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Evaluations of Repetitive Transcranial Magnetic Stimulation for Treatment-Resistant Depression

A Scan of Canadian Evidence

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Publication Date
October 2025

Acknowledgements
This project was undertaken by DataNB (formerly NB-IRDT) at the request of the Government of New Brunswick, Department of Health. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by the Government of New Brunswick or its partners is intended or should be inferred.

Project Data
Research analytic outputs were produced using secondary data extracted from literature sources accessed through databases (PubMed, PsycINFO, and Google Scholar) and organised into summary tables and narrative synthesis.

How to Cite This Product
Ndzeshang, S., & Carrillo-Balam, G. (2025). Evaluations of repetitive transcranial magnetic stimulation for treatment-resistant depression: A scan of Canadian evidence. Fredericton, NB: DataNB.

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Abbreviations and Definitions

AD	Antidepressants
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory (Second Edition)
CANMAT	Canadian Network for Mood and Anxiety Treatments
CGI-I	Clinical Global Impression Scale
cTBS	Continuous Theta Burst Stimulation
DLPFC	Dorsolateral Prefrontal Cortex
DMPFC	Dorsomedial Prefrontal Cortex
dTMS	Deep Transcranial Magnetic Stimulation
ECT	Electroconvulsive Therapy
GAD-7	General Anxiety Disorder (7-item)
HAM-A	Hamilton Anxiety Rating Scale
HAM-D-17	Hamilton Rating Scale for Depression (17-item)
HRDS-21	Hamilton Rating Scale for Depression (21-item)
iTBS	Intermittent Theta-Burst Stimulation
LH	Left Hemisphere
LiTBS	Low Intensity Theta Burst Stimulation
MADRS	Montgomery-Åsberg Depression Rating Scale
MDD	Major Depressive Disorder
MRI	Magnetic Resonance Imaging
NB-IRDT	New Brunswick Institute for Research, Data and Training

OCD	Obsessive Compulsive Disorder
OFC	Orbitofrontal Cortex
PDD	Persistent Depressive Disorder
PHQ-9	Patient Health Questionnaire–9
QIDS-SR16	Quick Inventory of Depressive Symptomatology - Self–Report (16-item)
RCTs	Randomised Controlled Trials
RH	Right Hemisphere
RcTBS	Repeated Continuous Theta Burst Stimulation
rTMS	Repetitive Transcranial Magnetic Stimulation
SDS	Sheehan Disability Scale
SETS	Stanford Expectancy of Treatment Scale
SNRIs	Serotonin-Norepinephrine Reuptake Inhibitors
SSRIs	Selective Serotonin Reuptake Inhibitors
TBS	Theta-Burst Stimulation
TRD	Treatment Resistant Depression

Executive Summary

Repetitive Transcranial Magnetic Stimulation (rTMS) is currently recommended as a first line neuromodulation treatment for individuals with treatment-resistant depression (TRD), a form of depression that does not respond adequately to standard treatments such as antidepressant medication and psychotherapy. There is robust evidence from clinical trials demonstrating its efficacy, highlighting the potential for expanding its application in depression treatment. However, evaluations of real-world programmes are critical to assess how rTMS performs in diverse clinical populations and settings. These evaluations can provide insights into programme outcomes and other components which are essential for informing service planning and policy development.

This evidence scan aimed to identify and synthesise available evidence on the evaluation of rTMS programmes, focusing exclusively on Canadian research. The findings are intended to inform future rTMS evaluations in the province of New Brunswick. To achieve this, we conducted a systematic search across three academic databases and synthesised the relevant literature on effectiveness and evaluation indicators.

Summary of findings

The scan identified a few studies on real-world evaluations of rTMS treatment for TRD in Canada. Studies were primarily focused on clinical outcomes such as depressive symptoms. The tools used to assess patient progress, timing of patient assessments, and treatment protocols varied significantly. For example, while some sites used both clinician-rated and patient-reported outcome measures, others relied on only one type. Additionally, some sites only treated patients with unipolar depression, while others treated patients with unipolar and bipolar depression.

Common indicators used across the studies measured various aspects of treatment effectiveness and patients' characteristics. These included response rates, remission rates, safety and tolerability, patient demographics, relevant medical history, and treatment parameters. Reported effectiveness ranged from modest to substantial improvements in depressive symptoms. Variations in response were attributed to the different treatment protocols and patient populations involved.

In general, rTMS was consistently well tolerated. Some minor side effects such as headaches or discomfort at stimulation sites were reported, with very few patients discontinuing treatment due to adverse events.

Key takeaways

- Few studies were identified, all of which focused exclusively on clinical outcomes.
- The inconsistency in assessment and delivery protocols highlights a lack of standardisation in rTMS service models, which may impact treatment comparability and outcomes.
- The observed outcomes generally support the use of rTMS as an effective and safe option for TRD, particularly given its high tolerability.
- Variation in effectiveness across patient groups may reflect differences in clinical populations and/or delivery settings. Some of the outcomes observed were similar to those reported in clinical trials, suggesting that rTMS can retain effectiveness in routine practice.
- There is a notable gap in the literature on implementation of rTMS programmes, including protocol adherence, service quality, and patient or provider experience. This limits the ability to make well-informed decisions on how to structure, fund, or scale rTMS programmes.
- Future evaluations could benefit from including a broader range of outcomes, including qualitative insights, to better capture the full scope of rTMS delivery and impact.

