Washington State Health Care Authority

Final Key Questions and Background

Transcranial Magnetic Stimulation for Treatment of Selected Behavioral Health Disorders

August 23, 2022

Background

Mental health conditions affect a large proportion of the American population, according to several nationally representative surveys.[1-4] Individuals suffering these conditions often experience decreased quality of life and impaired function across physical, emotional, and social domains. Over 14 million adults (5.6%) are estimated to have serious mental illness (SMI), in which the mental illness causes serious functional impairment interfering with one or more major life activities.[1,5]

Current treatment approaches for behavioral health disorders often begin with psychotherapy, pharmacotherapy, or both. However, many people do not achieve adequate clinical responses after the initial treatment attempt, and second and third-line medications or procedures (e.g., electroconvulsive therapy (ECT)) carry risk of adverse side effects that many individuals do not tolerate. Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that has been FDA approved for some behavioral health and neurologic conditions. There is a growing evidence base that TMS may be efficacious, with fewer or more tolerable side effects, and has led to growing interest in applying TMS to a broader set of conditions, most often those deemed treatment resistant.

This health technology assessment (HTA) reviews the efficacy, safety, and cost-effectiveness of TMS to assist the State of Washington's Health Technology Clinical Committee (HTCC) in determining coverage of TMS for the following selected behavioral health disorders: depression; anxiety disorders including generalized anxiety disorder (GAD); obsessive-compulsive disorder (OCD); post-traumatic stress disorder (PTSD); and addiction disorders including tobacco use disorder and substance use disorder (SUD).

Policy context

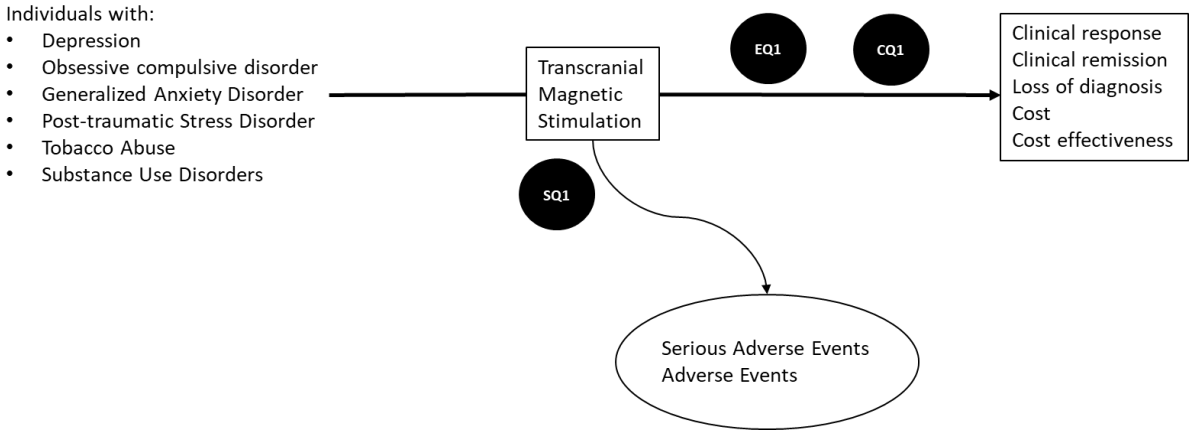
The State of Washington Health Care Authority selected TMS for selected behavioral health conditions for a health technology assessment (HTA) because of low/medium concerns of safety and medium/high concerns for efficacy and cost.

Washington State Health Care Authority

Scope of this HTA

The analytic framework (**Figure 1**), research questions, and key study selection criteria (**Table 1**) are listed in this section.

Figure 1. Analytic Framework Depicting Scope of this Health Technology Assessment



Abbreviations: SQ = safety question, CQ = cost question; EQ = efficacy question

Research Questions

Efficacy Question 1 (EQ 1). What is the efficacy of transcranial magnetic stimulation for the treatment of selected behavioral disorders?

Safety Question 1 (SQ 1). What are the harms associated with transcranial magnetic stimulation for the treatment of selected behavioral disorders?

Cost Question 1 (CQ 1). What are the costs and cost-effectiveness of transcranial magnetic stimulation for the treatment of selected behavioral disorders?

Study Selection Criteria

Table 1 provides the study selection criteria we will use to include studies in the HTA and are organized by population, intervention, comparator, outcomes, timing, setting, and study design (PICOTS) criteria.

