MEDICAL POLICY

Medical Policy Title	**Transcranial Magnetic Stimulation**
Policy Number	**3.01.09**
Current Effective Date	**January 23, 2025**
Next Review Date	**January 2026**

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

POLICY STATEMENT(S)

I. An initial course of transcranial magnetic stimulation (TMS) is considered **medically appropriate** as a treatment for major depressive disorder severe when **ALL** of the following have been met:

A. Aged 18 years or older;

B. Confirmed diagnosis of major depressive disorder severe (single or recurrent), documented by standardized rating scales that reliably measure depressive symptoms;

C. Documented failure of at least one (1) antidepressant medication in the current treatment episode, and any **ONE** of the following:

1. Failure of (4) four trials of psychopharmacologic agents, including (2) two different antidepressant agent classes and (2) two augmentation trials. (see Policy Guidelines);

2. Inability to tolerate a therapeutic dose of medications, as evidenced by (4) four trials of psychopharmacologic agents with distinct side effects; or

3. Is a candidate for electroconvulsive therapy (ECT), and ECT would not be clinically superior to repetitive TMS (rTMS) (e.g., in cases involving psychosis, acute suicidal risk, catatonia or life-threatening inanition, rTMS should NOT be utilized)

D. An adequate trial of evidence-based psychotherapy known to be effective in the treatment of major depressive disorder, without significant improvement in depressive symptoms, as documented by standardized rating scales that reliably measure depressive symptoms;

E. Absence of an absolute contraindication to TMS, and relative contraindications (if applicable) were assessed and deemed safe for administering TMS (refer to Policy Guideline IV).

F. TMS is administered by a U.S. Food and Drug Administration (FDA) cleared device and treatment modality, in accordance with the FDA label indications.

II. Repeat course of TMS is considered **medically appropriate** for the treatment of major depressive disorder severe when **ALL** of the following criteria are met:

A. All criteria for initial course of TMS treatment were met (see Policy Statement I);

B. Documentation of a new episode of severe major depression, as documented by standardized rating scales;

C. The member responded to prior treatments, as evidenced by a greater than 50% improvement in standard rating scale measurements for depressive symptoms;

D. It has been at least three (3) months since the end of the initial TMS treatment course.

E. TMS is administered by an FDA cleared device and treatment modality, in accordance with the FDA label indications.

III. TMS as a treatment for major depressive disorder that does not meet all the above criteria is considered **not medically necessary.**

IV. TMS sessions beyond the standard course of 36 sessions, either as continuation of initial acute course or as maintenance therapy is considered **investigational**.

V. TMS is considered **investigational** as a treatment for all other psychiatric and/or neurological disorders, including, but not limited to, bipolar disorder, borderline personality disorder, schizophrenia, obsessive-compulsive disorder (OCD), substance-related and addictive disorders (e.g., alcohol, caffeine, cannabis, tobacco, gambling), migraine headaches, or stroke.

RELATED POLICIES

Corporate Medical Policy:

1.01.55 Electrical Stimulation for Pain and Other Medical Conditions

3.01.13 Ketamine Therapy for the Treatment of Psychiatric Disorders

8.01.07 Tinnitus Treatment

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

I. Contraindications of TMS include the following:

A. Absolute:

1. presence of ferromagnetic or magnetic sensitive metal in the head or neck areas in close proximity to the TMS coil magnetic fields (e.g., metal/bullet fragments, cochlear implants, brain stimulators or electrodes, aneurysm clips or coils, vagus nerve stimulator);

2. presence of acute or chronic psychotic symptoms or disorders (e.g., schizophrenia, schizophreniform or schizoaffective disorder) in the current depressive episode.

B. Relative:

1. implanted cardiac pacemaker or implantable cardiac defibrillator (ICD);

2. history of seizures with increased risk of seizure);

3. neurologic conditions (e.g., epilepsy, cerebrovascular disease, dementia, increased intracranial pressure, history of repetitive head trauma or with primary or secondary

tumors in the central nervous system;

4. presence of a brain lesion (vascular, traumatic, neoplastic, infectious, or metabolic.

II. The recommended conventional/standard TMS treatment course protocols are FDA approved and involve high-frequency repetitive TMS (rTMS) treatments sessions daily over five days per week for up to six weeks, followed by an optional six treatment taper, for a total of 36 sessions.

III. Intermittent theta burst stimulation (iTBS) is an FDA approved accelerated TMS protocol for the treatment of refractory depression. The Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) protocol (also known as Stanford Neuromodulation therapy [SNT]) is an example of an accelerated iTBS treatment protocol, consisting of ten (10) daily sessions over five (5) consecutive days.

IV. Standardized rating scales considered reliable in rating depressive symptoms include validated depression monitoring scales such as: Geriatric Depression Scale (GDS); Personal Health Questionnaire Depression Scale (PHQ-9); Beck Depression Scale (BDI); Hamilton Rating Scale for Depression (HAM-D); Montgomery Asberg Depression Rating Scale (MADRS); Quick Inventory of Depressive Symptomatology (QIDS); and Inventory for Depressive Symptomatology Systems Review (IDS-SR).

