

Provincial Clinical Knowledge Topic Transcranial Magnetic Stimulation, Adult – Inpatient, Ambulatory V 1.2 April 2020

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Document History

Version	Date	Description of Revision	Completed By / Revised By
1.0	Mar. 2017	Initial document completion	Dr. Michael Demas
1.2	Jan. 2020	Change of tools from BDI to QID SR16 and Revised Protocols	Dr. Michael Demas

Important Information Before you Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

This topic is based on the following guideline(s):

- Canadian Network for Mood & Anxiety Disorders. Guidelines for the Management of Adults with Major Depressive Disorder
- National Institute for Health and Care Excellence Guideline Repetitive Transcranial Magnetic Stimulation for Depression.
- University of Calgary Health Technology Assessment Repetitive Transcranial Magnetic Stimulation for Treatment Resistant Depression

Rationale

In many studies conducted in the general population depression is a common mental condition with an annual prevalence rate from 5% to 12%. Depression is the leading cause of disability world-wide and is a major contributor to the overall global burden of disease⁴. Unfortunately not all patients respond to the available pharmaceuticals and treatment algorithms.

Repetitive Transcranial Magnetic Stimulation (rTMS) has been developed as a psychiatric treatment and was approved for clinical use by Health Canada in 2002. It involves the focal application of a magnetic field to the cerebral cortex, inducing small electrical currents which may alter brain functioning with therapeutic effect and without loss of consciousness or loss of memory.⁵ The term 'repetitive' is used to indicate the fact that the magnetic stimulation is delivered at regular intervals. It does not require anesthesia. Its therapeutic potential in psychiatry, and in other areas, is being studied in many countries throughout the world. By introducing rTMS in areas across AHS this could help to reduce rates of depressed persons, reduce practice variation, improve patient and provider experience, reduce inpatient admissions, reduce rates of suicide and suicide attempts, reduces rates of disabilities and improve fiscal management. Patient selection for rTMS is important.

The safety and side effects of rTMS have been extensively studied and rTMS has been shown to be safe. Guidelines for safe parameters have been published. The only common side effects are local discomfort at the site of the coil application, and mild headache. The risk of seizure is rare but may occur. This risk is reduced by careful safety screening. There is a small risk of hearing loss which can be minimized by the use of hearing protection and more modern, quieter devices. Other potential but rare side effects include: induction of mania in bipolar patients, burns from electrodes, local pain and paresthesia⁵. The treatment itself may have short efficacy effect for patients, may be only partially effective, and in some cases may not provide benefit at all.

rTMS therapy in Alberta will begin with a focus on the initial introductory indications as were outlined in the Health Technology Assessment Repetitive Transcranial Magnetic Stimulation for Treatment Resistant Depression 2014.⁶ Initial protocols were adapted based on the initial clinical trials of Mark George and Eric Wasserman published in the Journal of American Psychiatry 1997⁷ and also on the recent guidelines published by the Canadian Network for Mood and Anxiety Disorders¹ (2016). Additional guidelines also reviewed were the NICE Guidance², Clinical rTMS Society⁸, and the Clinical Neurophysiology recommendations for transcranial magnetic stimulation¹⁰.

Analytics

Baseline Analytic – Outcome Measure

Name of Measure	Order set Usage for: Transcranial Magnetic Stimulation, Adult – Inpatient, Ambulatory
Definition	<p>For all patients provided with transcranial magnetic stimulation therapy (rTMS) whether in the inpatient setting or in the ambulatory setting the following data is to be collected:</p> <ol style="list-style-type: none"> a. The number of times the order set is being used. b. Patient Demographics c. Site and Zone Identifiers d. Date and time of rTMS stimulation e. rTMS parameters – <ul style="list-style-type: none"> o machine utilized o Type of treatment – (e.g. continuous or intermittent Theta-burst treatment) o Coil type (magnetic field shape) o coil placement o stimulus intensity (as a % of motor threshold) o number of pulses/train o number of trains/block (if any blocks) o interpulse interval o intertrain (interblock) interval o total number of pulses
Rationale	<p>The data collected regarding rTMS protocols and the order set components utilized by clinicians across the province will provide consistent data that is being captured already in other provinces where rTMS is provided.</p> <p>The data will assist in evaluation of the therapy and provide further direction for implementation of the program across the province</p>
Notes for Interpretation	A comparison of the order set usage of ECT and TMS order sets would provide additional information for determining if there is increased access to appropriate antidepressant treatment, and if there is a change in the number of patients receiving ECT based on the implementation of TMS across the province.
Cited References	1. University of Calgary. <i>Repetitive Transcranial Magnetic Stimulation for Treatment Resistant Depression</i> . Health Technology Assessment. 2014 Apr. Accessed June 2016

Clinical Analytics – Outcome Measure #1

Name of Measure	Implementation of an rTMS model across AHS that demonstrates improved outcomes and effectiveness
Definition	The TMS model demonstrates: <ul style="list-style-type: none"> ○ a positive health/clinical impact ○ reductions in patient and clinician rated levels of depression ○ improvements in patient-related experience and quality of life
Rationale	<p>This is in response to an emerging issue based on accepted evidence and practice, approved by Health Canada for over a decade with therapeutic potential in psychiatry, and in other areas of medicine. It is being studied in many countries throughout the world. Introducing rTMS in areas across AHS could help to reduce rates of depressed persons, reduce practice variation, improve patient and provider experience, reduce inpatient admissions, reduce rates of suicide attempts, reduce rates of disabilities and improve fiscal management.¹</p> <p>The American College of Neuropharmacology²(ACNP) definitions for response, relapse, remission, and recovery will be utilized to define the effectiveness/efficacy of treatment</p> <ul style="list-style-type: none"> • Response – measured 1 month later – a 50% reduction in pre-treatment severity the patient is considered a responder. Less than 50% response then the patient is classified as a non-responder • Remission – ascribed after 3 consecutive weeks during which minimal symptom status (absence of both sadness and reduced interest/pleasure along with the presence of fewer than three of the remaining seven DSM-IV TR/DSM 5 diagnostic criterion symptoms (typically indicated by scores on the rating scale(s) within the non-depressed range) is maintained • Recovery – is ascribed after 4 months following the onset of remission without the occurrence of relapse • Relapse – a return of the index major depressive episode following the onset of remission
Notes for Interpretation	<p>The following clinician and patient rated assessment tools will be utilized to assist in measuring response, remission, recovery and relapse. The required assessments are to be completed immediately before the index treatment, after 10 sessions, midway through the treatment and at 1, 3 and 6 months post treatment.</p> <p><u>Clinician Rated Depression Symptoms</u></p> <ul style="list-style-type: none"> • Hamilton Depression Rating Scale³ (Ham-D) <p><u>Patient Rated Depression Symptoms</u></p> <ul style="list-style-type: none"> • Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16) • Columbia Suicide Severity Rating Scale⁵ (CSSR Lifetime/Recent & CSSR – since last visit) <p><u>Patient Rated Functional Quality of Life and Health Outcome</u></p> <ul style="list-style-type: none"> • EuroQol Five Dimensions Questionnaire⁶ (EQ-5D) • World Health Organization Disability Assessment Schedule⁷ (WHODAS 2.0)

	<p>Patient Rated Symptoms and Side Effects:</p> <ul style="list-style-type: none"> • Patient Rated Inventory of Side Effects (PRISE) • Frequency, Intensity and Burden of Scale Side Effects Rating (FIBSER)
Cited References	<ol style="list-style-type: none"> 1. University of Calgary. <i>Repetitive Transcranial Magnetic Stimulation for Treatment Resistant Depression</i>. Health Technology Assessment. 2014 Apr. Accessed June 2016 2. Rush John, Kraemer H, Sackeim H, Fava, Maurizio F, et al. Report by the ACNP Task Force on Response and Remission in Major Depressive Disorder. <i>Neuropsychopharmacology</i>. 2006; 31:1841-1863 doi: 10:1038/sjnpp. 1301 131 3. Canadian Network for Mood & Anxiety Disorders. Guidelines for the Management of Adults with Major Depressive Disorder: Section 4: Neurostimulation Treatments. <i>Can J of Psychiatry</i>. 2016: 61(9):561-575. 4. Hamilton, M. Rating depressive patients. <i>J Clin Psychiatry</i>. 1980; 41: 21-24 5. Beck A, Steer R, Brown G. "Manual for the Beck Depression Inventory-II". San Antonio, TX: 1996; Psychological Corporation 6. EuroQol Group. "EuroQol--a new facility for the measurement of health-related quality of life". <i>Health Policy</i> Amsterdam, Netherlands 1990; 16 (3): 199–208. doi:10.1016/0168-8510(90)90421-9 7. World Health Organization. <i>Disability Assessment Schedule 2.0</i>. Geneva, Switzerland. World Health Organization; 2014 8. Wisniewski S, Rush A, Balasubramani G, Trivedi M, Nierenberg A; Self rated global measure of the frequency, intensity and burden of side effects. <i>J Psychiatr Pract</i>. 2006 Mar; 12 (2):71-9.

