Webinar Title: Magnetizing the Mind: Exploring Transcranial Magnetic Stimulation

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Speaker 1: Hello and welcome to today's webinar, Magnetizing the Mind, Exploring Transcranial Magnetic Stimulation. This topical webinar is paid for by McLean Hospital, a top-ranked freestanding psychiatric hospital, a leader in psychiatric care, research, and education, and the largest psychiatric teaching hospital of Harvard Medical School. Some important points before we get started.

Doctors Jennifer Gatchel and Sanjali Kumar, the presenters for today's webinar, have working relationships with McLean Hospital. As such, they have both a financial and an intellectual interest in the webinar content. The purpose of this presentation is to provide a balanced view on the evolving role of TMS in the research and treatment of psychological disorders. APA does not endorse any products or services. The content was created by McLean Hospital and does not reflect the views of APA or its editorial staff. Email advertising@apa.org to learn more.

Next, this program does not offer CE. However, we will email everyone watching live today a certificate of attendance. Certificates will only be issued to those who watch for a minimum of 45 minutes. A recording of this presentation will be emailed to everyone in two weeks' time. The recording will include the presentation slides. During our time together, you will be on mute. You can communicate with us using the Q&A box located on your webinar screen. The Q&A is enabled for attendee interaction with submitted questions. Attendees can view all submitted questions and upload those they find important. This helps the presenter identify questions that many attendees want answered. A link to the presentation slides will be posted in the chat box of your webinar screen. If you miss them, don't worry. We will email them to you with the recording.

Now let me introduce our presenters. Dr. Jennifer R. Gatchel. Dr. Gatchel is an assistant psychiatrist in the Division of Geriatric Psychiatry at McLean Hospital and Massachusetts General Hospital and an instructor of psychiatry at Harvard Medical School. She holds an MD and PhD in neuroscience from Baylor College of Medicine and has received the DuPont Warren Fellowship and Livingston Award for her research on the neurobiology of depression and Alzheimer's disease.

Next, Dr. Sanjali Kumar. Dr. Kumar is a psychiatrist at McLean Hospital, an instructor in psychiatry at Harvard Medical School, and the associate medical director of McLean's Neurotherapeutics Clinic. She earned her MD from Creighton University and completed her residency at Brigham and Women's Hospital, Harvard Medical School. Welcome, Drs. Gatchel and Kumar.

Dr. Sanjali Kumar: Thank you. All right. Good morning, everyone, or good afternoon. It's wonderful to be here today. Thank you for joining us for Magnetizing the Mind. Over the next hour or so, we'll take a deep dive, and I hope an energizing one, into the evolving world of transcranial magnetic stimulation, or TMS. We'll start small and local, talking about the physics, the mechanisms, the neurons right under the coil, and then we'll zoom out, just like the magnetic fields themselves, to understand how TMS is transforming the treatment landscape in psychiatry.

These are the objectives. Here's where we're headed. By the end of the session, my hope is that you'll feel confident describing the mechanisms of TMS, not just in a theoretical sense, but how they relate to what you see clinically. I'd like to structure this talk the same way magnetic fields behave. Start focal and then expand. We'll begin at the level of neurons and circuits, move to how we deliver treatment, and end with the broader implications for psychiatry. We'll start small, physics, mechanisms, indications, and then get progressively "bigger," until we're talking about innovation and the future of neuromodulation.

This is just a visual map of that trajectory. Think of it as three concentric circles. The inner circle, the technical core of how TMS works. Then the middle circle, how we use it clinically, safety, populations, parameters, and the outer circle, the future. What's experimental, what's coming, and how can we think about TMS as part of a broader network-based approach to mental health care?

Let's start with a little context. Modern TMS was invented in 1985 by Anthony Barker in England. Psychiatry was actually not the first field to jump on it. It started as a neurophysiology tool for research and diagnostic purposes. Its therapeutic potential was a much later development. Fast forward to 2008, and we see FDA approval for treatment-resistant depression. That's when psychiatry truly entered the picture. By 2013, when major insurers began covering TMS, it stopped being an experimental curiosity and started being a real clinical option. We're now in an era where nearly every large academic department has a TMS program. In less than 40 years, we've gone from physics labs to standard psychiatric care. Not bad for a magnet and a coil.