V. When requesting TMS providers are required to submit documentation of medication trials, including the approximate dates and duration, dosing, and side effects, adequate trial of medication is based on a combination of duration, dosage, tolerance, and efficacy of medication. Duration is usually four to six weeks, as evidenced by the STAR*D trial.

VI. Augmentation trials may include co-administration of two antidepressants or treatment with one antidepressant and another agent known to improve outcomes in the treatment of depression.

VII. TMS must be performed by physicians who are adequately trained and experienced in the specific techniques used. The order for treatment (or re-treatment) should be written by a physician (MD or DO) who has examined the patient and reviewed the record. The treatment must be given under the direct supervision of the ordering physician, i.e., the physician must be in the area and be immediately available.

VIII. Motor threshold is initially assessed during the first treatment session. This allows for individualization of the intensity of stimulation. It is not medically necessary to check motor threshold at every treatment, but motor threshold may be reassessed if there is concern that it may have changed (e.g., change in medication). Requests for multiple motor thresholds during the course of rTMS treatment will require documentation to support medical necessity.

IX. Complementary/adjunct treatments (i.e., ketamine hydrochloride injection) are being investigated for the benefit-risk profile and safe-use conditions in the treatment of psychiatric disorders, including use with TMS. The U.S. Food and Drug Administration (FDA) has not determined the safety or efficacy of ketamine for the treatment of a psychiatric disorder(s) and is considered off-label use (FDA, 2023).

DESCRIPTION

Transcranial magnetic stimulation (TMS) is a noninvasive technique of delivering electrical stimulation to the brain. The technique involves the placement of a small coil over the scalp and passing a rapidly alternating current through the coil wire. The electrical current produces a magnetic field that passes unimpeded through the scalp and bone and stimulates neuronal function. TMS can be performed in an office setting, as it does not require anesthesia and does not induce a convulsion.

Repetitive TMS (rTMS) involves the delivery of repeated magnetic pulses, via an electromagnetic coil, to stimulate nerve cells in the region of your brain involved in mood control and depression. Deep TMS (dTMS) employs an H-coil helmet design to encompass and stimulate a broader surface area and deeper brain structures than conventional rTMS. Theta burst stimulation (TBS) is a form of rTMS where magnetic pulses are applied in bursts at a higher frequency and repeated at shorter intervals than conventional rTMS. TBS may be delivered as intermittent (iTBS) or continuous (cTBS) magnetic pulses. Accelerated TMS (aTMS) treatment protocol delivers more than one daily TMS session to reduce to treatment length and improve response time.

Continued and maintenance TMS treatment beyond the standard protocol of 36 sessions is being investigated as a treatment option to maintain improvement and/or prevent lapse following a full intensive course of TMS.

TMS is being investigated as a treatment option for other indications, including, but not limited to, schizophrenia, obsessive-compulsive disorder, bulimia, epilepsy, Parkinson's disease, Tourette's syndrome, migraines, chronic pain syndromes, and fibromyalgia.

SUPPORTIVE LITERATURE

TMS for Adults with Major Depression

The evidence for TMS in patients who have treatment-resistant depression includes numerous double-blind, randomized, sham-controlled, short-term trials. The evidence is sufficient to determine that TMS results in a meaningful improvement in net health outcomes and may be considered a treatment option in patients with treatment-resistant depression who meet specific criteria.

Lam and colleagues (2008) conducted a meta-analysis of 24 randomized, controlled trials (RCTs) comparing active versus sham repetitive TMS (rTMS) in patients with treatment-resistant depression, although there were varying definitions of treatment-resistant depression. Remission was reported for 17% of active rTMS and 6% of sham rTMS patients. The largest study (23 study sites) included in the meta-analysis was a double-blind, multi-center trial with 325 treatment-resistant depression patients randomized to daily sessions of high-frequency active or sham rTMS of the left dorsolateral prefrontal cortex. Loss to follow-up was similar in the two groups, with 301 (92.6%) patients completing at least one post-baseline assessment and an additional 8% of patients from both groups dropping out before the four-week assessment. Intent-to-treat analysis showed a trend favoring the active rTMS group in the primary outcome measure (two points on the Montgomery-Asberg Depression Rating Scale; $p = 0.057$) and a modest (two-point), but significant, improvement over sham treatment on the HAM-D. The authors reported that, after six weeks of treatment, the subjects in the active rTMS

group were more likely to have achieved remission than the sham controls (14% vs. 5%), although this finding is limited by loss to follow-up.

Kedzior and colleagues (2015) conducted a meta-analysis to examine durability of the antidepressant effect of high frequency rTMS of the left DLPFC in the absence of maintenance treatment. Included were double-blind, randomized, sham-controlled trials with a total of 495 patients. The range of follow-up was one to 16 weeks, but most studies only reported follow-up to two weeks. The overall effect size was small, with a standardized mean difference (SMD; Cohen's d) of -.48, and the effect sizes were lower in RCTs with eight- to 16-week follow-up (d = -.42) than with 1- to 4-week follow-up (d = -0.54). The effect size was higher when antidepressant medication was initiated concurrently with rTMS (5 RCTs, d = -.56) than when patients were on a stable dose of medication (9 RCTs, d = -.43) or were unmedicated (2 RCTs, d = -.26).