Clinical Analytics – Outcome Measure #2

Name of Measure	Implementation of an rTMS model that addresses patient safety, reduces harm and improves access to treatment for patients
Definition	<p>The TMS model demonstrates:</p> <ul style="list-style-type: none"> • reduction of harm to patient • reductions in wait times for patient to receive treatment for treatment resistant depression • reduces service pressures and unmet clinical need • reduction in the number of suicides and suicide attempts
Rationale	<p>The safety and side effect of rTMS have been extensively studied and rTMS has been shown to be safe. Guidelines for safe parameters have been published. The only noted common side effects are local discomfort at the site of the coil application, and mild headache. No anesthetic is required.</p> <p>rTMS has been shown to resolve the symptoms of depression and improve quality of life. Research has shown that there are decreased numbers of adverse events with rTMS.</p> <p>rTMS therapy is usually provided on an outpatient basis and the treatment time is generally no longer than an hour in total.</p>

	This supports capacity through upstream prevention by reducing demand for in-patient hospital treatment due to lower incidence of disease
Notes for Interpretation	<ul style="list-style-type: none"> • Wait time measurements for rTMS treatment and ECT therapy need to be captured for comparison • The number of all types of physician and psychiatrist visits should also be captured to demonstrate a reduction in service demands. • Capturing the rates of suicides and suicide attempts for those receiving rTMS therapy would provide additional data to support the measurement of improvement to patient safety.
Cited References	<ol style="list-style-type: none"> 1. University of Calgary. <i>Repetitive Transcranial Magnetic Stimulation for Treatment Resistant Depression</i>. Health Technology Assessment. 2014 Apr. Accessed June 2016 2. Canadian Network for Mood & Anxiety Disorders. Guidelines for the Management of Adults with Major Depressive Disorder: Section 4: Neurostimulation Treatments. <i>Can J of Psychiatry</i>. 2016; 61(9):561-575. 3. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. The Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. <i>Clin Neurophysiol</i> 2009;120:2008–39 4. National Institute for Health and Care Excellence. <i>Repetitive Transcranial Magnetic Stimulation for Depression</i>. London (UK): NICE; Updated December 2015. (Clinical Guideline 542) 5. Brain Stimulation. <i>The Clinical rTMS Society Consensus Review and Treatment Recommendations for Transcranial Magnetic Stimulation Therapy for Major Depressive Disorder</i>. 2016; Mar.

Goals of Management

1. A trained credentialed psychiatrist must determine the need for Transcranial Magnetic Stimulation (rTMS) therapy and prescribe the treatment.
2. rTMS is prescribed following a thorough psychiatric evaluation and assessment of any co-morbidities such as substance abuse, personality disorder and anxiety disorders.
3. Informed consent is obtained from the competent patient, or their legal decision maker, by the psychiatrist. The AHS/Covenant Health consent to treatment and procedures is followed. Consent can be withdrawn at any time during the treatment.
4. rTMS Therapy is primarily indicated for treatment of depressive disorders in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode or been non responsive to other recommended treatments such as cognitive behavioural therapy, and other psychotherapy.
5. rTMS Therapy can be administered with or without the concomitant administration of antidepressant or other psychotropic medications.
6. rTMS therapy can be reintroduced in patients who are relapsing into depression who previously responded to rTMS treatment and may be used to maintain a state of response/remission.
7. Any changes to what the person is taking, including prescription medications, over the counter medications, herbal supplements, and vitamins need to be reported to the treating psychiatrist.

Decision Making

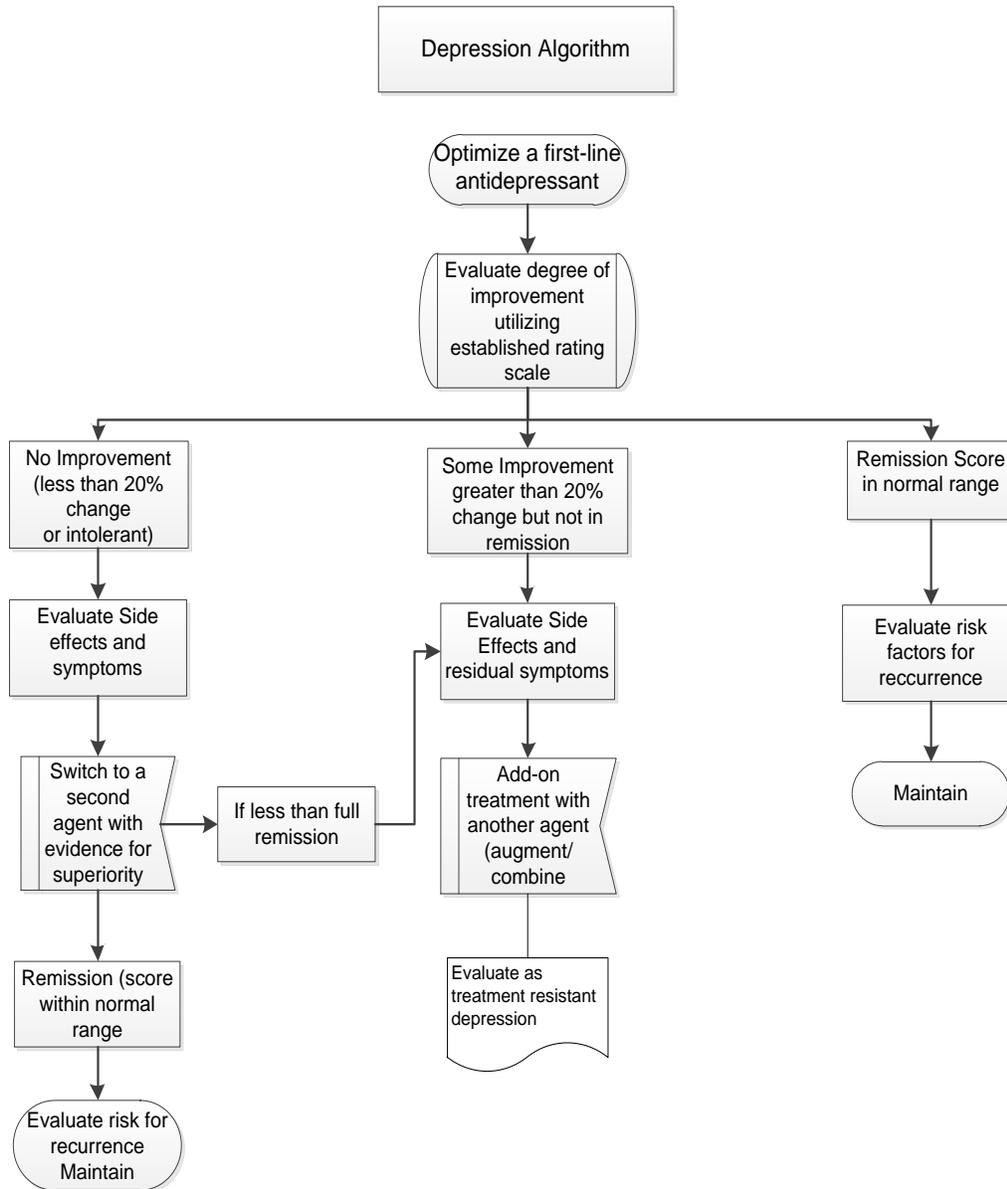
Principles of Care

Prior to exploring repetitive transcranial magnetic stimulation therapy (rTMS) consideration should be given to the level of treatment resistance, the likelihood for positive outcome with rTMS versus other treatments, and the severity and risk associated with the mental disorder being treated². Prior to recommending rTMS some suggested principles of care to consider are:

- Assess a person referred to specialist mental health services, including:
 - symptom profile, suicide risk, treatment history, whether treatment recommendations have been followed and the presence of any comorbidities such as substance use, personality disorder and anxiety disorder
 - psychosocial stressors, personality factors and significant relationship difficulties, particularly if the depression is chronic or recurrent
 - review the persons support network
- Consider reintroducing treatments that have been inadequately delivered or inadequately adhered to.
- Use a multidisciplinary approach to manage crises for people with severe depression who present significant risk, and to deliver high-quality acute care. Monitor risk appropriately
- Develop a multidisciplinary care plan with the person (and their family or care giver if the person agrees) which:
 - identifies the roles of all professionals involved
 - includes a crisis plan that identifies potential crisis triggers and strategies to manage them
 - is shared with the person, their Primary Care physician their other treatment providers and other relevant persons
- The patient must be able to comply with the rTMS therapy timeframe such being able to hold still, and attend daily treatment(s) (typically for 5 days a week for 20-30 treatment sessions) and be willing to comply with all evaluation procedures including follow-up evaluation at 1, 3 and 6 months post-treatment.

Clinical Depression Algorithm

Figure 1 Clinical Depression Algorithm¹



Adapted from CANMAT Journal of Affective Disorders

Transcranial Magnetic Stimulation (rTMS) Administration

Pre-Assessment

An evidence informed approach to the method of assessing the tolerability and efficacy of rTMS therapy and continuous quality improvement will be utilized. Patient and clinician driven tools that provide a common comparable outcome to other medical treatments, that are validated, reliable, generally comparable to the medical literature, that for the most part are in public domain, that are already in use, and produce a useful summary metric will be utilized.

The following are assessment tools that must be completed by the psychiatrist and the patient to assist with outcome measurements and improvement in quality of life. Additional instruments that could also be used in addition are noted. The required assessments are to be completed immediately before the first treatment, after 10 session's midway through the course of treatment, immediately after the last session of the index course of treatment and at 3 and 6 months post treatment. The information from the clinical decision support tools will be entered into the provincial monitoring system.

1. **rTMS Safety Screen:**

- A formalized safety screen must be done prior to rTMS using the Transcranial Magnetic Stimulation Adult Safety Screen¹¹ (TASS)

2. **Clinician Rated:**

- Required – Hamilton Rating Scale for Depression¹² (HAM-D)
- Optional – Montgomery Asberg Depression Rating Scale¹³ (MADRS)

3. **Patient Rated:**

- Required – Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16)

4. **Functional, Quality of Life and Health Outcomes:** Note both are required

- Required – EuroQol Five Dimensions Questionnaire¹⁶ (EQ-5D)
- Required – World Health Organization Disability Assessment Schedule¹⁷ (WHODAS 2.0)

5. **Suicide Assessment:**

- Required – The Columbia Suicide Severity Rating Scale Lifetime/Recent¹⁸ (CSSR)
A suicide risk assessment is to be completed prior to initiation of therapy and at least once during the index or maintenance course of treatment. The CSSR Lifetime/Recent is used before first treatment & the CSSR Since Last Visit for all other occasions.

6. **Symptom and Side Effects:**

- Required – Patient Rated Symptoms and Side Effects (PRISE)
- Required – Frequency, Intensity, and Burden of Side Effects¹⁹ (FIBSER/GRSEB [modified to replace the word “medication” with “rTMS”])

The following assessment tools have been recommended for additional assessments that the clinician feels are required based on clinical assessment of the patient.

7. Anxiety Rating Scales

- Recommended – Clinician rated – Hamilton Anxiety Rating Scale²⁰ (HAM-A) recommended
- Recommended – Patient rated – The Generalized Anxiety Disorder 7²¹ – item scale (GAD 7)
- Optional – Beck Anxiety Inventory²² (BAI)

8. Cognitive Assessment screening is generally not required. Clinicians might consider the following and/or the more formalized psychometric testing if the situation is clinically warranted:

- Optional – Montreal Cognitive Assessment²³ (MoCA)
- Optional – Folstein Mini-Mental Status Examination²⁴ (MMSE)

9. Screenings for Diagnosis – Formalized diagnostic instruments are not required beyond the proper clinical assessment by the psychiatrist. Clinicians might consider screening for diagnosis utilizing the following:

- Optional – M.I.N.I. International Neuropsychiatric Interview²⁵ (MINI)
- Optional – Brief Psychiatric Rating Scale²⁶ (BRPS)
- Optional – Structured Clinical Interview for DSM disorders²⁷ (SCID).

Inclusion Criteria

Good candidates for rTMS have been reported to have unipolar or bipolar depression as a primary diagnosis, have a history of episodic rather than chronic lifelong depression, have not previously failed to respond to ECT or rTMS, have had remediable life stressors (for example divorce or legal proceedings), at least somewhat optimized prior to treatment, and are sufficiently motivated and reliable to adhere to the schedule of treatments. A plan for psychiatric follow up (medications, individual and/or group therapy etc.) should be arranged prior to or during the course of treatment, to reduce the risk of relapse.

Inclusion criteria:

- Adults
- Adolescents are being considered under the care of rTMS experts only
- Major depressive episode in those who have failed to go into remission with at least two trials of antidepressant medications or those who have an intolerance to at least two trials of medications
- For patients who responded to rTMS previously and are experiencing a recurrence of their illness
- Special populations such as seniors and pregnant or lactating women require careful assessment
- Exceptional cases may exist and other special populations and indications are currently under study
- Informed written consent for treatment

Exclusion Criteria

- Presence of ferro-magnetic material anywhere on the head and neck, excluding the mouth. This includes but is not limited to cochlear implants, implanted brain stimulators or electrodes, aneurysm clips, and plates or screws
- Presence of increased intracranial pressure, such as after large infarctions

Precautionary Considerations

The following are reasons for caution as they may increase the risk of an adverse event or decrease the risk of response with rTMS therapy.

History of seizure activity, epilepsy should be assessed carefully. Seizure risk with rTMS is elevated in this population. Patients with a history of any seizures for any reason(s) should be assessed carefully and treatment should be provided in a setting where advance life support can be provided and is immediately available in a hospital setting.

Other considerations:

- The use of drugs that might potentially lower seizure threshold such as tricyclic anti-depressants, neuroleptic agents, and others.
- Cardiac Disease including arrhythmia. Patients with cardiac pacemakers and other implanted devices should be assessed carefully and treatment should be provided in a setting where cardiac support can be provided and is immediately available in a hospital setting. This includes treatment while on cardiac monitoring equipment
- Presence of any intra-cardiac lines or any indwelling catheter lines
- Psychotic features associated with depression
- Active concurrent substance use such as alcohol addiction
- Primary diagnosis of personality disorder
- Those who are unable to comply with treatment requirements such as patients with delirium/dementia or physical inability to hold still for the entire treatment session
- History of syncopal episodes
- Impairment or vulnerability of hearing
- Poor response or significant adverse reaction to rTMS

Procedure

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive, non-convulsive neuromodulation medical treatment that has been shown to produce changes in neuronal activity in the brain. rTMS does not require anesthesia and can be done on an outpatient basis. rTMS uses targeted repeated pulses of magnetic energy. During stimulation, an electromagnetic coil is held against the scalp with the intention of inducing electrical currents in the cerebral cortex via powerful, focused magnetic field pulses. rTMS stimulates the brain with targeted repeated pulses or stimuli of magnetic energy. These pulses are delivered in trains of repeated stimuli. There is a pause or space between pulses and between trains. A series of trains comprises a treatment of stimulation applied to the target area. Trains may be organized into blocks of trains. The number, timing, strength and interval of each parameter are all important in defining the rTMS protocol. rTMS protocols pay close attention to the target area(s) of the brain, the duration of the stimulus or pulse, the number and frequency (speed) of pulses per train, the number of trains per block (if any), the inter stimulus/interpulse interval (ISI or IPI), the inter train interval (ITI), the interblock

interval (IBI), the total number of pulses, and the stimulus strength as a percentage of motor threshold.