Let's get into the fun part, the physics, but a very distilled version. At its core, TMS is simply the application of electrical current through a metal coil, which produces a rapidly alternating magnetic field. That field passes through the skull and induces a small electrical current in the brain tissue below. What's fascinating is that it does this non-invasively. No surgery, no implants, no electrodes under the skin. You can almost think of it like a wireless connection between the coil and the cortex.

Again, it's when that magnetic field alternates that it generates what we call an induced electrical field. That's what actually depolarizes the neurons. The magnetic field itself doesn't stimulate neurons directly. It's the electrical current that induces the work. It's a beautiful application of Faraday's law, physics in service of psychiatry. Now here's where it gets interesting. The strength of that magnetic field drops off exponentially with distance. Not because it's absorbed by the tissue, but simply because of how magnetic fields behave in space. The deeper you go into the brain, the weaker that magnetic field becomes. In turn, the electrical currents that were induced by that magnetic field also decrease the deeper they get into the tissue.

This begs the question, if the magnetic field strength decreases exponentially, with downstream effects of the induced electrical field and tissue stimulation also decreasing, how can we affect deeper regions of the brain distal to the location immediately underneath the coil? The answer is neuronal circuits. Even though the field weakens as it travels, the effects can reach deeper structures indirectly through connected neuronal circuits.

For example, stimulating the DLPFC, or the dorsolateral prefrontal cortex, doesn't just activate local neurons, it modulates the networks they're a part of. Networks that project to things like the limbic system, to the anterior cingulate, to the subcortical mood and reward regions. While TMS may look focal, its effects are network level. Again, to summarize, the electrical current goes through the coil, which induces a magnetic field, which induces an electrical current, which then depolarizes neurons and leads to circuit-level modulation. That's our overall foundation.

Building from there, we'll now talk about how those circuits actually change behavior and mood. Let's zoom out from physics to physiology. How does all this electrical activity translate into remarkable clinical changes we see in patients? Now that we've covered the physics, the literal sparks, we're going to move on to how those sparks affect the brain. There's no single mechanism of action for TMS. Instead, we have several well-supported hypotheses that together explain its antidepressant and neuroplastic effects.

As discussed before, stimulating a cortical region can affect parts of the brain much further away via neuronal circuits. Stimulation of the left DLPFC can influence distant regions via neuronal circuits. For example, over time, TMS can decrease the hyperconnectivity between the default mode network and the anterior cingulate cortex. Interestingly, recent studies have shown that if you have a baseline higher connectivity between the default mode network and the ACC, there's a slightly higher chance that you will respond to TMS.

Rather than thinking that TMS changes the DLPFC, or the dorsolateral prefrontal cortex, we now think that TMS normalizes network communication between cortical and limbic regions. If you've ever looked at a patient's fMRI after TMS and wondered why symptom change doesn't always map perfectly onto the local activation, this is why. It's about circuit tuning, not just cortical stimulation.

This slide's one of my favorites because it captures the essence of why TMS works long after the last pulse. Repeated TMS sessions promote long-term potentiation and long-term depression, strengthening some synaptic pathways and pruning others. Recent research in 2024 and 2025 continues to confirm that TMS promotes metaplasticity, meaning it not only changes existing synapses, but adjusts the threshold for future plasticity as well, so the brain in general becomes more adaptable and more receptive to new learning and therapy. This is why combining TMS with psychotherapy can sometimes amplify outcomes, because you're literally priming the brain for change.

And another possible hypothesis is that patients with depression often have low BDNF levels, it's a protein in the brain, which can normalize with psychiatric treatment, including antidepressants and TMS. BDNF is implicated in neuronal growth, survival, and plasticity. In fact, newer data suggests that there's even a bit more of a nuance. Recent studies have shown that the degree of BDNF increase may correlate with the durability of remission, meaning patients who show larger BDNF upswings after TMS tend to maintain their clinical gains longer.

Another aspect of molecular effects is increased monoamine turnover and changes in GABA and glutamate, with normalization of the HPA access. When conceptualizing it, it's less about monoamines "increasing" and more about network

level neurochemical rebalancing. For example, TMS seems to enhance GABAergic inhibition in parts of the brain that are hyperactive, and can increase glutamate signaling where underactivity exists.

TMS also increases local cerebral perfusion, especially in targeted prefrontal regions. In fact, we now think that blood flow changes are not just passive, they actually reflect neuronal plasticity processes and metabolic demands in newly activated circuits. Increased blood flow as both a marker and a mechanism of enhanced network health. It reflects the brain actively rewiring itself.

