17(5):336-342.
11. Berlim MT, van den Eynde F, Tovar-Perdomo S, Daskalakis ZJ. Response, remission and drop-out rates following high-frequency repetitive transcranial magnetic stimulation (rTMS) for treating major depression: a systematic review and meta-analysis of randomized, double-blind and sham-controlled trials, *Psychol Med* 2014;44:225-239.
12. Simpson KN, Welch MJ, Andrew Kozel F, Demitrack MA, Nahas Z. Cost-Effectiveness of Transcranial Magnetic Stimulation in the Treatment of Major Depression: a Health Economics Analysis, *AdvTher* 2009;26(3):346-368.
13. Berlim MT, Van den Eynde F, Daskalakis ZJ. Efficacy and Acceptability of high Frequency Repetitive Transcranial Magnetic Stimulation (rTMS) Versus Electroconvulsive Therapy (ECT) for Major Depression: A Systematic Review and Meta-Analysis of Randomized Trial. *Depress Anxiety* 2013;00:1–10.
14. UK ECT Review Group. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. *Lancet* 2003;361:799-808.
15. Knapp M, Romeo R, Mogg A, Eranti S, Pluck G, Purvis R, et al. Cost-effectiveness of transcranial magnetic stimulation vs. electroconvulsive therapy for severe depression: A multi-centre randomised controlled trial, *J Affect Disord* 2008;109:273-285.
16. Keshkar M, Ghazizadeh A, Firoozabadi A. Repetitive Transcranial Magnetic Stimulation Versus Electroconvulsive Therapy for the Treatment of Major Depressive Disorder, A Randomized Controlled Clinical Trial, *J ECT* 2011;27:4.
17. U.S. Food and Drug Administration. Neurological Devices Panel of the Medical Devices Advisory Committee. FDA Executive Summary. Available online at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4273b1_01-FDAExecutiveSummary.pdf. 2007.
18. McLoughlin DM, Mogg A, Eranti S, Pluck G, Purvis R, Edwards D. The clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depres-

sion: a multicentre pragmatic randomized controlled trial and economic analysis. *Health Technol Assess* 2007;11:24.

19. Iranian Statistics Centre, 2011, Iranian Population and Housing Census, available: <http://www.amar.org.ir/Default.aspx?tabid=765>. Access: July 2014.

20. Khosravi A, Najafi F, Rahbar MR, Motlagh MI, Kabir MJ. Health profile indicators in the Islamic Republic of Iran, Iranian Ministry, Tehran, Iran 2009:44.

21. Eranti S, Mogg A, Pluck G, Landau S, Purvis R, Brown RG, et al. A Randomized, Controlled Trial with 6-Month Follow-Up of Repetitive Transcranial Magnetic Stimulation and Electroconvulsive Therapy for Severe Depression. *Am J Psychiatry*

2007;164:73–81.

22. Fitzgerald PB, Hoy K, Gunewardene R, Slack C, Ibrahim S, Bailey M, et al. A randomized trial of unilateral and bilateral prefrontal cortex transcranial magnetic stimulation in treatment-resistant major depression. *Psychol Med* 2010;41:1187-1196.

23. Kozel FA, George MS, Simpson KN. Decision Analysis of the Cost-Effectiveness of Repetitive Transcranial Magnetic Stimulation versus Electroconvulsive Therapy for Treatment of Nonpsychotic Severe Depression. *CNS Spectr* 2004;9(6):476-482.

24. Prudic J, Olfson M, Marcus SC, Fuller RB, Sackeim HA. Effectiveness of electroconvulsive therapy in community settings. *Biol Psychiatry*. 2004;55:301-12.