Neuroimaging may be used to help target specific areas of the brain, although more commonly, scalp landmarks are used for coil positioning. Stimulation is delivered either unilaterally, or less commonly bilaterally, over the target region(s). In major depression, the most common targets are the left or right dorsolateral prefrontal cortex (DLPFC), or in some cases, the dorsomedial prefrontal cortex (DMPFC). Other areas of the brain can be targets of interest. The rationale behind choosing these target brain area stems from neuroimaging and other studies that indicated depression is associated with dysfunctional brain activity in, among other regions, the dorsolateral and dorsomedial prefrontal cortex.

The dorsolateral prefrontal cortex (DLPFC) can be located using the International 10-20 electroencephalograph (EEG) system to locate scalp site F3 or the BEAM (F3) method. Another procedure locates the DLPFC site by measuring 5 or 6 cm anterior to the motor 'hotspot' site at which the strongest movements of the contralateral thumb are elicited; this site is convenient as it is used to determine motor threshold. In some cases, MRI-guided neuronavigation may be used to define the stimulation site. This is most commonly used when stimulation of non-standard sites is required. The prescribing psychiatrist will advise on the technique to be utilized to locate the region.

A standard course of treatment usually involves a series of daily treatments lasting for 20 to 30 sessions. As with any medical procedure, an informed consent must be obtained from the patient or decision maker prior to performing the procedure, detailing the nature of the treatment, the reason for its being proposed for the patient, the possible benefits and risks of the treatment, and alternatives. If the patient elects to proceed, the psychiatrist will use clinical experience and clinical judgement to determine the placement of the coil, the intensity, frequency, train duration, and all other parameters. The psychiatrist normally also performs the initial motor threshold testing in order to determine the settings of stimulation in each patient.

This document details the options available to the providing psychiatrist. All persons are informed before beginning rTMS therapy that their anonymized data will be part of a provincial data set used to monitor safety, efficacy, and quality and will be available for analytics purposes.

rTMS Process

rTMS therapy is always prescribed by and delivered under the supervision of an appropriately qualified psychiatrist. The psychiatrist always supervises the treatment. The rTMS operator may be an appropriately trained and credential individual who is under a medical delegation in a manner similar to a phlebotomy technician drawing blood for a laboratory investigation ordered by a physician. Treatment programs should be appropriately and adequately staffed and trained with ongoing training to ensure fidelity to the protocols and processes required.

Stimulation intensity is determined according to a measure of cortical excitability known as *motor threshold* (MT). Stimulation applied to the scalp overlying the motor cortex induces overt motor activity in the contralateral hand (or leg) muscle that can be identified visually or recorded using an electromyogram (EMG) as a motor evoked potential (MEP). Motor Threshold is defined as the minimum stimulation intensity applied to motor cortex required to induce a reliable motor response in a predefined muscle of the contralateral hand in at least 50% of a series of stimulations. In the

clinical setting motor responses are assessed based on visible responses; by recording the EMG response (e.g. greater than 50 microvolts).

The intensity of stimulation in rTMS protocols is determined on an individual basis, as a percentage of the motor threshold (MT). Determining MT is relatively straightforward and objective. Motor threshold is determined at the beginning of each treatment course at the beginning of the first treatment session. Some authors report MT is fairly stable overtime and usually does not need to be re-established unless the protocol needs to be changed while others recommend reassessing MT every 5 sessions and some every treatment session.

The literature recommends that MT be determined using single TMS pulses resulting in a motor response of a hand muscle, typically abduction of the contralateral abductor pollicis brevis or abductor pollicis longus, sometimes the first dorsal interosseous muscle, measured as a motor evoked potential (MEP) of at least 50 microvolts in at least 50% of 10–20 consecutive stimuli, or as can be visually observed. The stimulations should be performed at least 5 seconds apart during the determination, as more frequent stimulation may change the excitability of the brain area being stimulated. Some recommend if the site of the stimulation is to be the dorsomedial prefrontal cortex, MT may be determined by stimulating the medial motor cortex over the vertex, and observing movements of the lower extremity rather than the upper extremity.

Standardization of stimulation protocols is essential for safety, comparison of rTMS effects between participants and protocols, for quality improvement and other purposes. A wide variety of treatment protocols are in clinical use around the world, and the optimal treatment protocol may vary based on patient presentation. One widely used treatment is the Food and Drug Administration approved protocol (2008) which consists of 3,000 pulses delivered at 10 pulses per second in a series of 75, 4-second trains, with 26-second pauses between trains, for a total stimulation time of 37.5 minutes.

Protocols are defined generally utilizing the following terms:

- Target: area of the brain (coil placement) stimulated directly by the treatment
- Pulse: a single stimulus
- Train: a series of pulses
- Block: a series of trains
- Interstimulus interval (ISI): the interval between the onset of one stimulus to the onset of another stimulus (also known as IPI)
- Intertrain interval (ITI): the interval between sets of trains
- Interblock interval (IBI): the time between blocks of trains
- Interpulse interval (IPI): the time between magnetic pulses (also known as ISI)

Theta burst stimulation (TBS) is a patterned form of rTMS that mimics the brain's endogenous theta rhythms (~5 Hz rhythms) by delivering 5 bursts of stimulation per second, with each burst consisting of three pulses at 50 Hz. It can produce either an excitatory or inhibitory effect, depending on the specific parameters of delivery. Continuous theta-burst stimulation (cTBS) for example typically delivers 600 pulses of theta burst stimulation as a single 40 sec train and is considered inhibitory. Intermittent theta-burst stimulation (iTBS) delivers 600 pulses of theta burst stimulation in 20 trains (2 seconds on, 8 seconds off) over approximately 3 minutes. Theta burst carries the advantages of a shorter treatment session, and thus enables each device and operator to treat more persons in a day as long as the rTMS machine is TBS capable and is actively cooled.

Hearing protection should be offered to both patient and operator during the procedure depending on the noise output of the machine. In addition, the rTMS operator and the supervising psychiatrist should be familiar with first aid procedures for managing a seizure, and the process for managing a seizure should be determined in advance. All ferro-magnetic material should be removed from the patient's head area prior to the procedure. Dental implants, orthodontic devices, or other implanted metal hardware in the mouth area are not a contraindication to treatment. However, the patient should remove electronic devices such as mobile phones or medication pumps and magnetic sensitive items such as bank and credit cards, and keep them away from the stimulator coil (a distance of greater than 1 meter is recommended) during treatment to avoid disruption of the functioning of these devices.

rTMS Protocols

The most recent CANMAT Guidelines¹ (September 2016) reviewed and suggested various types of rTMS as first line, second line, and so on, based on the literature ([see Table 1](#)). The 2016 Clinical TMS Society Consensus Review and Treatment Recommendations for TMS Therapy for Major Depressive Disorder and the 2104 evidence based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS) also provide guidance for rTMS including that rTMS therapy is recommended as an acute treatment for symptomatic relief of depression in the indicated patient population. rTMS therapy is recommended for use as a subsequent option in patients who previously benefited from an acute course and are experiencing a recurrence of their illness (continuation or maintenance). rTMS therapy can be administered with or without the concomitant administration of antidepressant medication or other psychotropic medications. The review indicated that there is a probable antidepressant effect of low frequency (LF) rTMS of the right dorsolateral pre frontal cortex (RDLPFC). Similarly that there is probably no difference in the antidepressant effect between high frequency (HF) rTMS of the left dorsolateral prefrontal cortex (LDLPFC) and LF RDLPFC, and there was no recommendation for the antidepressant effect of bilateral rTMS combining high frequency rTMS of the LDLPFC and low frequency rTMS of the RDLPC.