Now we're going to transition to talk about indications for TMS use. Unipolar treatment-resistant depression remains a primary FDA indication. We all know that there are several ways to clinically assess treatment-resistant depression, but often in the real world, insurance definitions end up dictating access to treatment. This is a moving target, with each insurance carrier having their own definition for treatment-resistant depression, but often it is four or more antidepressant trials across two different med classes with at least two augmenting agents.

In March 2024, the FDA cleared TMS as a first-line add-on for depression for adolescents aged 15 to 21 years old. That's a major milestone. So far, the early real-world data from NeuroStar, it's one of the TMS companies, shows about 78% clinical improvement and no safety concerns in this group. There's also some early research exploring developmentally sensitive dosing, adjusting stimulation intensity for cortical thickness, which tends to be different in adolescents, but this is still in early stages.

All right, so other indications. Some other FDA cleared indications are migraines, OCD, smoking cessation, and comorbid anxiety in adult patients with MDD. Here, I just want to add another quick reminder that unfortunately, even if a treatment is FDA cleared, it doesn't mean that it's necessarily covered by insurance. That's just something to keep in the back of your mind in the real world, unfortunatley.

This is where we stand on what TMS does and who it helps. Before we put everyone under the coil, let's talk safety because even though it is a relatively benign treatment, there are important precautions and contraindications that every clinician should know. This slide shows the classic 13-item safety screening questionnaire, which remains our standard checklist. It's from the original international safety consensus, and we still use it almost verbatim today.

You can think of this questionnaire as your seatbelt. It covers seizure history, syncope, head trauma, hearing issues, metallic implants, pregnancy, pacemakers, infusion devices, all the way down to prior TMS or MRI experiences. Generally, this safety screening isn't a one-and-done situation. Most clinics recheck these questions at regular intervals, especially because patients may not always know what change is pertinent, such as a medication titration.

The only true absolute contraindication is non-removable metallic objects in or around the head within 30 centimeters of the coil. That includes things like aneurysm clips, cochlear implants, and certain neurostimulators. Dental fillings and braces are generally safe because those are usually non-ferromagnetic. More recently, some new implants will come as TMS conditional, much like MRI conditional devices. Generally, it's always a good idea to look up the manufacturer's specs, and we often

reach out to them as well if we have further questions. These conditional devices are still far from standard, though, so the safest policy is still, if it's metal, near the brain, and it's not removable, we tend not to treat.

Then this slide goes more into those gray zone situations. Implanted stimulators, aneurysm coils, cochlear implants, intracranial stents, bullet fragments, vagus nerve stimulators. These remain in the proceed only after specialist consultation category. Some research groups have started joint safety registries tracking TMS in patients with implanted devices, and that will probably inform future consensus guidelines, but for now, we generally do our own homework.

These are some more nuances to consider. Even if a device is 30 centimeters away, be cautious if it's affected by physiological cues, such as pacemakers, insulin pumps, et cetera. This is generally another question for the specialist and/or manufacturing company. Can it be turned off? Things like that. Those questions are generally determined on a case-by-case evaluation. Other things like tattoos, permanent makeup, same thing, case-by-case. If metallic ink was used, it could heat up, for example. Piercings, if precious metal is ceramic, they don't need to be removed, but it's always good to play it safe. TMS and concurrent Botox for migraines, wait 24 hours before doing TMS so you don't disturb the binding site.

This is a helpful tidbit because it comes up a lot. They said it was okay for an MRI, so it should be safe for TMS. While this does increase the chances that it will be safe, we have to remember that the intensity of TMS treatment is strong enough to cause nerves to fire, which isn't the case for MRIs. We can't just assume. We need to go through these safety steps.

All right. This slide goes more into relative seizure risk. If there are any concerns, we often reach out to the patient's neurologist if they have one. It's important to remember and share with the patient that the raw numbers are reassuring. TMS seizure risk is still around 0.1% overall, far below many psychotropics. New data shows that the history of epilepsy roughly doubles that to about 0.2%, but still very low. Other things like sleep deprivation and abrupt benzo or alcohol withdrawal remain the strongest modifiable triggers.

Concurrent ketamine therapy. This combination is currently done on a research-only basis, but you would do the TMS before ketamine if it is done on the same day since ketamine generally lowers seizure threshold. You generally try and separate that by a few hours. Another thing that's become increasingly common is cannabis use. There's still no direct safety concern, but emerging evidence shows that heavy, chronic THC use may dampen response by blunting neuroplasticity. Not necessarily unsafe, but possibly less effective.