Blumberger and colleagues (2018) published findings from a multi-center, randomized, non-inferiority trial (THREE-D) that compared 10-Hz rTMS with iTBS. Between 2013 and 2016, 414 patients with treatment-resistant major depressive disorder were enrolled and randomized to four to six weeks of rTMS (n=205) or iTBS (n=209). Treatment resistance was defined as failure to tolerate two or more antidepressant trials of inadequate dose and duration or no clinical response to one antidepressant trial of an adequate dose and duration. Patients who failed more than three antidepressant trials of adequate dosage were excluded from the trials. Patients could alter their medication during this trial. Treatment with rTMS (37 minutes) and iTBS (three minutes) was delivered five times per week for four to six weeks. The primary outcome measure was the 17-item HAM-D, for which scores for patients treated with rTMS improved by 10.1 points and scores for patients treated with iTBS improved by 10.2 points (adjusted difference, 0.103; lower 95% CI, -1.16; p=0.001). Treatment with iTBS resulted in a higher self-rated intensity of pain (mean score, 3.8) than treatment with rTMS (mean score, 3.4; p=0.011). Headache was the most common treatment-related adverse event for both groups (rTMS=64% [131/204]; iTBS=65% [136/208]). Serious adverse events were noted in patients treated with rTMS (one case of myocardial infarction) and iTBS (one case each of agitation, worsening suicidal ideation, worsening depression); there was no significant difference in the number of adverse events in the two groups. The trial lacked a treatment group with placebo.

Cole and colleagues (2020) studied the Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) protocol in an open-label clinical trial to evaluate the use of intermittent theta burst stimulation (iTBS) treatment using functional connectivity MRI (fcMRI)-guided targeting to delivery treatment. Participants (n=21) received 60 cycles of ten bursts of three pulses at 50 HZ. Ten sessions were applied per day (18,000 pulses/day) for five consecutive days with the overall pulse dose being five times greater than the FDA-approved iTBS protocol (18,000 pulses in six weeks). On average, the participants met the standard response criteria in 2.30 days of SAINT (equivalent to approximately 23 ten-minute sessions). Despite the small sample size, significant reductions in suicidality were noted using the Columbia Suicide Severity Rating Scale, suicidal ideation subscale (C-SSRS) (p<0.001). The response rate (a reduction of 50% or greater improvement from baseline) was 90.48%, all responders were in remission immediately following the SAINT protocol and 70% remained in remission one month following treatment. In the intent-to-treat group, 86.4% met remission, and 80-100% of participants remained in remission one month after treatment completion. It was identified that participants with a history of conventional rTMS nonresponse took more time to

reach a response; however, 83% responded by the end of the 5-day protocol. There were no adverse events or negative cognitive effects on any neuropsychological batteries following treatment with the SAINT protocol. The authors recommend larger RCTs to confirm results, concluding that the study demonstrated that the iTBS protocol is preliminarily safe, feasible, and associated with high rate of remission from depression.

In 2021, a systematic review and meta-analysis that comprised of ten RCTs comparing TBS to sham treatment, and the Blumberger study comparing TBS to conventional rTMS (Voigt 2021). The studies included 667 patients with a diagnosis of major depressive disorder. The authors compared the response rates and found that TBS was superior to sham on response and that there was no statistically significant difference between TBS and conventional rTMS, including the incidence of adverse events. The authors concluded that the positive outcomes and the noninferiority of TBS versus standard rTMS, support the continued development of TBS for the treatment of depression.

Ontario Health (2021) conducted a technology assessment to evaluate the effectiveness, safety, cost-effectiveness, and the budgetary impact if rTMS was to be publicly funded. The study included ten systematic reviews which incorporated 58 primary studies and one network meta-analysis. Inclusion criteria were adults 18 years of age and older with treatment resistant depression who had received any of seven rTMS modalities: low-frequency (1Hz) stimulation, high-frequency (10-20 Hz), unilateral stimulation, bilateral stimulation, iTBS, and deep TMS and then measured changes from baseline in depression scores, remission rate, response rate (defined as ≥50% reduction in depression score), relapse rate, and adverse events. Most rTMS modalities were more effective than sham treatment for all outcomes, and all rTMS modalities were similar to one another in response and remission rates (which are similar to ECT response and remission rates). Additionally, the authors highlighted that rTMS or iTBS, followed by ECT for patients who did not respond to initial pharmacological treatment were less expensive and more effective than ECT alone.

Cole and colleagues (2022) conducted a double-blind randomized sham-controlled study (n=14 active group; n=15 sham group) to evaluate the antidepressant efficacy of the accelerated Stanford Neuromodulation Therapy (SNT) protocol, also known as the SAINT protocol, which delivers intermittent theta burst stimulation (iTBS). Before starting iTBS treatment sessions, each participant underwent a structural MRI and resting-state functional MRI (fMRI). Participants diagnosed with major depressive disorder received 10 sessions of active or sham iTBS, delivered daily for five consecutive days, for a total of 18,000 pulses per day. Stimulation was delivered at 90% of resting motor threshold, adjusted for depth of the identified functional connectivity MRI (fcMRI) target. The trial was halted at the midpoint since the planned interim analysis demonstrated a large effect size of active compared with sham treatment (d>0.8). A large antidepressant effect of SNT was observed, with 79% of participants in the active SNT group (11 of 14 participants) achieving remission from their depressive episodes at some point during the 4-week follow-up, compared with 13% (two of 15 participants) in the sham treatment group. No severe adverse events occurred during the trial. A greater incidence of headache was reported in the active SNT group compared with the sham treatment group. Study limitations include a small sample size, single study site, and 45% of participants had comorbid psychiatric diagnoses. The authors concluded that the SNT protocol induced a significantly greater reduction in depressive symptoms than an identical course of sham stimulation after 5 days of treatment in a treatment resistant sample. The authors concluded that

studies will be needed that compare the efficacy of SNT parameters with and without fcMRI-guided targeting to determine the importance of this targeting method.