Appendix

Appendix 1. The rTMS strategy costs components and description

Costs	Monetary value of costs	Description and source
Costs related to the device:		All costs were based on a self-report of a manager at rTMS private center, except for costs related to the depreciation that are based on tax laws of the country, the annual depreciation rate was 10%.
• Cost of purchase	90000000	
• Cost of deployment and commissioning	2000000	
• The annual cost of repair and service	80000	
• The annual cost of depreciation	9000000	
• Cost of special seat	600000	
• Cost of the noise reduction tool(two)	30000	
• Cost of cooling	2000000	
Total cost of the device	106710000	
Costs related to Human Resources:		Human resources costs were calculated only for psychiatrists. According to the Iran Health Insurance Organization, wages and expected earnings for a psychiatrist is equal to 10.5 million in 1392. It is for 250 working days and 6 hours per day. Also two sessions were considered for clinical psychologist and psychiatrist.
• Cost of per minute intervention by a psychiatrist.	2527	
• Cost for 10 sessions of 25-minute intervention by a psychiatrist.	631750	
• Costs of evaluation by a clinical psychologist	40400	
• Cost of evaluation by a psychiatrist	303600	
Total cost of Human Resources	975750	
Total cost of physical space	120000000	According to the rTMS center, About 12 meters of space were allocated or TMS. Other spaces were included a waiting room, service room, secretary location and a computer system and furniture. Also these spaces were used for other disorders, including sensory-motor disabilities, Parkinson, Bipolar disorder and Schizophrenia. But, approximately 70% of patients had major depression.
Annual energy costs	16800000	
Total costs for initial phase of treatment (10sessions of therapy, 4sessions of counseling)	975750	
Costs for Maintenance period (6months follow-up)		
• Three sessions of counseling by a psychiatrist	75900	
• Two sessions of counseling by a clinical psychologist (Depending on a psychiatrist recommendation)	40400	
• Cost of fluoxetine	9450	
Total cost of maintenance period (follow-up)	125750	
Total cost of initial treatment and maintenance phase by rTMS	1101500	

Appendix 2. The ECT strategy costs components and description

Costs	Monetary value of costs	Description and source
Costs related to the device:		
• Cost of purchase	11000000	
• The annual cost of depreciation and services	1100000	
Total cost of the device	12100000	
Costs related to Human Resources:		
• Annual salary of a psychiatrist	75000000	Wage was calculated for a psychiatrist, an anesthesiologist and a nurse in a private center in one year.
• Annual salary of an anesthesiologist	36000000	
• Annual salary of a nurse	15000000	
• Cost of examination by a psychiatrist	101200	
• Costs of care by a nurse	3182400	
Total cost of Human Resources	129283600	
Total cost of physical space		
• The cost of physical space allocated to ECT	120000000	About 14 meters of space were allocated to ECT. Of this cost, 20% is related to other costs including administrative space for ECT.
Annual energy costs	2920000	
Medication costs:		
• Cost of Thiopental sodium 5.2mg/kg	5300	This drug is injected as an anesthetic and a muscle relaxant.
• Cost of Esculin 1-1.5mg/kg	800	
Total cost of Medication	6100	
Costs of anesthesia:		
• Costs related to the respiratory devices	60000000	These costs include purchase of equipment, depreciation, energy and annual maintenance.
• Cost of monitoring devices	20000000	
• costs related to anesthesia Supplies	51600	
Total cost of anesthesia:	8051600	
Total costs of hospitalization:	5168000	Costs are related to hospitalization in a private hospital in 1392.
Total cost of treatment with ECT	360529300	
Cost of one session of ECT	123500	This cost is calculated by dividing the costs of treatment with ECT in 8 intervention sessions on 2920 hospital beds.
Cost of eight sessions of ECT	988000	
Costs for Maintenance period (6 months follow-up)		
• Cost of referring to a psychiatrist for 6 months after treatment	151800	The costs of 6-month follow-up period, including 6 sessions of psychiatric examination, daily use of Asentra and Lorazepam once every two days.
• Cost of Asentra 50mg	30600	
• Cost of Lorazepam 1mg	3870	
Costs for Maintenance period (6 months follow-up)	186270	
Total cost of treatment and maintenance phase by ECT.	1174270	