Patients with active psychosis or mania generally do better with ECT or medication stabilization first. There is some new pilot work that is cautiously exploring TMS for bipolar depression using right-sided inhibitory protocols, but that's still in the research world and not mainstream practice yet. The safest way to currently practice is that TMS and mania don't mix. If a patient starts to drift hypomanic midcourse, stop, reassess, and usually get in contact with their outpatient providers if that is not who you are.

Then I think these numbers are helpful to put out there during a consult to provide context and put things in perspective for patients. As of 2025, we now have tens of thousands of treatment courses tracked across registries, and the overall seizure rate has not budged, still 0.1%. That's actually lower than many antidepressants, including Wellbutrin. It's a great reassurance point. In the hierarchy of seizure risk, TMS sits below Wellbutrin.

This is one of the most comforting facts for both patients and staff, that if a seizure were to happen, it happens while getting the treatment, while in the chair, under supervision, and is almost always brief and self-limited. It doesn't increase the patient's chances of developing epilepsy. It's not going to happen on their drive home. In recent years, some clinics have started doing mock TMS seizure trials, just so everyone in the clinic knows the overall flow of events that should occur if this very rare outcome happens. We'll go more in-depth about that in a bit, but generally it is to stop stimulation, support airway, place the patient in a side position, and call for help and document.

These factors, epilepsy, TBI, threshold-lowering meds, substance withdrawal, sleep deprivation, excessive caffeine, increase seizure risk. There's also growing recognition that severe eating disorders can increase risk transiently, mostly via electrolyte abnormalities. If you're treating someone with active purging or severe restriction, make sure metabolic labs are up to date. What can you do to mitigate risk? This is another thing we monitor for throughout the treatment course. Generally, at every session, we ask the patient about medication changes, use of substances, and hours of sleep. If there are any concerns, we can hold treatment for some time, check in with their outpatient team, and recheck motor threshold.

This slide walks through what to do if a seizure does occur. Terminate treatment, assess airway, breathing, and circulation, your general ABCs. Then after the convulsion ends, turn patient on their side to clear their airway and prevent aspiration. Call emergency services as quick as possible. Most TMS clinics are in free standing outpatient clinics, so this is generally 911. Lastly, carefully document everything before, during, and after. Again, for reassurance, across the literature, there have been no reports of status epilepticus, no long-term sequelae, and no secondary injuries from TMS-related seizures. They're startling, but self-limited.

All right. These are the most common side effects. We went through the most dangerous and intense ones, but these are the more common ones. Facial muscle twitching and scalp pain. We generally start by slightly readjusting the coil or decreasing intensity. I also mentioned at the beginning of the treatment that these symptoms generally improve as the treatment progresses, and our body habituates to it.

Some patients also take prophylactic over the counter analgesics before treatment, especially in the beginning of the course. For teeth grinding, most clinics have mouth guards to offer the patients. It's also important to avoid any loose particles like food, gum, and dentures during treatment to avoid choking and aspiration risk. For transient effects on hearing, it's mandatory for both patients and staff to wear ear plugs during treatment.

Similar to responding when there is seizure activity, if you start to see signs of mania or hypomania start to develop, reassess, gather collateral from the outpatient team and social contacts, and possibly consider alternative treatments such as ACT. Overall, if this were to happen, it is generally a slow process, so it can be caught in its early stages. Overall, our safety profile remains one of TMS's strongest selling points. Minimal systemic effects, no anesthesia, no cognitive impairment, and a remarkably low risk of serious events. You can drive yourself to treatment, so you can generally fit it into even a workday.

Now that we've covered how to keep patients safe before and during treatment, we're going to shift gears and talk about what the treatment itself looks like in practice, how we set parameters, map targets, and tailor protocols to each patient. The treatment itself, this is a pre-treatment workflow. There's an initial consult where the prescriber performs the initial evaluation, confirms indications and safety, all the stuff we've been talking about. Then the overseeing provider prescribes the treatment, oversees the treatment, and completes the initial mapping procedure, and generally, at least one other motor threshold re-evaluation during the course of treatment. Most clinics also get baseline rating scales because tracking these throughout treatment is an increasingly important quality metric for insurers.