Maintenance TMS for Adults with Major Depression

A variety of maintenance schedules are currently being studied, with the role of maintenance TMS not been fully established and high heterogeneity in administration between studies.

Fitzgerald and colleagues (2013) reported a prospective, open-label trial of clustered maintenance rTMS for patients with treatment-resistant depression. All patients had received a second successful course of rTMS following relapse and were then treated with monthly maintenance therapy consisting of five rTMS treatments over a 2.5-day period (Friday evening, Saturday, and Sunday). Of 35 patients, 25 (71%) relapsed at a mean of 10.2 months (range, 2- 48 months).

In 2014, Dunner and colleagues reported one-year follow-up with maintenance therapy from a large, multi-center observational study (42 sites) of rTMS for patients with treatment-resistant depression. A total of 257 of the 307 patients initially studied who were treated with rTMS agreed to participate in the follow-up study. Of these, 205 patients completed the 12-month follow-up, and 120 patients met the Inventory of Depressive Symptoms-Self Report response or remission criteria at the end of treatment. Ninety-three of the 257 patients (36.2%) who enrolled in the follow-up study received additional rTMS (mean, 16.2 sessions). Seventy-five of the 120 patients (62.5%) who met response or remission criteria at the end of the initial treatment phase (including a two-month taper phase) continued to meet response criteria through follow-up.

Two RCTs investigated outcomes of maintenance TMS sessions, concluding that periodic TMS appears feasible in some cases, but once-monthly TMS is not superior to “watchful waiting” (Philip et al., 2016) and rTMS could represent a novel strategy for preventing relapse in treatment resistant depression (Benadhira 2017). Further studies are needed to confirm the benefits of rTMS maintenance and to clarify effectiveness and feasibility.

D’Andrea and colleagues (2023) report that the role of maintenance TMS has not been fully established and there is a lack of global consensus on how a maintenance protocol should be carried out. The authors conducted a systematic review to identify, characterize, and evaluate the current maintenance TMS protocols for patients diagnosed with major depressive disorder (MDD) and treatment resistant depression. Literature published through March 2022 yielded 14 eligible articles (3 randomized sham-controlled trial, 8 open label studies, 2 case reports, 1 case series).

The authors found that most included studies highlighted the significant efficacy of maintenance protocols in decreasing relapse risk; however, with a wide heterogeneity of maintenance protocols applied the authors found it difficult to unequivocally identify which parameters can mostly affect the capacity of maintenance TMS to prevent relapses. Included studies started maintenance TMS from one week to one month after acute treatment and had a wide difference in duration of maintenance protocols spanning from 12 weeks to more than one year. The risk of study bias included three low risk, four moderate risk, and three studies with severe risk of bias. This systematic review found the risk of relapse was most pronounced after five months from the acute treatment and no superior efficacy has been observed in different RCTs involving left, right, or bilateral dorsolateral prefrontal cortex (DLPFC) acute stimulation. The author found no available evidence about the type of

maintenance protocol (i.e., cluster rTMS, tapering rTMS, continuous rTMS, or rescue rTMS) able to guarantee higher levels of effectiveness; however, it was stated that cluster and continuous rTMS studies seem to exhibit lower risks of relapse compared to the others maintenance protocols. Limitations include small sample sizes (range n=1 to 281 subjects) and a small number of studies, which makes the results still inconclusive per the authors. Despite a lack of randomization and the heterogeneity of studies in the current literature, the authors concluded that maintenance TMS appears to be a resourceful strategy to maintain acute antidepressant treatment effects and significantly reduce the risk of relapses over time.

Yamazaki and colleagues (2023) published a study protocol for a multicenter open-labelled parallel-group trial with a planned recruitment of 300 patients with MDD who have responded or remitted to acute rTMS therapy. This study aims to evaluate whether maintenance rTMS is effective in maintaining the treatment response in patients with MDD with a large sample size and feasible study design. The protocol of maintenance rTMS therapy is once a week for the first six months and once biweekly for the second six months.

TMS for Adults with Obsessive-Compulsive Disorder (OCD):

For individuals with a diagnosis of obsessive-compulsive disorder (OCD) who receive TMS, the evidence includes small-to-moderate sized randomized, sham-controlled, double-blind trials, and meta-analyses of these studies.