The Alberta guidelines for rTMS provide specific initial protocols within the general categories as recommended in the CANMAT and other Guidelines (see table below). The most recent adjustments are in keeping with the principles outlined in the creation of the document including the need to have a basket of set protocols from which the prescribing psychiatrist can choose using appropriate clinical judgement but not from an infinite number of protocols thus allowing for standardization for purposes of fidelity to the principles of the Guideline, for quality improvement, and for clarity, in keeping with the current medical literature. Importantly CANMAT Guidelines recommendations remain emphasized to the prescribing psychiatrist in the Guideline.

Also remaining in true fidelity to the principles of the Guideline is the purposeful method of providing room for reasonable disagreement about the importance, value, and reliability of the evidence in the medical literature while keeping the number and types of protocols within a limited set of recommended-approved protocols.

Some recent updates in the field include the United States of America Food and Drug Administration approvals of the shorter standard FDA high frequency protocol from 37.5 to 19 minutes, the FDA approval of a theta burst protocol, the 2018 Consensus Recommendations for the Clinical Application of Repetitive Transcranial Magnetic Stimulation (rTMS) in the Treatment of Depression by McClintock et al from the Journal of Clinical Psychiatry, the 2018 Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with

depression (THREE-D): a randomized non-inferiority trial by Blumberger, *et al*, in the Lancet, the 2018 Response and Remission Rates Following High-Frequency vs. Low-Frequency Repetitive Transcranial Magnetic Stimulation (rTMS) Over Right DLPFC for Treating Major Depressive Disorder (MDD): A Meta-Analysis of Randomized, Double-Blind Trials, by Cao, *et al* in Frontiers in Psychiatry, Durability of antidepressant response to repetitive transcranial magnetic stimulation: Systematic review and meta-analysis, by Senova, *et al*, January 2019 in Brain Stimulation, and other papers.

Experts have some disagreement about Right Sided Low Frequency Protocols. This illustrates the room for reasonable scientific disagreement. For example for some experts in general it is now thought that Right Sided Low Frequency rTMS protocols need to have sufficient numbers of pulses (>1200) per session in order for this type of protocol to be efficacious whereas other experts have evidence for their own peer reviewed published research showing that 360 or 600 pulses as Continuous 1 Hz stimulation is efficacious.

Tolerability and clinical efficacy assist in decision making around stopping the treatment and/or changing protocols. In general after two weeks there should be evaluation of the clinical efficacy of a protocol and if no adequate response then the protocol could be changed.

The decision of actual protocol(s) and any adjustments will remain between the treatment provider and the patient based on clinical factors and may need to be adjusted as treatment progresses. Reasons for the choice of protocol should be documented. It is recognized that there will be legitimate reasoned disagreements among experts as to what is considered first line, second line, and so forth. In order to achieve fidelity to the overarching goals of these guidelines the protocols have been specified in detail for treatment providers to follow. Expert centres may use other protocols or target areas. Other protocols supported in the literature are presented in [Appendix A](#) and are at present to be reserved for the expert rTMS sites. The guidelines will be reviewed on a yearly basis.

Table 1 CANMAT Recommendations for rTMS Stimulation Protocols ⁸

Recommendation	Frequency	Site
<i>First Line</i>	<ul style="list-style-type: none"> High Frequency rTMS Low Frequency rTMS 	<ul style="list-style-type: none"> Left DLPFC Right DLPFC
<i>Second Line</i>	<ul style="list-style-type: none"> Bilateral rTMS Low frequency rTMS (in non-responders to high frequency left DLPFC) OR High frequency rTMS(in non-responders to low frequency) 	<ul style="list-style-type: none"> Left DLPFC – high frequency and Right DRPFC – low frequency Right DL:PFC Left DLPFC
<i>Theta burst</i>	<ul style="list-style-type: none"> Intermittent iTBS Bilateral Left Intermittent and right continuous TBS Bilateral Intermittent TBS 	<ul style="list-style-type: none"> Left LPFC Right and Left DLPFC Right and Left DMPFC
<i>Third Line</i>	<ul style="list-style-type: none"> Bilateral High Frequency rTMS 	<ul style="list-style-type: none"> Right and Left DMPFC

Legend:

DLPFC – dorsolateral left prefrontal cortex DRPFC – dorsolateral right prefrontal cortex
DMPFC – dorsomedial prefrontal cortex

On day one of the treatment it is recommended to begin at 30–50% of the target intensity and subsequently increasing the intensity on each train as tolerated by the patient until the target is reached. Subsequent days can be started at full intensity, if tolerated. The goal is to reach the target threshold within 3–5 treatments. Some persons may need a lower stimulus intensity of 100 or 110% of motor threshold.

To provide guidance for toleration of the treatment the patient is asked to rate the pain of stimulation on a scale of 1-10 (10 being the maximum tolerable). By staying at a rating of no more than 9 this generally ensures the stimulation is within the patient's pain tolerance.

Recommended First Line

- A. High Frequency AB – HF(LL) – 37.5 minute duration**
 - 10 Hz Protocol – Excitatory Stimulation
 - Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 26 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses

- B. High Frequency AB – HF2(LL) – 19 minute duration**
 - 10 Hz Protocol – Excitatory Stimulation
 - Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 11 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses
 - 19 minute duration

- C. Low Frequency AB – LF (RL)4**
 - 1 Hz Protocol – Continuous Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 60 pulses/train
 - Intertrain Interval (ITI): 0 seconds (no ITI)
 - Number of trains: 20 trains
 - Total number of pulses: 1200 pulses
 - 20 minutes

- D. Intermittent Theta-burst (iTBS) AB – iT(LL)**
 - 50 Hz Intermittent (iTBS) Protocol – Excitatory Stimulation

- Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
- Stimulus Intensity: 120% of motor threshold
- Triplet Pulse Duration: 2 seconds
- Number of triplet pulses: 5 triplet bursts per second
- Intertrain Interval (ITI): 8 seconds
- Number of Trains: 20 trains
- Total number of Pulses: 600 pulses
- 3 minute duration

Recommended Second Line

- E. Bilateral rTMS AB – B2 (LHF/RLF4)** This is a combination of Left and Right sided protocols: Left High Frequency **AB – HF2(LL)** and Right Low Frequency **AB – LF (RL)4** (Use **both** in each treatment session).

Left High Frequency – 37.5 minute duration **AB – HF2(LL)**

- 10 Hz Protocol – Excitatory Stimulation
 - Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 26 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses

Right Low Frequency **AB – LF (RL)4**

- 1 Hz Protocol – Continuous Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 60 pulses/train
 - Intertrain Interval (ITI): 0 seconds (no ITI)
 - Number of trains: 20 trains
 - Total number of pulses: 1200 pulses
 - 20 minutes duration

- F. Non-responders to High frequency rTMS LDLPFC trial Low Frequency AB – LF (RL)4**
Low Frequency **AB – LF (RL)4**

- 1 Hz Protocol – Continuous Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 60 pulses/train
 - Intertrain Interval (ITI): 0 seconds (no ITI)
 - Number of trains: 20 trains
 - Total number of pulses: 1200 pulses
 - 20 minutes duration

- G. Non-responders to Low frequency rTMS RDLPC trial High Frequency AB – HF(LL)**

High Frequency **AB – HF(LL)** – 37.5 minute duration

- 10 Hz Protocol – Excitatory Stimulation
 - Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 26 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses

H. Right Low Frequency **AB – LF (RL)**

- 1 Hz Protocol – Continuous Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 60 pulses/train
 - Intertrain Interval (ITI): 0 seconds (no ITI)
 - Number of trains: 10 trains
 - Total number of pulses: 600 pulses
 - 10 minutes duration

I. Right Low Frequency **AB – LF (RL)2**

- 1 Hz Protocol – Intermittent/Continuous Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 60 pulses/train
 - Intertrain Interval (ITI): 30 seconds
 - Number of trains: 6 trains
 - Total number of pulses: 360 pulses
 - 8.5 minutes duration

Second Line Theta-burst Protocols

J. Continuous Theta-burst (iTBS) **AB – cT(RL)** – 3 minute duration

- 50 Hz Continuous (iTBS) Protocol – Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Triplet Pulse Duration: 2 seconds
 - Number of triplet pulses: 5 triplet bursts per second (bursts of 3 X 50 Hz pulses at 200 ms intervals for 40 seconds)
 - Intertrain Interval (ITI): 8 seconds
 - Number of Trains: 20 trains
 - Total number of Pulses: 600 pulses

K. Bilateral Mixed Theta-burst – AB – BiT(iL/cR) This is a combination of Left intermittent and Right continuous Theta-burst protocols. Left Intermittent Theta-burst (iTBS) **AB – iT(LL)** and Continuous Theta-burst (iTBS) **AB – cT(RL)** (*Use **both** in each treatment session*).