Then outpatient procedure logistics. Important considerations for practicality, logistics, and often whether or not a patient can access the treatment include patients can drive themselves, this is the big one. The length of the appointment depends on the procedure and machine. The appointments generally last about 20 to 40 minutes total, so it's something that usually people can build into their workday. The most common protocol is Monday through Friday for 30 treatments and then a six-treatment taper. Even though you can drive yourself, it is definitely a time commitment.

Then I'm sure that a lot of people have heard of the rise of the accelerated protocols, such as the SAINT protocol, which is like a TMS bootcamp where you do several treatments throughout the day, which can compress an entire course of TMS, which generally takes six weeks to one week. The development of these types of protocols are swift, and some have FDA clearances. Some insurers have started to cover these treatments, but it's rare, and they're generally more of an out-of-pocket expense at this time. In general, the field is moving towards shorter, denser courses, mostly for increased patient convenience and accessibility.

The treatment itself. The standard techniques of providing TMS include surface cortical stimulation, deep stimulation, and theta burst stimulation. The surface stimulation remains the most used worldwide, and insurance still reference it as the benchmark. That's generally the figure 8 coil that if you've seen in the past. Then deep TMS uses specialized coils that reach broader networks, including sub-cortical limbic structures. In common practice, that's generally referring to using a BrainsWay device, which is usually more of the helmet method. Then theta burst stimulation. It continues to prove equivalent in efficacy, but in one-tenth of the time. As of 2025, several studies show no difference in long-term remission or relapse rates between the surface stimulation and the theta burst, which is a much shorter treatment.

These are the backbone parameters of every treatment. In short, frequency is the number of magnetic pulses per second. That's measured in Hertz. The most

common protocol is excitatory and takes place in the dorsolateral prefrontal cortex. Less common for people with high risk for seizure, poor tolerability, or anxious features. Experienced clinicians will sometimes use an inhibitory protocol, which is less than or equal to one Hertz. The excitatory protocol is greater than one Hertz. The inhibitory protocol would take place in the right DLPFC.

Intensity is the percentage of resting motor threshold, which is evaluated during the initial mapping procedure. You stimulate the motor cortex and find the minimum amount of energy required to evoke a motor response in the contralateral small hand muscle. Then we usually treat at 100% to 120% of this motor threshold. We generally work up to the 120% based on patient tolerability. There's continued advancement in how we do this initial mapping procedure from geographical calculations to more connectivity-based targeting, but this requires a more updated machine and access to MRI-guided or EEG-informed targeting. Again, it's not quite mainstream yet, but is starting to develop.

The most common depression regimen is generally 10 Hertz, 3,000 pulses, 100% to 120% of that MT for 4 to 6 weeks. Like I said before, this continues to be an ever-developing field. There is continued discussion around maintenance and retreatment. We now have evidence that shows that half of responders will maintain benefit for 6 to 12 months without further session. For the other half, booster sessions every 3 to 6 months have been shown to prolong remission. Some clinics now run maintenance schedules, weekly or biweekly sessions for high relapse risk patients. Sometimes you just need a tune up, but in the real world, this is generally also affected by what insurance will cover.

These are the efficacy numbers. About 50% to 60% of patients with treatment-resistant depression respond, and about 30% to 35% achieve full remission. The real-world registry data for response rates to accelerated TMS is even higher, with numbers closer to 80% response rate and 50% remission, but we need much more information about this treatment modality at this point. In an era of modest antidepressant response rates, these are extraordinary numbers, and they come without systemic side effects.

Durability also remains excellent thus far. Benefits are stable four weeks after treatment and can last up to one year. A meta analysis of 732 patients who responded to TMS were tracked, and the proportion of initial responders who sustained response were at the three-month mark, 67%, six months, 53%, and 12 months, 46%. As we've been saying, this is a developing field, and recent meta analyses show that when clinics schedule a short retune at three and six months, roughly 70% of initial responders maintained remission at one year, up from the mid-40s we have here, but this information is still developing.

So far, we've covered what TMS is, how it works, how to keep it safe, and how it's delivered. Now we're going to talk about how to make it better, how to optimize response, and tailor protocols to special populations. Special populations. TMS can be helpful for the GERI population, especially if inherent prefrontal atrophy is taken into account, which could mean higher frequency treating or deep TMS. If accessible, neuro-navigation can also be helpful for these calculations. Also worth noting is that there's no increased seizure or cognitive impairment risk in the GERI

cohorts, even those on polypharmacy, which becomes a very important thing in the real world.