In 2018, Carmi and colleagues published a small double-blinded pilot study comparing low-frequency deep TMS (LF-DTMS; 1 hertz [Hz]) to high-frequency deep TMS (HF-DTMS; 20 Hz) and to sham deep TMS in patients with OCD. A total of 41 adults with a score of 20 or more on the Yale Brown Obsessive Compulsive Scale (YBOCS) were recruited at the Chaim Sheba Medical Center in Israel. Participants were randomly assigned to receive one Hz stimulation (LF), 20 Hz stimulation (HF), or a sham stimulation, using a computer program. All groups were treated five times per week for five weeks (for a total of 25 sessions). Final analysis included only the 16 participants in the HF group and 14 participants in the sham group, based on a lack of response in the LF group. A higher proportion of participants from the HF group (n=7; 43.75%) compared to the sham group (n=1; 7.14%) reached the pre-defined response criteria after five weeks of treatment. However, at the one-month follow-up, significance was lost, with four participants in the HF group and none from the sham group defined as responders. The authors concluded that HF DTMS is safe, tolerable, and effective in reducing OCD symptoms, but larger studies are needed. Limitations included a small sample size, single center, and short follow-up period.

Carmi and colleagues (2019) reported therapeutic effect findings of deep TMS (dTMS) in a multicenter randomized double-blind placebo-controlled trial for patients diagnosed with OCD. A total of 94 eligible patients were randomized to active treatment with high-frequency (n=47) or sham (n=47) dTMS for six weeks. Clinical response to treatment was determined using the Yale-Brown Obsessive-Compulsive Scale (YBOCS). At the 6-week posttreatment assessment the YBOCS score decreased significantly from baseline in both the active (−6.0 points) and sham (−3.3 points) treatment groups. YBOCS scores between the two groups was statistically significant at the posttreatment assessment (2.8 points, p=0.01), for an effect size of 0.69. The rate of full response at the follow-up assessment was 45.2% (19/42) in the active treatment group, compared with 17.8%

(8/45) in the sham treatment group (p=0.006). The rate of partial response at the follow-up assessment was 59.5% (25/42) in the active treatment group, compared with 42.2% (19/45) in the sham treatment group (p=0.106). The Clinical Global Impressions improvement scale (CGI-I) categorical analyses demonstrated a significant difference between the active and sham treatment groups at the posttreatment assessment. In the active treatment group, 49% of participants (20/41) reported feeling moderate to "very much" clinical improvement, as compared with only 21% (9/43) of participants in the sham treatment group (p=0.011). The Clinical Global Impressions severity scale (CGI-S) score was statistically significant at the posttreatment assessment, with higher rates of patients rating improvement in the active treatment group as compared with the sham treatment group (61% [25/41] and 32.6% [14/43], respectively; p=0.022). Trial limitations include that the effect of provocation was not controlled, and the relevant brain activity was not recorded, which limits the understanding of the exact contribution of the exposure procedure. The authors concluded that the option of adding dTMS as a treatment option for OCD should be considered when the response to proper psychological or pharmacological intervention is inadequate.

Fitzsimmons and colleagues (2022) conducted a systematic review and pairwise/network meta-analysis to evaluate the efficacy and safety of rTMS as a treatment option for obsessive-compulsive disorder (OCD). Study eligibility criteria included published, peer-reviewed, randomized sham-controlled trials enrolling patients with a primary diagnosis of OCD, and any form of rTMS intervention with at least 5 treatment sessions. A database search, up to February 2021, resulted in a total of 21 eligible studies, involving 662 patients (n=368 active rTMS; n=294 sham rTMS). Eleven different stimulation protocols were investigated across the 21 studies. The GRADE certainty rating for all studies is rated as Moderate, due to the presence of likely publication bias. Post-treatment Yale-Brown Obsessive-Compulsive Scale (YBOCS) meta-analysis showed a significantly greater improvement in YBOCS scores following active rTMS than following sham rTMS (Hedges g=-0.502). There was no difference between dropout rates for active vs sham rTMS. For depression severity, as measured by the Hamilton Depression Rating Scale and the Montgomery Aberg Depression Rating Scale, scores showed a small but statistically significant improvement in comorbid depression symptoms following active rTMS compared with sham rTMS (g=-0.21). Due to relatively few studies reporting depression symptom scores, the authors did not carry out a subgroup or network meta-analysis for this outcome. For symptom severity, as measured by the Clinical Global Impression – Severity (CGI-S), the pairwise meta-analysis found a large and significant improvement in CGI-S following active rTMS compared with sham rTMS (g=-0.86). Identified study limitations include primary outcome data lacking from three studies, moderate heterogeneity, and variability in methodology (12 different stimulation protocols). The authors concluded that rTMS is an efficacious treatment for OCD given an average of a 4-point decrease in YBOCS compared with sham, and that their findings are reportedly in agreement with previous systematic reviews and meta-analyses of rTMS for OCD that show efficacy for rTMS against sham.

