



Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic:	Transcranial magnetic stimulation for depression
Topic exploration report number:	TER247

Introduction and aims

Transcranial magnetic stimulation (TMS) is an intervention that involves the placement of an electromagnetic coil against the head. The coil sends repetitive pulses of magnetic energy at fixed frequency to specific areas of the brain. The stimulation can improve symptoms of depression and anxiety. Treatment is usually considered for patients with depression that has not responded to antidepressant medications or patients for whom antidepressant medication is not suitable.

Health Technology Wales researchers searched for evidence on transcranial magnetic stimulation for the treatment of depression.

Summary of evidence

Technology Assessment/Guidance

The National Institute for Health and Care Excellence (NICE) Interventional Procedures Guidance 542 on "Repetitive transcranial magnetic stimulation for depression" (NICE 2015) concludes that the evidence for the procedure show no major safety concerns and its efficacy in the short-term is adequate, although the clinical response is variable. For the evaluation of the clinical efficacy, NICE considered a number of systematic reviews of both randomised and non-randomised clinical trials as well as some sources of primary evidence. The guidance reports the following sources of secondary evidence:

- Slotema et al. (2010) - systematic review of 40 RCTs including 1592 patients with depression treated by repetitive TMS (rTMS) or sham stimulation. Their meta-analysis if the mean changes in unspecified depression rating scales showed a significant effect in favour of rTMS.
- Lepping et al. (2014) - systematic review of 63 studies including 3236 patients treated by rTMS, sham stimulation of electroconvulsive therapy (ECT). The review shows that for patients with any type of depression as well as for patients with treatment-resistant depression, there was a reduction in the Hamilton Depression Rating Scale (HDRS) in the

rTMS group in comparison to the sham stimulation group. However, when rTMS was compared against ECT in patients with any type of depression, the mean percentage reduction in HDRS score was reported to be higher in the ECT group.

- Zhang et al. (2015) - systematic review of ten RCTs including 634 patients with treatment-resistant depression treated by bilateral rTMS, unilateral rTMS or sham stimulation. The meta-analysis of the clinical response rates in patients treated by bilateral rTMS or sham stimulation favoured the intervention with bilateral rTMS. Within the same study, the meta-analysis of the remission data showed no significant difference between patients treated with bilateral rTMS or sham stimulation.
- Ren et al. (2014) - systematic review of ten RCTs including 429 patients with a primary major depressive episode treated by rTMS or ECT. The meta-analyses of clinical response data and remission data showed that the intervention favoured the treatment with ECT.

The authors acknowledge that their literature search identified a large number of systematic reviews, RCTs, non-randomised comparative studies and case series that could be potentially relevant for this topic.

The EUnetHTA OTCA05 rapid assessment of “Repetitive transcranial magnetic stimulation for treatment-resistant major depression” (EUnetHTA 2017) evaluated the clinical effectiveness and safety of interventions with rTMS for treatment-resistant major depressive disorder that does not respond satisfactorily to at least two trials of antidepressant monotherapy in comparison to sham stimulation or ECT. For the comparison of rTMS vs sham, the authors identified 25 studies covering a population of 1180 participants. Only six studies that use ECT as a comparator were found covering a population of 266 participants. The authors conclude that the body of evidence indicates that rTMS is generally safe and well-tolerated but it has a short-term effect for improving depression in comparison with sham, with follow-up studies not showing that the small effect continues for longer periods. They also highlight that the evidence is not sufficient to prove if rTMS is as effective and safe as ECT although rTMS patients had less and not clinically relevant decreases in depression scores as compared to ECT patients.

Areas of uncertainty

A large body of relevant evidence was found on the effectiveness of TMS for the treatment of depression. However, there are uncertainties regarding the following aspects and these will be explored in full during appraisal:

- More clarity is needed in order to decide the population potentially suitable for TMS. In particular, what constitutes “major depression disorder” and what previous treatments would be tried before TMS.
- Similarly, in the majority of studies, TMS was compared to ECT, or no further treatment. It is not known what represents standard care in Wales. In cases of no further treatment, the intervention could be used as a standalone or in combination with pharmaceutical treatment.
- One TMS device (Magstim Horizon TMS Therapy systems) is confirmed as having relevant regulatory approval. It is unclear any other TMS devices are CE-marked and what evidence exists to support the use of different devices.

