

Repetitive transcranial magnetic stimulation for depression

Interventional procedures guidance

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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with

those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

This guidance replaces IPG242.

1 Recommendations

- 1.1 The evidence on repetitive transcranial magnetic stimulation for depression shows no major safety concerns. The evidence on its efficacy in the short-term is adequate, although the clinical response is variable. Repetitive transcranial magnetic stimulation for depression may be used with normal arrangements for clinical governance and audit.
- 1.2 During the consent process, clinicians should, in particular, inform patients about the other treatment options available, and make sure that patients understand the possibility the procedure may not give them benefit.
- 1.3 NICE encourages publication of further evidence on patient selection, details of the precise type and regime of stimulation used, the use of maintenance treatment and long-term outcomes.

2 Indications and current treatments

- 2.1 Depression is a common disorder that can have a debilitating effect on a person's life. It is characterised by persistent sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep, appetite and libido, tiredness and poor concentration. It is also often accompanied by feelings of hopelessness and suicidal thoughts, and can lead to suicide. Depression can last from weeks to years, and can be recurrent. It can substantially impair an individual's ability to

function at work or cope with daily life. Treatments for depression include a range of psychological therapies and antidepressant medications. In severe depression that has not responded to other treatments, electroconvulsive therapy is sometimes used.

3 The procedure

- 3.1 Repetitive transcranial magnetic stimulation (rTMS) does not need anaesthesia and can be done on an outpatient basis. A purpose-made electromagnetic coil is held against the scalp with the intention of inducing electric currents in the cerebral cortex. Imaging may be used to help target specific areas of the brain. Treatment is usually considered for patients with depression that has not responded to antidepressant medication or patients for whom antidepressants are not suitable.
- 3.2 In rTMS, repetitive pulses of electromagnetic energy are delivered at various frequencies or stimulus intensities. Conventional rTMS is a repetition of individual pulses at a pre-set interval (train of pulses), whereas theta-burst rTMS is a repetition of short bursts of pulses at a pre-set interval (train of bursts). Stimulation can either be delivered unilaterally, over the left or right dorsolateral prefrontal cortex, or bilaterally over both cortices. Bilateral stimulation may be done sequentially or simultaneously. Treatment with rTMS usually comprises daily sessions lasting about 30 minutes, typically for 2 to 6 weeks.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a systematic review of 40 randomised controlled trials including 1592 patients with depression (type unspecified) treated by repetitive transcranial magnetic stimulation (rTMS, n=751) or sham stimulation (n=632), meta-analysis of mean changes in unspecified depression rating scales showed a significant effect in

favour of rTMS (Hedges' g value of 0.55, $p < 0.001$).

- 4.2 In a non-randomised comparative study of 185 patients with treatment-resistant depression treated by conventional rTMS ($n=98$) or theta-burst rTMS ($n=87$), Hamilton Depression Rating Scale (HDRS) scores (lower scores indicate less depression) decreased from 22.1 ± 6.9 to 12.3 ± 8.9 and from 21.1 ± 5.1 to 12.7 ± 7.9 respectively at 1-month follow-up (p value within groups < 0.001 , p value between groups not significant). In the same study, Beck Depressive Inventory scores (scores range from 0 to 63, with lower scores indicating less depression) decreased from 35.4 ± 10.8 to 22.4 ± 15.5 in the conventional rTMS group and from 35.9 ± 9.9 to 20.2 ± 13.3 in the theta-burst rTMS group at 1-month follow-up (p value within groups < 0.001 , p value between groups not significant).
- 4.3 In a systematic review of 63 studies including 3236 patients treated by rTMS ($n=2330$), sham stimulation ($n=806$) or electroconvulsive therapy (ECT; $n=100$), percentage changes in HDRS scores (lower scores indicate less depression) were pooled and converted to Clinical Global Impression – Improvement scale (CGI-I) scores. CGI-I scores range from 1 to 7: a score of 4 means no change, scores of less than 4 indicate improvements in depression and scores of more than 4 indicate worsening depression. For patients with any type of depression, the mean percentage reduction in HDRS scores was 37% (CGI-I equivalent 2.8) in the rTMS group and 22% (CGI-I equivalent 3.4) in the sham stimulation group ($p < 0.05$). For patients with treatment-resistant depression, the mean percentage reduction in HDRS scores was 48% (CGI-I equivalent 2.4) in the rTMS group and 23% (CGI-I equivalent 3.4) in the sham stimulation group ($p < 0.05$). When rTMS was compared against ECT in patients with any type of depression, the mean percentage reduction in HDRS scores was 34% (CGI-I equivalent not reported) in the rTMS group and 46% (CGI-I equivalent 2.45) in the ECT group ($p < 0.05$).
- 4.4 In a systematic review of 10 randomised controlled trials including 634 patients with treatment-resistant depression treated by bilateral rTMS, unilateral rTMS or sham stimulation, clinical response data (defined as more than a 50% improvement in HDRS or Montgomery–Åsberg Depression Rating Scale scores) were compared between groups. Meta-analysis of clinical response rates in patients treated by bilateral rTMS or sham stimulation revealed a risk ratio of 3.29 in favour of bilateral rTMS (95% confidence interval [CI] 1.69 to 6.38, $p=0.0004$). In the same study, meta-analysis of remission data (classified according to

predefined criteria in each included study) revealed no significant difference between patients treated by bilateral rTMS or sham stimulation (risk ratio 0.5; 95% CI 0.19 to 1.31, $p=0.16$).