Steuber and McGuire (2023) conducted a meta-analysis of RCTs to examine the therapeutic benefit of rTMS in patients with OCD and to explore moderators of its treatment effects. Clinical characteristics and effect sizes were extracted from 25 randomized controlled trials (n=860 participants) published up to December 2022. A random effects model calculated the effect sizes for treatment efficacy and treatment response using the clinician-rated Yale-Brown Obsessive-

Compulsive Scale (YBOCS). Across RCTs, rTMS exhibited a moderate therapeutic effect (g = 0.65; p<.001) on OCD symptom severity and a large effect on the average treatment response (39.5% for rTMS and 8.8% for the sham conditions; p<.0001). Trials that had longer rTMS sessions (in minutes) were associated with greater improvement in OCD severity and accounted for 24% of the variance in treatment effects. There was a negative relationship between reductions in OCD severity and the number of rTMS sessions, which accounted for 28% the modeled treatment effects. There was no significant relationship between the total number of pulses in rTMS treatment sessions and reductions in OCD severity. This study was limited by heterogeneity of an OCD diagnosis, four RCTs were excluded for a lack of pre-post treatment data, and lack of long-term follow-up assessments (ranged between 1 and 12 weeks). The authors concluded that there is a 3-fold increased likelihood of treatment response compared with sham conditions, and findings related to efficacy, favorable safety profile, accessibility, and treatment-refractory status suggest that rTMS represents a novel therapeutic option for patients with OCD, particularly those who are unresponsive to first line treatments.

Fitzsimmons and colleagues (2024) published findings of a blinded, randomized, proof-of-concept trial to characterize and compare treatment-induced changes in task-based functional magnetic resonance imaging (tb-fMRI) activation caused by 3 different protocols. Participants (n=61) diagnosed with OCD resistant to first-line treatments were randomized to three different parallel arms: rTMS to left dorsolateral prefrontal cortex (DLPFC) (n=19), rTMS to left supplementary motor area (preSMA) (n=23), or the control low-intensity rTMS to the vertex (n=19). Participants received 16 sessions of rTMS immediately before exposure and response prevention (ERP) psychotherapy over 8 weeks, with task-based functional magnetic resonance imaging scans and clinical assessments before and after treatment. OCD symptom severity was assessed using the Yale-Brown Obsessive-Compulsive Scale (YBOCS) before treatment (T0), after rTMS-ERP session 8 (4 weeks of treatment, T1), after rTMS/ERP session 16 (8 weeks of treatment, T2), and 12 weeks following the end of treatment (T3). Mean OCD symptom severity decreased significantly in all treatment groups, across all three time points, compared to baseline (p< .001), with no significant differences between groups. Depression symptoms decreased significantly in the entire sample following treatment (p = .0006) and in all groups separately. Average Patient Exposure and Response Prevention Adherence Scale (ERP adherence) scores across all 16 treatment sessions did not differ between the groups for either homework or in-session exposure exercises. There was no difference between groups in terms of frequency of different side effects and no serious adverse events were reported. The authors concluded that in this proof-of-concept randomized trial, combined rTMS/ ERP led to a substantial reduction in symptoms (57.4% responders), but there was no difference in symptom improvement between patients with OCD receiving HF rTMS to left DLPFC, left preSMA, or vertex. The study is limited by the limited number of treatment sessions, short follow-up period, and insufficient power to detect differences in clinical effects between groups, which the authors state could hinder any firm clinical conclusions.

<u>TMS for Adults with Migraine Headaches:</u>

Short and colleagues (2011) conducted a pivotal randomized, double-blind, multicenter, sham-controlled trial (n=201) with the Cerena TMS device to demonstrate the safety and effectiveness of a de novo application. Post hoc analysis showed a benefit of the device for the primary endpoint

(37.74% pain free after 2 hours for Cerena vs. 16.67% for sham; p=.018) and for the proportion of subjects who were pain free after 24 hours (33.96% for Cerena vs. 10% for sham; p=.002). Active treatment was not inferior to sham for the proportion of subjects free of photophobia, suggesting that the device does not worsen photophobia. However, the device was not inferior to sham for the proportion of subjects free of nausea and phonophobia.

Saltychev and colleagues (2022) conducted a systematic review and meta-analysis of eight RCTs (n=339 participants) that compared rTMS to sham stimulation in patients with migraine. All RCTs applied high-frequency rTMS to the left dorsolateral prefrontal cortex, and all studies except one included patients with chronic migraine. All studies except one had a low risk of bias and the risk of publication bias was nonsignificant. Results for the frequency of migraine days per month and the intensity of migraine pain both favored rTMS; however, the authors stated that the difference in migraine pain intensity was clinically insignificant.

TMS for Smoking Cessation

TMS to aid in smoking cessation is currently being investigated as a non-pharmacological treatment option. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome (Li 2020; Shevorykin 2022).

Bellini and colleagues (2024) conducted a double-blind, randomized, sham-controlled trial to test the effect of deep TMS (dTMS) on adult smokers. A total of 100 participants were randomized to active (n=50) or sham (n=50) treatment of up to 21 sessions administer over 6 weeks. Participants completed abstinence, mood, and cognition scales at determined timepoints during follow-up. No serious adverse events occurred during this study. Three participants in the active treatment group were withdrawn from the study in the first week for forearm movements during the application of the pulse series. Based on study results the authors concluded that that use of rTMS, with the parameters used and the H4 coil, was not effective in treatment smoking cessation.

In a randomized sham-controlled trial evaluating the clinical efficacy and safety of administering iTBS for tobacco use disorder, 38 patients received 28 sessions of active (n=25) or sham (n=13) iTBS over 14 visits (Addicott 2024). Both active and sham groups reported reduced cigarette consumption, cigarette craving, and tobacco withdrawal symptoms. The authors concluded that there were no differences in cigarette consumption between the active and sham iTBS groups, both groups decreased cigarette consumption similarly, and further research is needed to compare iTBS to standard high-frequency rTMS.