TMS has been shown to be helpful as an adjunct treatment to general care for post-stroke patients. They're also conducting studies that show that deciding what parameters to use could be dictated by time since stroke. People are also exploring using TMS prior to PT or OT to maximize neuroplasticity windows, priming the brain, like we mentioned before. Then earlier we touched on the fact of the FDA clearance for adolescents. So far it has been effective, and there hasn't been an observed increase in suicide, negative neurocognitive effects, or structural brain changes. It's still a growing field and clearly very pertinent.

For pregnant patients, it has been found to be safe for the fetus because the magnetic field rapidly drops off after 30 centimeters, as discussed in the beginning of the talk. You should check motor thresholds more often, essentially weekly, and monitor for hypotension in pregnant patients. In 2024, a systemic review of all published cases found zero obstetric complications attributable to TMS, and symptom remission rates similar to non-pregnant patients. Clinicians are also increasingly using left-sided ITBS protocols in pregnancy just because they're shorter, less tiring, and equally effective. For many pregnant patients, TMS offers a path forward when medication isn't an option. It's non-systemic, non-sedating, and evidence-based.

Optimizing response. Patients come in five days a week for six weeks. That's 30 opportunities for therapeutic engagement. It's a captive audience. Studies have started suggesting that pairing TMS with CBT or behavioral activation yields synergistic improvement, especially in executive function and emotional regulation. Mechanistically, it makes sense. TMS boosts plasticity. Therapy provides the new wiring. You could think of it as TMS is opening a window and psychotherapy is deciding what breeze we let in. Clinics are now experimenting with CBT modules that patients can complete during or right after sessions. Early results look promising.

What if it isn't working? First, keep treating if the insurance allows you to. Sometimes people need more pulses. Like we've been saying, the idea of a maintenance schedule is being studied. Then consider, is depression the priority pathology to be managing at this point? Is that what's really leading the bus in the presentation here? Recheck motor threshold. Switch protocols or use image-guided targeting available to you.

This is when you provide general quality psychiatric care. If TMS isn't working. The same way you would consider a different medication if one wasn't effective. Assess safety. Contact collaterals. Consider other neurotherapeutic treatments. This ends up being a significant aspect of care in neurotherapeutics because inherently, by the time the patient makes it to your clinic, they've trialed and failed several different medications and treatments. Your main goal here is to help the patient see that they are not at the end of the road in terms of a combination of ways of things that we can think of to help.

To an extent, so much of what we've talked about today would lend itself to what's to come and has been dovetailed throughout the talk. To highlight some, the next

priority pathologies to treat with TMS are bipolar depression, anxiety, PTSD, addiction, schizophrenia, ADHD, chronic pain, tinnitus, Tourette's, and Alzheimer's. Accelerated TMS protocols, whether that be the full inked version of 10 treatments per day or now clinics are trialing fewer treatments per day so it doesn't take the whole day but still shortens overall treatment course.

A couple of these have gained FDA clearance recently. Treatment protocols with more pulses, including maintenance schedules, connectivity-based targeting via individualized MRI maps, combination neuromodulation, pairing it with other modalities, using D-cycloserine or D-serine to augment the treatment via long-term potentiation. Using real-time guided EEG systems to synchronize pulses to the patient's ongoing brain rhythm. Cerebellar TMS for movement and cognitive disorders, and so many others. All right, so that is the end of the official talk and we'll start talking about some Q&As. Thank you so much for listening.

Speaker 1: We're now moving into the live Q&A. Thank you to everyone who submitted questions during registration and to those adding them in the Q&A box today. Drs. Gatchel and Kumar will do their best to answer as many as possible, so they may not get to all of them. Your questions are appreciated. Let's dive in. Are there any clinical trials associated with the use of TMS?

Dr. Kumar: Yes, there's been several. A lot of what I summarized in the talk today thus far have been based on clinical trials that have been done. There's been both open-label and then there's also been the more double-blind controlled placebo versions as well.

Speaker 1: Brilliant. We have another question that asks, can clinical psychologists use this? Would they need a special license?

Dr. Kumar: As of right now, it might be state-to-state, so I can speak most confidently about Massachusetts. You do need an MD overseeing the treatment, so essentially writing that initial prescription and being present in the area for all treatments. Then generally, TMS techs and nursing can provide the actual treatment on a day-to-day basis. I don't think they can be initially prescribed, but we generally work in close contact with therapists and outpatient teams of our patients because the outpatient team knows the patient so much more. It can generally be advocated by a therapist to use TMS. I think it depends on the clinic as to who can put in a referral, but the process can generally be started. We often depend on an outpatient team in the community to start that process.