- **Left** 50 Hz Intermittent (iTBS) Protocol – Excitatory Stimulation **AB – iT(LL)**
 - Coil Placement: **left** dorsolateral prefrontal cortex
 - Stimulus Intensity: 120% of motor threshold
 - Triplet Pulse Duration: 2 seconds
 - Number of triplet pulses: 5 triplet bursts per second
 - Intertrain Interval (ITI): 8 seconds
 - Number of Trains: 20 trains
 - Total number of Pulses: 600 pulses
- **Right** 50 Hz Continuous (TBS) Protocol – inhibitory Stimulation **AB – cT(RL)**
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse duration: 40 seconds
 - Number of triplet pulses: 5 triplet bursts per second (bursts of 3 X 50 Hz pulses at 200 ms intervals for 40 seconds)
 - Total number of pulses: 600 pulses

L. Bilateral Intermittent Theta-burst **AB – B iT(M)** – 3 minute duration which uses Left Intermittent **and** Right Intermittent Theta-burst protocols. Left Intermittent Theta-burst (iTBS) **AB – iT(LL)** and Right Intermittent Theta-burst (iTBS) **AB – iT(RL)** (*Use **both** in each treatment session*).

- 50 Hz Intermittent (iTBS) Protocol – Excitatory Stimulation . Left Intermittent Theta-burst (iTBS) **AB – iT(LL)**
 - Coil Placement: **left** dorsomedial prefrontal cortex (LDMPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Triplet Pulse Duration: 2 seconds
 - Number of Pulses: 5 triplet bursts per second
 - Intertrain Interval (ITI): 8 seconds
 - Number of Trains: 20 trains
 - Total number of Pulses: 600 pulses
- 50 Hz Intermittent (iTBS) Protocol – Excitatory Stimulation Right Intermittent Theta-burst (iTBS) **AB – iT(RL)**
 - Coil Placement: **right** dorsomedial prefrontal cortex (RDMPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Triplet Pulse Duration: 2 seconds
 - Number of Pulses: 5 triplet bursts per second
 - Intertrain Interval (ITI): 8 seconds
 - Number of Trains: 20 trains
 - Total number of Pulses: 600 pulses

Recommended Third Line

M. Bilateral High Frequency **AB – B HF(M)** – 37.5 minute duration per side uses both Left and Right Protocols as Left High Frequency **AB – HF(LL)** and Right High Frequency **AB – HF(RL)** (*Use **both** in each treatment session*).

- 10 Hz Protocol – Excitatory Stimulation High Frequency **AB – HF(LL)**
 - Coil Placement: **left** dorsomedial prefrontal cortex (LDMPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 26 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses

10 Hz Protocol – Excitatory Stimulation Right High Frequency **AB – HF(RL)**

- Coil Placement: **right** dorsomedial prefrontal cortex (RDMPFC)
- Stimulus Intensity: 120% of motor threshold
- Pulse Duration: 4 second
- Intertrain Interval: 26 seconds
- Number of Trains: 75 trains
- Total number of pulses: 3000 pulses

The following protocol can be considered in patients where tolerability is an issue or where there are concerns over safety such as a risk of seizure. This protocol has been used safely in patients with epilepsy.

N. Low Frequency AB – LF(RM) – 8 minute duration

- 1 Hz Protocol – Inhibitory Stimulation
 - Coil Placement: **right** dorsomedial prefrontal cortex (RDMPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 10 pulses/train
 - Intertrain Interval (ITI): 30 seconds
 - Number of trains: 6 trains
 - Total number of pulses: 360 pulses

Post Procedure Management

These should be carried out following each treatment and at the end of the course of treatment:

- Monitoring of any adverse events
- Assessment of response to treatment using:
 - Completion of the Hamilton Rating Scale for Depression (HAM-D) at the end of the index course of treatment, after 10 sessions or midway through the index course of treatment and at 1, 3 and 6 months following the index course of treatment
 - Completion of Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16) after 10 sessions or midway through the index course of treatment, after the index course of treatment and at 1, 3, and 6 months post treatment
 - Functional, Quality of life and Health Outcome Measurement scales following index course of treatment and at 1, 3, and 6 months post treatment
 - EuroQol Five Dimensions Questionnaire (EQ-5D)
 - World Health Organization Disability Assessment Scale (WHODAS 2.0)
- Completion of Columbia Suicide Severity Rating Scale Lifetime/Recent (CSSR), after 10 sessions or midway through the index course of treatment, at the end of the index course of treatment, and at 1, 3, and 6 months following the index course of treatment
- Follow-up treatment plan for rehabilitation and recovery are provided and documented
- Communication is essential and is to be provided to the primary care physician about response to treatment and the follow up treatment plan

Continuation and Maintenance Transcranial Magnetic Stimulation (rTMS)

rTMS should be discontinued in the event of an intolerance to treatment, significant adverse reactions and inadequate or no response after 30 treatments. All adverse reactions should receive appropriate treatment, be documented on the patient record and entered into the rTMS monitoring system.

Index Treatment

An index course of treatment is defined as the initial series of treatment given to relieve acute symptoms of the illness

An extended index treatment course can be recommended beyond 30 treatments in specific circumstances:

- In patients who experience only partial improvement and the clinicians believe that a clear plateau of benefit has not been reached
- Rarely in patients who have had no meaningful benefit after 30 treatments but who have had a history of late response to treatment in prior episodes, or are highly treatment resistant

Continuation/Maintenance Treatment

A continuation course of treatment is defined as a course of treatment that is an extension of, and begins after the index course, that is intended to prevent a relapse of the episode, and/or further response on to remission.

A maintenance course of treatment is defined as a course of treatment that begins after the end of the continuation or index course of treatment, and is intended to prevent recurrence of a new episode.

- Continuation/Maintenance treatment may be recommended for patients where:
 - Pharmacotherapy has been ineffective or unsafe in preventing relapse or recurrence
 - The patient prefers to continue with rTMS and is unwilling to pursue other treatment options
 - The patient has responded well to previous rTMS therapy
- Written consent must be obtained prior to initiation of maintenance rTMS therapy. Prerequisites include:
 - Assessment of the proposed benefits against possible risks, including the patient's current response to rTMS
 - Re-examination of the patient's medical history, physical examination and appropriate investigations
- Maintenance Protocols may vary based on the patients initial response to index treatment and might include a series of consecutive treatments followed by an interval or individual treatments spaced out over time.
- All required clinical support tools (rating scales) are required to be used in the Index course, and continued to be used in any continuation treatment every 5 treatments. For any maintenance treatment the rating scales are required to be used in the same fashion as in an index course if consecutive treatments are utilized, and for every treatment if single sessions are spaced one week or more apart.

Clinical Documentation

Physician Assessment and Documentation

Assessment

This section contains specific considerations related to this topic. Standard assessment and documentation practices should still be followed.