TMS for Other Indications

In an updated Cochrane Review (Walton ~~et al.~~ 2021) assessed the evidence for use of TMS in individuals with drug-resistant epilepsy compared with other available treatments in reducing seizure frequency, epileptiform discharges, anti-epileptic medication use and side effects, as well as improving quality of life. Included eight RCTs (n=241 participants), seven of which were blinded. Two of the studies showed a statistically significant reduction in seizure rate from baseline (72% and 78.9% reduction of seizures per week from the baseline rate). The remaining six studies did not show a significant reduction in seizure frequency with rTMS compared to controls. Three studies did show a statistically significant reduction in epileptic discharges after active rTMS treatment and

adverse events were rare, but an increase in seizure frequency did occur in a small number of individuals. No significant change in medication use was reported. The authors concluded that even though there is reasonable evidence that rTMS is effective at reducing epileptiform discharges, the evidence for the efficacy of rTMS for seizure reduction is low, and further research is needed.

Evidence related to the efficacy of rTMS is limited for other indications, such as gambling (Concerto 2023), amyotrophic lateral sclerosis (ALS) (Fang 2013; Di Lazzaro 2024), anxiety (Trevizol 2021), insomnia (Krone 2023). Tourette syndrome (Kwon 2011), fibromyalgia (Short et al., 2011; Knijnik 2016; Salychev and Laimi 2017), Alzheimer's disease (Ahmed 2012), stroke (Yang 2013), Parkinson disease (Benninger 2012; Xie 2020), tinnitus (Peng 2012), migraine (Lan 2017), schizophrenia (Matheson 2010; He 2017; Guan 2020; Hua 2022; Johnstone 2022), and chronic pain (O'Connell 2018). Studies have methodological limitations, such as small samples sizes and limited follow-up. The role that TMS has in the treatment of these indications has not yet been established.

PROFESSIONAL GUIDELINE(S)

Major Depressive Disorder

Consensus recommendations for the application of rTMS were published in 2018 by the National Network of Depression Centers (NNDC) rTMS Task Group and the American Psychiatric Association Council on Research (APA CoR) Task Force on Novel Biomarkers and Treatments (McClintock et al., 2018). A total of 118 publications, including three multi-center RCTs, from 1990 through 2016, were included in the review. The consensus states:

- rTMS is appropriate for patients with major depressive disorder even if the patient is medication resistant or has significant comorbid anxiety; however, patients with co-morbid psychotic symptoms or acute suicidal ideation should be considered for other established antidepressant treatments, such as ECT;
- the preferred length of acute TMS treatment is depended upon the risk-benefit ratio for clinical response and remission, with a likely standard acute course of 20 to 30 treatments over six weeks, to achieve results consistent with published trials;
- motor threshold (MT) determination should occur at baseline and be rechecked when there have been medication changes that could affect the MT;
- there is limited RCT evidence regarding maintenance strategies following response or remission with acute rTMS. It is recommended that available evidence-based antidepressant strategies (e.g., repeat rTMS, pharmacotherapy, exercises) be used after successful acute rTMS treatment.

In 2022, the Department of Veterans Affairs Department of Defense (VA/DoD) issued clinical practice guidelines for the management of MDD. A weak recommendation was made for rTMS for treatment for patients who have demonstrated partial or no response to two or more adequate pharmacologic treatment trials. The VA/DoD found that there is insufficient evidence to recommend for or against theta-burst stimulation. A weak recommendation against choosing Ketamine as an initial pharmacotherapy and for augmentation use of Ketamine for patients with MDD who have not responded to several adequate pharmacologic trials.

The American Psychiatric Association clinical practice guideline for treatment of patient with major depressive disorder supports the use of TMS as a safe and well tolerated treatment in the acute phase (2010).

Obsessive-Compulsive Disorder

In 2020, the National Institute for Health and Care Excellence (NICE) published interventional procedures guidance for TMS for OCD, stating that the evidence on the safety of TMS raises no major safety concerns; however. the evidence on efficacy is inadequate in quantity and quality. NICE recommends that TMS should only be used in the context of research.

The American Psychiatric Association 2013 practice guideline for the treatment of patient with OCD states that the overall strength of evidence for somatic therapies (e.g., rTMS) is low and the therapies should be considered only after first- and second-line treatments, and well-supported augmentation strategies have been exhausted.

Other Indications

The American Psychiatric Association published several clinical practice guidelines to provide evidence-based recommendation for the assessment and treatment of psychiatric disorders. TMS requires further study for use in treating bipolar disorder (2002) and TMS is not addressed in the practice guidelines for borderline personality disorder (2024), eating disorders (2023), schizophrenia (2020), post-traumatic stress disorder (2000), Alzheimer's disease (2000).

The 2018 NNDC and APA CoR consensus recommendation for the application of rTMS reported that there is some evidence of the safe and therapeutic use and clinical benefit of TMS for other neuropsychiatric disorders, but the current evidence is insufficient to support routine clinical rTMS in these populations.