Speaker 1: Brilliant. Thank you. We have another question that asks, what can counselors, therapists, and clinicians do to help extend the benefit of TMS long-term after the treatment ends?

Dr. Kumar: Like we were saying earlier about how TMS can help prime the brain for therapy. Again, this is still something that's being studied. Almost everything involving TMS is still in that stage, but it can prime the brain to be a bit more plastic and a bit more open to different types of therapy. Optimizing that timing and starting therapy or doing therapy while getting TMS and continuing it could potentially help with the long-term potentiation aspects of TMS.

Dr. Jennifer R. Gatchel: Some others that have come up are, is it true that TMS is not yet conclusive in terms of its benefit for ADHD? Are any preliminary findings optimistic? Then there are a few other questions related to TMS for neurodegenerative conditions like Alzheimer's disease. For ADHD, and I believe Dr. Kumar commented on this, there are some promising findings, but nothing conclusive or definitive. It's not a standard of care approach as of yet for ADHD, but it's an area of ongoing investigation. Yes, preliminary findings are optimistic.

For neurodegenerative conditions like Alzheimer's disease and Parkinson's disease, a similar situation. An area, as you can imagine, of intense research, especially for Alzheimer's disease, with the advent of disease-modifying therapies, which don't benefit all patients and come with a great degree of potential risks and side effects. Could TMS be an augmenting treatment or could it be another way to enhance or prevent cognitive decline or slow cognitive decline? Early results are promising, but this largely may involve targeting different brain regions, and the one we might target in depression or OCD. It's currently not, again, part of the standard of care, but I think we're increasingly going to see clinical trials in this area and further investigation.

Similar for Parkinson's disease and Parkinson's disease depression and anxiety are very common comorbidities in addition to the motor symptoms. We have treated patients with Parkinson's disease depression, but TMS is not, again, the gold standard or the FDA-cleared recommended treatment for Parkinson's disease depression, but it's certainly a population that you could consider referring for TMS if they're not responding to psychotherapy or pharmacotherapy.

Dr. Kumar, did you want to comment any further on--

Dr. Kumar: That's perfect.

Dr. Gatchel: Okay, great. Another question that came up in the pre-submitted questions that was a common theme was, how does the efficacy of TMS compare to-- for treatment-resistant depression, how does it compare to using psychotherapy or using pharmacotherapy? Dr. Kumar, did you want to comment on this? I can also chime in as well.

Dr. Kumar: Go for it.

Dr. Gatchel: Okay. There haven't been a great deal of head-to-head studies that have investigated TMS versus specific type of psychotherapy or medication trials, but based on the studies investigating these therapies alone, response rates and efficacy seems to be similar. There are, of course, different safety profiles for each of these treatments and risks and benefits.

There's different time to experience the treatment effects. For example, with pharmacotherapy, this can be on the range of weeks, and you also are dealing with side effects given that this is a systemic effect on the body. Versus for TMS, we can see response sometimes sooner, and there are really few, if any, long-term negative physical or somatic side effects or downstream consequences of the treatment. There are no negative effects on memory or thinking or cognition.

Then for psychotherapy, again, not many direct head-to-head studies, but as Dr. Kumar went over, there's increasing interest in the synergy of these approaches together. Often, it's not an either-or in our clinical practice. We often recommend a trial of TMS, but also continuing to explore the benefits of, again, augmenting with psychotherapy or pharmacotherapy because, again, if we can target different pathways, the different mechanisms by which these treatments are working, we're more likely to see a response.

Then there's also a question about-- there are more and more med-spa-type facilities offering exomind treatments, and curious about our thoughts on that. I'm not as familiar with the exomind treatment. Then as Dr. Kumar mentioned and came up in a previous question, in many states, an MD is required to be present for an actual TMS treatment. There are other types of non-invasive brain stimulation like transcranial direct current stimulation or TDCS. Those are things that can be done portably and without an MD present, so that might be part of what the exomind treatment is.

Again, for TDCS, if it's done in a really rigorous way, there are mixed results in terms of its efficacy for depression, but some of those results are promising. It also has a good safety profile and is well-tolerated and could be done remotely. Again, there could be some benefits there. It's been increasingly studied in combination with cognitive remediation and psychotherapy, that combination.