Washington State Health Care Authority

Table 1. Proposed Population, Intervention, Comparator, Outcome, Timing, and Setting for Health Technology Assessment

PICOTS	Include	Exclude

Population	• Individuals of all ages with eligible clinical diagnosis:
	  • Depression, major depressive disorder (MDD)
	  • Obsessive compulsive disorder (OCD)
	  • Generalized Anxiety Disorder (GAD)
	  • Post-traumatic stress disorder (PTSD)
	  • Tobacco Use Disorder, or regular smoker
	  • Substance Abuse Disorder (SUD)
	• Subgroups: Individuals who are peri- or post-partum, elderly, age < 18 years
		• Individuals with ineligible mental health diagnosis
		• Individuals with no mental health diagnosis (e.g. healthy controls)
		• Individuals with a primary medical (i.e., non-psychiatric) diagnoses
		• Studies conducted in animals, *in vitro*, or *in silico*

Intervention	• Repetitive TMS (rTMS) with or without concurrent pharmaco- and/or psychotherapy delivered over more than 1 session • Deep TMS (dTMS) with or without concurrent pharmaco- and/or psychotherapy	• Single session TMS (TMS) • Other non-invasive neuromodulation procedures (e.g. transcranial direct current stimulation, neurofeedback; transcutaneous vagus nerve stimulation) • Invasive neuromodulation therapies (e.g. implanted vagus nerve stimulation, deep brain stimulation, brain surface implants)
Comparator	• Sham TMS with or without concurrent pharmaco- and/or psychotherapy	• Head-to-head comparisons between alternative TMS protocols, with medications, psychotherapy, other neuromodulation procedures (e.g. ECT), o complementary or alternative therapies • Waitlist control • No comparator
Outcomes	• EQ: Primary study outcome or outcome used for determining power or sample size is a clinical outcome: response (e.g. symptom scales or indices), remission, or loss of diagnosis as measured by validated instruments or clinical evaluation. Clinical outcomes from studies where the primary outcome is an intermediate or biomarker but that also report a validated clinical outcome will only be included if the study was also adequately powered for the clinical outcome. • SQ: Serious adverse events (e.g., seizure), adverse events (e.g., headache), side effects including device-related complications (e.g., scalp pain) • CQ: Cost; cost-effectiveness	• Non-validated measures of clinical response or remission • Individual symptom response outside of a validated scale (e.g. guilt, hopelessness) • Intermediate or biomarker outcomes, such as electrophysiologic or functional imaging outcomes, lab measures, craving measures
Timing & Language	• No timing restrictions • English language articles	• No timing exclusions • Non-English language articles
Study Design	• EQ: RCTs, non-randomized controlled trials, crossover trials • SQ: same as EQ plus we will consider prospective controlled cohort studies if evidence from trials is insufficient • CQ: CEA, CUA, or CBA performed from the	• Editorial, commentaries, narrative reviews, or letters; conference abstracts; case reports or case series; retrospective controlled cohort studies; case-control studies; other observational study designs without a comparator group not already specified

	societal or payor perspective	• Relevant systematic reviews will be excluded but will be hand searched to identify potentially eligible primary studies • Studies with fewer than 10 individuals in each arm will be excluded.
Setting	• Countries categorized as "very high human development" on the United Nations Development Programme's HDI Report6[a] • Inpatient settings • Outpatient settings, community and residential (e.g. group homes, long-term care facilities) • For Cost Outcomes, primarily rely on US studies	• Countries not categorized as "very high human development" according to the United Nations Development Programme's 2018 Human Development Report6 • No exclusions based on care setting

Abbreviations: CBA = cost-benefit analysis; CEA = cost-effectiveness analysis; CQ = cost question; CUA = cost-utility analysis; EQ = efficacy question; PICOTS = population, intervention, comparator, outcome, timing, and setting; RCT = randomized controlled trial; SQ = safety question

[a] Andorra, Argentina, Australia, Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Brunei Darussalam, Bulgaria, Canada, Chile, Costa Rica, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hong Kong China (SAR), Hungary, Iceland, Ireland, Israel, Italy, Japan, Kazakhstan, Korea (Republic of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Mauritius, Montenegro, Netherlands, New Zealand, Norway, Oman, Palau, Panama, Poland, Portugal, Qatar, Romania, Russian Federation, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Taiwan, Turkey, United Arab Emirates, United Kingdom, United States, Uruguay.

References

1. Substance Abuse and Mental Health Services Administration. *Key substance use and mental health indicators in the United States: results from the 2020 National Survey on Drug Use and Health.* Rockville, MD; 2021.
2. Centers for Disease Control and Prevention. BRFSS prevalence & trends data. https://www.cdc.gov/brfss/brfssprevalence/. Published 2017. Updated Sept. 13, 2017. Accessed June 8, 2022.
3. Brody DJ, Pratt LA, Hughes J. *Prevalence of depression among adults aged 20 and over: United States, 2013–2016.* Hyattsville, MD; 2018.
4. Terlizzi EP, Villarroel MA. *Symptoms of generalized anxiety disorder among adults: United States, 2019.* Hyattsville, MD; 2020.
5. National Institute for Mental Health. Prevalence of Serious Mental Illness. https://www.nimh.nih.gov/health/statistics/mental-illness. Published 2022. Accessed August 23, 2022.
6. Human Development Reports. Towards 2021/2022 HDR. https://hdr.undp.org/towards-hdr-2022. Published 2021. Accessed June 8, 2022.