In 2023, the Department of Veterans Affairs Department of Defense (VA/DoD) issued clinical practice guidelines for the management of bipolar disorder. A weak recommendation was made to offer rTMS as an adjunctive treatment for individuals with bipolar disorder who have demonstrated partial or no response to pharmacologic treatment for depressive symptoms.

Maintenance TMS

The 2018 NNCD and APA CoR consensus recommendations for the application of rTMS found limited evidence regarding maintenance strategies following response or remission with acute rTMS (McClintock et al., 2018). One RCT compared a once-monthly scheduled approach with a re-introduction approach and found that both approaches were approximately equivalent in prolonging clinical benefits. The study also found that "rescue therapy" (re-introduction of daily rTMS triggered by symptom relapse) was effective in 69% of instances.

The Clinical TMS Society (2021) indicates that for patients who demonstrate a late response to TMS, subsequent treatment extensions in ten (10) treatment increments are allowed based on clinical need.

REGULATORY STATUS

Devices for TMS have been cleared for marketing by the U.S. Food and Drug Administration (FDA) for the treatment of major depressive disorder in adults who have failed to achieve satisfactory improvement from prior antidepressant medication in the current episode. In 2024 the FDA cleared the first TMS therapy device for use as an adjunct for the treatment of MDD in adolescent patients aged 15-21. Some of these devices use deep TMS or theta burst stimulation (TBS) protocols.

In 2013, the FDA cleared the first TMS device for acute treatment of pain associated with migraine headache with aura and approved the first device for adjunct treatment of adults diagnosed with OCD in 2018.

TMS protocols are FDA approved and include conventional/standard and accelerated protocols. The Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) TBS treatment protocol was FDA cleared in 2018 for severe major depressive disorder and utilizes intermittent theta burst stimulation (iTBS). TBS treatment protocol is supported by the Clinical TMS Society (2023).

FDA cleared TMS Devices for the Treatment of Major Depressive Disorder:

Device	Manufacturer	FDA Clearance	Clearance Date
NeuroStar Advanced Therapy System *ages 15-21	Neuronetics	K231926	03/22/2024
Horizon 3.0 TMS Therapy System	Magstim	K222171	01/13/2023
Magnus Nueromodulation System with SAINT Technology	Magnus Medical	K220177	09/01/2022
ALTMS Magnetic Stimulation Therapy System	REMED Co., Ltd	K220625	04/06/2022
Horizon TMS Therapy System (with iTBS protocol)	Magstim	K182853	03/15/2019
Mag Vita TMS Therapy System with Theta Burst Stimulation	Tonica Elektronik	K173620	8/14/2018
Apollo	Magstim	K180313	05/04/2018
Nexstim	Magstim	K171902	11/10/2017
Horizon	Magstim	K171051	09/13/2017
Neurosoft	TeleEMG	K160309	12/22/2016
Magvita	Tonica Elektronik	K150641	07/31/2015
Rapid Therapy System	Magstim	K143531	05/08/2015
Brainsway H-Coil Deep TMS System	Brainsway	K122288	01/07/2013
NeoPulse, now known as Neurostar	Neuronetics	K083538	12/16/2008

FDA cleared TMS Devices for the Treatment of Adults with Obsessive-Compulsive Disorder (OCD):

Device	Manufacturer	FDA Clearance	Clearance Date
CloudTMS for OCD	TeleEMG	K221129	03/10/2023
Horizon 3.0 TMS Therapy System	Magstim	K222171	01/13/2023
Neurostar	Neuronetics	K212289	05/06/2022
MagVenture TMS Therapy	Tonica Elektronik	K193006	08/09/2020
Brainsway H-Coil Deep TMS System	Brainsway	K183303	03/08/2019

FDA cleared TMS Devices for the Treatment of Adults with Migraine Headache with an Aura:

Device	Manufacturer	FDA Clearance	Clearance Date
Savi Dual Migraine Therapy	ENeura	K230358	05/16/2023
Brainsway H-Coil Deep TMS System	Brainsway	K183303	03/08/2019
Springtms Total Migraine System	Eneura	K140094	05/21/2014
Cerena	eNeura Therapeutics	K130556	03/05/2013

FDA cleared TMS Devices to Aid in Smoking Cessation for Adults

Device	Manufacturer	FDA Clearance	Clearance Date
Brainsway Deep TMS System	Brainsway	K200957	08/21/2020

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
90867	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial, including cortical mapping, motor threshold determination, delivery, and management

Code	Description
90868	subsequent delivery and management, per session
90869	subsequent motor threshold re-determination with delivery and management

ICD10 Codes

Code	Description
F32.0-F32.9	Major depressive disorder, single episode (code range)
F33.0-F33.9	Major depressive disorder, recurrent (code range)

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SEARCH TERMS

Not applicable

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Transcranial Magnetic Stimulation (LCD) L33398 accessed 12/20/24.

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid

guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.

- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION	
Committee Approval Dates	
07/15/10, 08/18/11, 11/15/12, 12/19/13, 12/18/14, 10/15/15, 12/15/16, 12/21/17, 12/20/18, 01/16/20, 01/21/21, 01/20/22, 01/19/23, 01/18/24, 01/23/25	
Date	**Summary of Changes**
01/23/25	• Annual review, revision to Policy Statement and Policy Guidelines, policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
08/20/09	• Original effective date