For other types of brain stimulation treatment like exomind, I feel like those are in the more explor-- I don't know exactly what that is, but that may be in a more exploratory range. We'd want to really get a detailed assessment of what is being stimulated, what is the device that's being used, and getting more detailed info on that before recommending that or evaluating that. What might be the cost? There's some questions about what is the out-of-pocket cost. Dr. Kumar, do you want to comment on that?

Dr. Kumar: I don't know. Obviously, it'll be person to person. I know that most of the accelerated protocols right now are out-of-pocket, and I want to say they're around $40,000 or so.

Dr. Gatchel: Yes, that's my understanding as well. I think in the future, there's a robust body of evidence for the accelerated protocols, but the insurance approval piece is lagging behind. I think in the future, we will see insurance covering that procedure more, but it's totally out-of-pocket, like in the range of $40,000, like Dr. Kumar mentioned. For non-accelerated, I want to say it would also be in that range. It is quite expensive, and for most patients, it's prohibitively expensive for them to do it if insurance were not going to cover it. Can you go over how long each treatment takes? Did you say the whole day?

Dr. Kumar: Again, that depends on the machine that's being used. Some of them, the actual treatment can last for about three minutes, and others, about 20 minutes. The full-day thing is more if you're doing that accelerated protocol where you're doing 10 treatments per day with an hour in between. If you're doing the most common protocol that is currently being used, it's usually about a 20-minute to 45-minute appointment, including in the door, out the door, talking to the clinician, et cetera. Like we said earlier, it could be fitted into a workday or a school day or something like that, which makes it a bit more accessible.

Dr. Gatchel: I'm just reviewing some of the other questions, make sure we get-- Could TMS be applicable in managing functional neurological disorders and sleep problems? Again, I think this is also an area of active investigation but not robust evidence. If solely thinking about functional neurological disorders without comorbid depression or isolated sleep problems, so I think it's not yet part of standard of care area of investigation, still very early.

Certainly, with functional neurological disorders and sleep problems, they're often comorbid with depression, so that's not uncommon that we might see a patient with a functional neurological disorder and he's experiencing significant distress. We will evaluate that patient the risk and benefits for treating with TMS. That can be more complicated when there's a question of functional neurological disorder related to seizures, because as Dr. Kumar mentioned, seizures are rare, but uncommon, potentially serious side effect of TMS.

We definitely do a very thorough screening history during consults about any history of seizure, any family history of epilepsy, all of which can increase the risk for this complication during treatment. We rigorously monitor patients throughout their treatment to ensure that they're being treated safely and not having a seizure. In the case of functional neurological disorder, if seizures or pseudo seizures are part of that, it can be more complex in terms of monitoring and ensuring safety and efficacy, but it is not a contraindication.

Let's see. It seems like there are some questions about just the angle of the coil placement during treatment and how can that be adjusted if there's pain or difficulty tolerating treatment? How much leeway is there in making adjustments to that while still ensuring that the treatment is effective? Dr. Kumar, do you want to mention anything about that and I can chime in?

Dr. Kumar: Yes, absolutely. Again, that depends on the type of machine that you're using. I think we talked earlier about how there's a deep TMS version, which is more of a helmet model, and then most of them are more of a coil model. The helmet has probably a bit more leeway in a more subjective sense of placement. I think there's always a little bit of leeway, just moving it slightly while still being in the general area. There's the moving of the actual coil, but you can also decrease the intensity at the time and work more slowly in building that, which can also help with some of that discomfort.

Dr. Gatchel: Does Medicare cover TMS? Yes, it does. I believe it covers TMS for major depression. I don't think it yet covers it for OCD. Is it recommended or contraindicated for a patient to undergo EMDR treatment while also receiving TMS treatment? Yes. That's, again, I think on a case-by-case basis and just evaluating the patient's clinical stability and the tolerability of those treatments. They both can be very intensive treatments, especially the TMS coming daily. In some cases, we might want to adjust the TMS treatment target to take into account symptoms of PTSD or trauma so we don't worsen those symptoms.

It would be important to communicate with the TMS clinic to come up with a collaborative plan around considering those treatments if you want to do them in combination or sequentially. There's no absolute contraindication saying that you

couldn't do it during a course of EMDR. I think we covered most of the questions, but let us know also if **[unintelligible 00:52:48]**

[00:53:20] [END OF AUDIO]