1. History of Present Illness
 - Current treatment regimen and response
 - Current symptoms and level of functioning
2. Past History
 - History of any co-morbidities such as substance abuse, personality and/or anxiety disorder
 - Prior depressive episodes, treatment trialed and response(s) including any side-effects or adverse effects to treatment
 - History of metal work, welding, shrapnel, surgery on the head, neck, and brain including any implanted devices, wires, clips, pacemaker or other implanted cardiac device
 - History of seizures for any reason
3. Medications & Allergies
 - Medication Reconciliation completed
 - Medication review and response to current regimen (consider medications that have the potential to lower seizure threshold)
4. Physical examination completed
 - General Appearance and vital signs
 - Potential pregnancy (last normal menstrual period [LNMP], known gestation)
5. Family History
 - Family history of depressive episodes, other mental health conditions, and other significant medical conditions
6. Social History
 - Alcohol / substance use
 - Current living circumstances
7. Patient and Family Experience and Expectations
 - Patient and family aware of all available treatment options and possible side effects
 - Plan of care provided to referring physician
8. Scoring Tools / Risk Scores ([see Pre-Assessment](#))
 - Transcranial Magnetic Stimulation Adult Safety Screen (TASS)
 - Hamilton Rating Scale for Depression (HAM-D)
 - Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16)
 - Columbia Suicide Severity Rating Scale Lifetime/Recent (CSSR)
 - EuroQol Five Dimensions Questionnaire (EQ-5D)
 - World Health Organization Disability Assessment Schedule (WHODAS 2.0)
 - Patient Rated Inventory of Side Effects (PRISE)
 - Frequency, Intensity, and Burden of Side Effects Rating (FIBSER)
 - Hamilton Anxiety Rating scale (HAM-A if indicated)
 - Montreal Cognitive Assessment (MoCA if indicated)
 - Other scales if indicated

9. Mental status examination
10. Formal diagnostic instruments if indicated (e.g. MINI, BPRS, SCID)

Documentation

- Informed consent obtained
- The clinical treatment plan, the course of rTMS treatment and the clear indication for the recommendation of the treatment
- rTMS session parameters:
 - unilateral or bilateral
 - position of the coil
 - type of pulses
 - number of pulses per train
 - number of trains per block if any
 - interstimulus/interpulse interval
 - Interblock interval (if any)
 - motor threshold
 - stimulus intensity
 - total number of pulses
- Adverse events during the course of the treatment
- Objective response to the treatment and follow up including continuation and/or maintenance therapy, pharmacotherapy, psychotherapy, etc.
- Follow-up treatment rTMS sessions scheduled and any additional therapeutic interventions and therapy
- Patient compliance with rTMS and other treatments
- Medication regimen and any changes along with compliance with medication treatment regimen and similarly for any psychotherapy

Nursing/Technician Assessment and Documentation

Initial Assessment Nursing/Technician Interventions

Assessment

- Assesses orientation, level of consciousness, presence of confusion and any general concerns, complaints
- Mental status examination unless completed by the psychiatrist
- Columbia Suicide Severity Rating Scale Lifetime/Recent (CSSR) Assessment completed
- Transcranial Magnetic Stimulation Adult Safety Screen (TASS) completed
- Hamilton Rating Scale for Depression (HAM-D) completed by the psychiatrist before the first course of treatment, after 10 sessions, after the last treatment and at 1, 3 and 6 months post treatment
- Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16) completed by the patient before the first course of treatment, after 10 sessions, after the last treatment and at 1, 3 and 6 months post treatment
- Functional, Quality of Life and Health Outcome measurements completed

- EuroQol Five Dimensions Questionnaire (EQ-5D) before the first course of treatment, after 10 sessions, after the last treatment and at 1, 3 and 6 months post treatment
- World Health Organization Disability Assessment Schedule (WHODAS 2.0) before the first course of treatment, after 10 sessions, after the last treatment and at 1, 3 and 6 months post treatment
- Any other additional assessments required by the psychiatrist completed
- Patient able to confirm understanding of the procedure, process
- Vital signs including temperature, pulse, respirations and BP recorded

Planning

- Patient information about rTMS, written and verbal provided
- Informed consent obtained by the psychiatrist
- Rationale, risks and benefits of rTMS discussed where appropriate with the patient, family, or guardian
- Pre-checklist completed and any concerns discussed with the physician
- Follow up continuation or maintenance treatment if required has been planned with the psychiatrist and communicated to the patient, family or guardian

Interventions

- Medications documented on the patients chart by the physician
- Medication reconciliation completed unless done by the physician
- All metal objects and any magnetic sensitive items have been removed – rings, watches, jewellery, studs and any magnetic sensitive items such as bank cards
- Hearing protection offered
- Monitoring for any signs of adverse events

Evaluation

- Response to rTMS session and any adverse events
- Follow up sessions and ongoing therapy scheduled
- Follow up assessments are completed and documented on the chart

Documentation

- Informed consent obtained from patient, or legal representative
- Mental status exam including risk of suicide, signs of mania, hypomania, or mixed states, as relevant on the patient record
- Vital signs pre and post treatment
- Patient response during and after the treatment
- Any adverse events recorded
- Follow up instructions provided, and any additional appointments as required

Order Set: Transcranial Magnetic Stimulation

Risk Assessment / Scoring Tools / Screening:

The required assessments are to be completed immediately before the first treatment, after 10 session's midway through the course of treatment, immediately after the last session of the index course of treatment and at 1, 3 and 6 months post treatment. They must also be completed at least every 5 sessions during continuation treatment and with any maintenance treatments (with each treatment if single sessions spaced apart one week or more, or following the repeated index course if maintenance is a repeat of a series of treatments).

Clinician Rated:

- Transcranial Magnetic Stimulation Adult Safety Screen (TASS)
- Hamilton Rating Scale for Depression (HAM-D)

Patient Rated:

- Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16)

Functional, Quality of Life and Health Outcomes:

- EuroQoL Five Dimensions Questionnaire (EQ--5D)
- World Health Organization Disability Assessment Schedule (WHODAS 2.0)

Suicide Risk Assessment:

- Columbia Suicide Severity Rating Scale Lifetime/Recent (CSSR) before first treatment. Since last seen for all other occasions

Symptom and Side Effects:

- Patient Rated Symptoms of Side Effects (PRISE)
- Frequency, Intensity, and Burden of Side Effects (FIBSER) modified to use the word "rTMS" instead of "medication"

Patient Care

Goals of Care Designation

- Appropriate goals of care designation assigned
- Goals of care designation required

Safety and Precautions

- Offer hearing protection
- Seizure precautions and monitoring

Monitoring

Vital Signs

- Monitor vital signs pre and post treatment including temperature (T), pulse (P), respirations (R) and blood pressure (BP)
- Monitor for signs of seizure activity throughout the treatment

Psychosocial

- Cognitive behavioural therapy
- Other forms of Psychotherapy

Laboratory Investigations

Ensure completed, prior to Transcranial Magnetic Therapy Index course of treatment, a proper set of clinically indicated investigations has been completed by the primary care physician or psychiatrist, if not already documented on the patient record.

Hematology

- Complete Blood Count (CBC)

Chemistry

- Thyroid Stimulating Hormone (TSH)
- Sodium
- Potassium
- Chloride
- Carbon Dioxide
- Creatinine
- Magnesium
- Phosphate
- Vitamin B12
- Folate

Urine Tests

- Urinalysis Random

Diagnostic Investigations

General Radiology (*if clinically indicated*)

- MR Brain

Advanced Imaging

- Electroencephalography (EEG) (*if clinically indicated*)

Medications

- Maintain patient on current medication regimen unless otherwise reviewed by Psychiatrist

Treatment Schedule

- rTMS treatment daily or _____ for _____ days then reassess

Treatment Protocol (Refer to rTMS Protocols)

rTMS

- High Frequency Protocol (10 Hz) – **AB – HF(LL)**
- High Frequency Protocol (10 Hz) – **AB – HF2(LL)**
- Low Frequency **AB – LF (RL)4**
- Low Frequency **AB-LF (RL)**
- Low Frequency **AB-LF (RM)**
- Bilateral Protocol (10 Hz/1 Hz) – **AB – B2 (LHF/RLF4)**
- Low Frequency Protocol (1 Hz) – **AB – LF(RL) 2**
- Bilateral Protocol (10 Hz/1 Hz) – **AB – B3 (LHF2/RLF4)**
- Bilateral High Frequency Protocol (10 Hz) – **AB – B HF (M)**