Conclusions

The body of evidence found is extensive and suggests that TMS could be an effective intervention for the treatment of depression, although some evidence reported clinically non-significant results compared to other treatments. From the last technology assessment presented in the context of this review (2017), it is possible that the body of evidence expanded and a further evaluation could be feasible in order to determine the clinical and cost-effectiveness of interventions with TMS for the treatment of depression or to identify the best suited populations that could benefit of such interventions.

Brief literature search results

Resource	Results
HTA organisations	
Healthcare Improvement Scotland	We did not identify any relevant guidance from this source.
Health Technology Assessment Group	We did not identify any relevant evidence from this source.
Health Information and Quality Authority	We did not identify any relevant guidance from this source.
EUnetHTA	EUnetHTA. (2017). Repetitive transcranial magnetic stimulation for treatment-resistant major depression. Rapid assessment of other technologies OTCA05. Diemen (The Netherlands): EUnetHTA. Available at: https://eunetha.eu/wp-content/uploads/2018/01/OTCA05_Repetitive-transcranial-magnetic-stimulation-for-TRD.pdf [Accessed March 31].
International HTA Database	Ontario Health - Repetitive transcranial magnetic stimulation (rTMS) for people with treatment-resistant depression. Anticipated publish date in 2021.
UK guidelines and guidance	
SIGN	We did not identify any relevant evidence from this source.
NICE	NICE. (2015). Repetitive transcranial magnetic stimulation for depression [IPG542]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ipg542/ [Accessed 31.03.2021].
Secondary literature and economic evaluations	
https://www.epistemonikos.org/en/	Not searched due to the large body of suitable evidence already identified in the previous searches conducted.
https://www.tripdatabase.com/	Not searched due to the large body of suitable evidence already identified in the previous searches conducted.
Cochrane library	Rodriguez-Martin JL, Barbanoj JM, Schlaepfer TE, et al. (2002). Transcranial magnetic stimulation for treating depression. Cochrane Database of Systematic Reviews. (2). doi: 10.1002/14651858.CD003493
Medline	Lepping P, Schönfeldt-Lecuona C, Sambhi RS, et al. (2014). A systematic review of the clinical relevance of repetitive transcranial magnetic stimulation. Acta psychiatrica scandinavica. 130(5): 326-41. Ren J, Li H, Palaniyappan L, et al. (2014). Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: a systematic review and meta-analysis. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 51: 181-9. Slotema CW, Blom JD, Hoek HW, et al. (2010). Should we expand the toolbox of psychiatric treatment methods to include Repetitive Transcranial Magnetic Stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. The Journal of clinical psychiatry. 71(7): 873-84. Zhang Y, Zhu D, Zhou X, et al. (2015). Bilateral repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and meta-analysis of randomized controlled trials. Brazilian Journal of Medical and Biological Research. 48(3): 198-206.
Primary studies	
https://www.epistemonikos.org/en/	Not searched due to the large body of suitable evidence already identified in the previous searches conducted.
https://www.tripdatabase.com/	Not searched due to the large body of suitable evidence already identified in the previous searches conducted.
Cochrane library	We did not identify any additional relevant primary evidence from this source.

Medline	Not searched due to the large body of suitable evidence already identified in the previous searches conducted.
Ongoing primary or secondary research	
PROSPERO database	Leandro Valiengo Valiengo, Sara Vacas, Ana Maia, André Brunoni, Orestes Forlenza, Albino J. Oliveira-Maia. Transcranial magnetic stimulation for major depression in the elderly: study protocol for a systematic review with meta-analysis and meta-regression. PROSPERO 2017 CRD42017079619 Available from: https://www.crd.york.ac.uk/prospERO/display_record.php?ID=CRD42017079619
Clinicaltrials.gov	A large body of ongoing/completed clinical trial that could be potentially relevant for this topic have been identified.
Other	
Evidence provided by topic proposer	NICE. (2015). Repetitive transcranial magnetic stimulation for depression [IPG542]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ipg542/ [Accessed 31.03.2021].
Evidence used for background	NHS. (2019). Treatment - Clinical depression. Online. Available at: https://www.nhs.uk/mental-health/conditions/clinical-depression/treatment/ [Accessed 31 March].

Date of search:	March 2021
Concepts used:	Transcranial magnetic stimulation AND depression