- 4.5 In a systematic review of 10 randomised controlled trials including 429 patients with a primary major depressive episode treated by rTMS ($n=217$) or ECT ($n=212$), meta-analysis of clinical response data (defined as more than a 50% improvement in HDRS scores) revealed a risk ratio of 1.52, in favour of ECT (95% CI 1.18 to 1.95, $p=0.001$). Meta-analysis of remission data (classified according to predefined criteria in each included study) revealed a risk ratio of 1.42 in favour of ECT (95% CI 1.16 to 1.75, $p=0.0007$).
- 4.6 A case series evaluated 120 patients who had at least a partial response (that is, at least a 25% improvement in HDRS scores); 99 patients were recruited from the active rTMS arm of a randomised sham-controlled trial, while 21 patients initially had sham stimulation and subsequently received active rTMS. For patients originally in the active rTMS arm of the trial, the mean HDRS score was 9.1 ± 6.2 at the end of rTMS therapy and 9.0 ± 7.1 at 6-month follow-up ($p=0.537$), indicating a maintained treatment effect. No pre-treatment scores were reported. No mean HDRS scores were reported for patients who initially had sham stimulation and subsequently received active rTMS. In the same study, the relapse rate (Kaplan–Meier estimate) at 6-month follow-up was 13% in patients who were originally in the active rTMS arm of the trial and 16% in patients who initially had sham stimulation and subsequently received active rTMS (no p value reported).
- 4.7 Specialist advisers listed improvements in depressive symptoms and health-related quality of life as efficacy outcomes.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 A self-limiting complex partial seizure was reported in 1 patient who had unilateral repetitive transcranial magnetic stimulation (rTMS), at a frequency of 20 Hz and

- at 110% of the motor threshold. The patient was awake after 8 seconds; she was alert with no postictal confusion and had no memory of what happened. No subsequent physical sequelae were reported.
- 5.2 A hypomanic episode was reported in 1 patient, soon after completion of therapy, in a randomised controlled trial of 130 patients treated by 1 Hz or 2 Hz rTMS. The exact timing of occurrence was not reported.
- 5.3 Headache was reported in 10% (46/472) of patients treated by high-frequency rTMS, 4% (4/109) treated by low-frequency rTMS and 3% (12/461) given sham stimulation in a systematic review of 40 randomised controlled trials that included 1592 patients with depression (type unspecified).
- 5.4 Scalp discomfort was reported in 9% (45/472) of patients treated by high-frequency rTMS, 2% (2/109) treated by low-frequency rTMS and 2% (9/461) given sham stimulation in the systematic review of 40 randomised controlled trials that included 1592 patients with depression (type unspecified).
- 5.5 Pain at the rTMS application site was reported in 6% (6/99) of patients in a case series of 120 patients with major depressive disorder treated by rTMS.
- 5.6 Facial twitching was reported in 2% (9/472) of patients treated by high-frequency rTMS, none treated by low-frequency rTMS (n=109) and none given sham stimulation (n=461) in the systematic review of 40 randomised controlled trials that included 1592 patients with depression (type unspecified).
- 5.7 Local erythema was reported in 1% (6/472) of patients treated by high-frequency rTMS, none treated by low-frequency rTMS (n=109) and none given sham stimulation (n=461) in the systematic review of 40 randomised controlled trials that included 1592 patients with depression (type unspecified).
- 5.8 Drowsiness was reported in 3% (12/472) of patients treated by high-frequency rTMS, none treated by low-frequency rTMS (n=109) and none given sham stimulation (n=461) in the systematic review of 40 randomised controlled trials that included 1592 patients with depression (type unspecified).
- 5.9 Vertigo was reported in no patients in the conventional rTMS (n=98) group and

- 1 patient in the theta-burst TMS group (n=87) in a non-randomised comparative study of 185 patients with treatment resistant depression.
- 5.10 Increasingly hostile thoughts were reported in no patients in the conventional rTMS group (n=98) and 1 patient in the theta-burst rTMS group (n=85) in the non-randomised comparative study of 185 patients with treatment-resistant depression. The timing of occurrence was not reported.
- 5.11 Device-related insomnia was reported in 1 patient in the case series of 120 patients with major depressive disorder treated by rTMS.
- 5.12 Device-related arthralgia was reported in 1 patient in the case series of 120 patients with major depressive disorder treated by rTMS.
- 5.13 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: discomfort, unpleasant twitching, worsening psychomotor agitation in patients with mixed affective disorder, transient confusion, transient problems with concentration and/or working memory, and transient hearing loss. They did not suggest any theoretical adverse events.

6 Committee comments

- 6.1 The Committee recognised the difficulties in conducting research on repetitive transcranial magnetic stimulation (rTMS) for depression, in the context of the variable natural history of depression, the challenges of providing sham treatment, and a variable and often small response. Despite large numbers of patients in the published studies, there were difficulties in assessing the effect size. Nevertheless, the Committee noted consistently positive outcomes in many studies and a good safety profile. These considerations underpinned the recommendations in 1.1 and 1.2.
- 6.2 The Committee was advised that the procedure may not be appropriate for treating some kinds of depression and that patient selection is therefore most

important.

6.3 The Committee noted that commentary from patients was positive and described significant benefits to their quality of life, including the advantages, for some patients, of being able to stop the use of oral antidepressant medications.

6.4 The Committee was informed that the technology is evolving.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).