Theta-burst

- Intermittent Theta-burst Protocol (50 Hz) – **AB – iT (LL)**
- Bilateral Theta-burst Protocol (50 Hz) – **AB – B iT (iL/cR)**
- Continuous Theta-burst Protocol - **AB-cT(RL)**
- Bilateral Mixed Theta-burst Protocol - **AB-BiT(iL/cR)**
- Bilateral Intermittent theta-burst Protocol (50 Hz) – **AB – B iT (M)**

Transitions and Referrals

- Consult _____ for transitional and/or follow-up care planning

Discharge

- Follow up with Primary Care Physician
- Provide results of treatment to Primary Care Physician

Disposition Planning

Physician

1. Considerations for hospital admission
 - Seizure during Transcranial Magnetic Stimulation therapy (rTMS)
 - Initiation of a manic or mixed state for patient with bipolar disorder
 - Acutely suicidal/risk of suicide, other risk of harm to self or others
 - Worsening condition
2. Outpatient follow-up
 - Follow up instructions provided to primary care physician and follow-up date arranged. Options discussed for continuing on going therapy e.g. psychotherapy such as cognitive behavioral therapy
 - Medication regimen documented
 - Scheduled follow up rTMS sessions
 - Patient provided with instructions re follow up treatment including completing self-assessments, appointments and to report any adverse events

Nursing/Technician

1. Patient checklist for discharge readiness from the clinic:
 - Treatment record form completed
 - Assessments completed by the patient or psychiatrist using the following assessment tools:
 - Hamilton Rating Scale for Depression (HAM-D)
 - Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16)
 - EuroQol Five Dimensions Questionnaire (EQ-5D)
 - World Health Organization Disability Assessment Schedule (WHODAS 2.0)
 - Columbia Suicide Severity Rating Scale (CSSR)
 - Patient Rated Inventory of Side Effects (PRISE)
 - Frequency, Intensity, and Burden of Side Effects Rating (FIBSER)
2. Education to be provided prior to discharge from the clinic:
 - Patient aware of follow up rTMS appointments
 - Reporting any adverse events to the psychiatrist, primary care physician and rTMS team
 - Detailed follow up of any psychotherapy treatment
 - Medication regimen reviewed
3. Education tools/resources to be provided prior to discharge
 - Written instructions regarding the treatment and what to expect
4. Follow-Up Instructions
 - Instructions provided with continuing on going treatment
 - Follow up scheduled with treating psychiatrist
 - Follow up scheduled with primary care physician
 - Report any adverse events, worsening condition, mental status
 - Complete the Quick Inventory of Depressive Symptom¹⁵ (QIDS – SR 16) at 1, 3 and 6 months post treatment
 - Complete the EuroQol Five Dimensions Questionnaire (EQ-5D) at 1, 3 and 6 months post treatment

- Complete the World Health Organization Disability Assessment Schedule (WHODAS 2.0) at 1, 3 and 6 months post treatment
- Complete the Patient Rated Inventory of Side Effects (PRISE) at 1, 3 and 6 months post treatment
- Complete the Frequency, Intensity, and Burden of Side Effects Rating (FIBSER) at 1, 3 and 6 months post treatment

Rural Considerations

1. Nearest referral site for rTMS therapy
2. Patient ability to travel to site for rTMS therapy and concurrent sessions
3. Ability to access required resources for on-going therapy/treatment

Transcranial Magnetic Stimulation, Adult – Inpatient, Ambulatory Clinical Knowledge Topic Working Group Member List

We would like to acknowledge the contributions of the Provincial Clinical Knowledge Working Group members as follows. Your participation and time spent is appreciated.

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Thank you to the following clinicians who participated in the colleague review process. Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated.

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22 March 2019 FDA Approval letter Nexstim Navigated Brain Therapy (NBT) System 2

8 March 2019 FDA Approval letter Brainsway Deep TMS System

3 August 2018 FDA Approval letter Magstim Horizon TMS Therapy System Theta Burst

Protocol

14 August 2018 FDA Approval letter Mag Vita TMS Theta Burst Protocol

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Appendix A – Transcranial Magnetic Stimulation Protocols

Table 1 Transcranial Magnetic Stimulation Protocol Examples

Location	Session Length	No & Amount of Sessions	Site/ Coil Placement	Frequency	Stimulus Intensity	Pulses in Train	# of Trains	Interval	Time On	Time Off	Total No. of Pulses
<i>Toronto UHN</i>	15 - 30	Mon – Fri 4 - 6 Weeks 20 – 30 Sessions	DMPFC/ DLPFC	1 Hz	DMPFC 60-65% MT	60	6	30	60	30	360/per side
			DMPFC /DLPFC	20 Hz	DLPFC 35-45% MT	50	30	10	2.5	60	1500
<i>CCHMBI</i>	30	Mon – Fri 4 Weeks – 20 Sessions	DLPFC	1 Hz			25-50	3			
			DLPFC	10 Hz							
<i>Riverview Medical Clinic</i>	60	Mon – Fri 4 Weeks 20 Sessions	DLPFC /DRPFC	1 Hz	100-110% MT	10	90				90
			DLPFC /DRPFC	10 Hz	100-120% MT	40	75	30			3000
			DLPFC /DRPFC	20 Hz	80-110% MT	40	40	28			1600
<i>ACH</i>	60	Mon – Fri 3 Weeks 15 Sessions)	DLPFC	10 Hz			75				3000
Alternate	37.5	20 Sessions	DLPFC	20 Hz	120% MT		30	10			1500

Legend:

DMPFC – dorsomedial prefrontal cortex
 DLPFC – dorsolateral left prefrontal cortex
 DRPFC – dorsolateral right prefrontal cortex
 MT – Motor threshold

ACH – Alberta Children’s Hospital – Calgary Alberta
 CCHMBI – Centennial Health Centre for Mental Health & Brain Injury
 Riverview Medical Clinic – Calgary, Alberta

Table 2 Transcranial Magnetic Stimulation Theta-Burst Protocol Examples

Location	Hz	Delay	Wave Form	Burst Pulses	IBI	Rep Rate	Train Pulses	# Trains	Time On	Time Off	Total No. of Pulses
Toronto UHN	iTBS	8	Biphasic Burst	3	20	5	10	10	2	8	600
Toronto UHN	Space Paired		Biphasic Burst	5	10	2		20	40	8	600
Riverview Medical Clinic	50			10		8-15		20			600
Spaced Paired	50				10	5		2			600

The following are retired protocols that have appeared in previous versions of this Guideline:

Low Frequency Protocol (1 Hz) – AB – LF(RL)

Right Low Frequency – 8 min duration

• 1 Hz Protocol – Inhibitory Stimulation

- Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
- Stimulus Intensity: 120% of motor threshold
- Pulse Duration: 60 seconds
- Number of Pulses/train: 10 pulses/train
- Intertrain Interval (ITI): 30 seconds
- Number of trains: 6 trains
- Total number of pulses: 120 pulses

Bilateral Protocol (10 Hz/1 Hz) – AB – B (LHF/RLF)

Bilateral rTMS AB – B(LHF/RLF) (Use **both** in each treatment session)

Left High Frequency – 37.5 minute duration

- 10 Hz Protocol – Excitatory Stimulation
 - Coil Placement: **left** dorsolateral prefrontal cortex (LDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 4 second
 - Intertrain Interval: 26 seconds
 - Number of Trains: 75 trains
 - Total number of pulses: 3000 pulses

Right Low Frequency – 8 min duration

- 1 Hz Protocol – Inhibitory Stimulation
 - Coil Placement: **right** dorsolateral prefrontal cortex (RDLPFC)
 - Stimulus Intensity: 120% of motor threshold
 - Pulse Duration: 60 seconds
 - Number of Pulses/train: 10 pulses/train
 - Intertrain Interval (ITI): 30 seconds
 - Number of trains: 6 trains
 - Total number of pulses: 120 pulses