Introduction

Background

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive brain stimulation technique in which short magnetic pulses are directed to specific regions of the brain to stimulate nerve cells involved in mood regulation.[1] rTMS is most widely used as a treatment for major depressive disorder (MDD), where it has become an established therapeutic option. Its clinical use is also being explored in other psychiatric and neurological conditions, such as post-traumatic stress disorder, neuropathic pain, obsessive-compulsive disorder (OCD), and anxiety disorders. However, the supporting evidence in these areas is still evolving.[2–5]

rTMS received regulatory approval from Health Canada in 2002, followed by approval from the U.S. Food and Drug Administration in 2008 as a therapy for treatment-resistant depression (TRD).[6] The Canadian Network for Mood and Anxiety Treatments (CANMAT), which provides national clinical guidelines for the use of rTMS in mood disorders, currently lists rTMS as one of the first-line neuromodulation treatments recommended for patients with MDD who have not responded adequately to at least one antidepressant, with electroconvulsive therapy (ECT) listed as another option.[7]

Typically delivered in outpatient settings, rTMS does not require anaesthesia or hospitalisation, making it a practical non-pharmacological treatment option for TRD. The standard treatment protocol involves daily sessions, five days per week over four to six weeks.[7] In Canada, rTMS services are delivered through a mix of public and private providers, which reflects varied service models.

In relation to its efficacy, meta-analyses of randomised controlled trials (RCTs) and clinical evidence reviews have consistently demonstrated that rTMS outperforms sham treatment (a form of placebo) in reducing depressive symptoms and improving remission rates among individuals with TRD.[3,8–10] Expert guidelines have endorsed several effective protocols for unipolar depression treatment, including high-frequency rTMS applied to the left dorsolateral prefrontal cortex (DLPFC), low-frequency stimulation of the right DLPFC, and intermittent theta burst stimulation (iTBS) when used as part of a combined protocol.[11]

Although RCTs offer strong internal validity (high confidence in cause-and-effect findings), real-world evaluations are critical for assessing how rTMS performs in different clinical populations and settings. These evaluations can provide insights into effectiveness in practice, cost-effectiveness, access and equity issues, and implementation challenges, all of which are essential for informing service planning and policy decisions.

Purpose

In New Brunswick (NB), a publicly funded rTMS two-year pilot programme was launched in May 2024 to improve access to innovative, evidence-based treatment for individuals with MDD who have not responded to conventional therapies such as antidepressants or psychotherapy.[12] This report was developed as part of preliminary work to support the evaluation of rTMS services in NB. It aims to identify and synthesise available evidence on how rTMS has been evaluated across other Canadian provinces. Although international studies were initially considered in case Canadian data was limited, this report includes only Canadian evidence.

The findings are intended to help develop a framework for evaluating rTMS in NB, focusing on key elements such as service characteristics, data collection methods, and outcome measures. In addition to informing the evaluation design, this scan provides insight into how rTMS is delivered in real-world settings. In addition, it presents an overview of operational and clinical factors that may inform assessments of programme effectiveness and support broader implementation in the province.

Scan questions

This evidence scan was guided by the following questions:

1) Has there been any evaluation of the implementation and/or outcomes of rTMS in other jurisdictions within Canada or internationally?

2) What are the indicators evaluated, and what are the results?

Methods

Eligibility criteria

This scan focused on real-world studies. This refers to evaluations of rTMS as it is delivered in routine clinical practice, rather than in controlled research or experimental settings. The criteria presented in the following sub-sections were used to select studies relevant to rTMS service delivery.

Inclusion criteria

Studies were included if:

1) They reported real-world process or outcomes evaluations of rTMS service delivery.
2) The patient population was comprised of adults with major depression or TRD.

3) Evaluations addressed at least one of the following domains:
    a. Implementation processes
    b. Clinical outcomes
    c. Safety
    d. Cost-effectiveness
    e. Patient experience

When more than one study was available from the same rTMS provider, studies with significantly different protocols or objectives (e.g., comparing once-daily versus twice-daily treatments) were included to capture meaningful variation in delivery. Otherwise, only the most recent publication was included to avoid duplication.

Exclusion criteria

Studies were excluded if:

1) They focused exclusively on paediatric populations.
2) They were based on theoretical models or clinical trials.
3) They described feasibility studies, experimental protocols, or case series not integrated into routine service delivery.
4) They represented earlier versions of reports already included.

Search scope

The search focused on recent publications (within the past ten years) with the primary aim to identify evaluations conducted in Canada. International studies were considered only if there was limited Canadian evidence to address the scan questions. To ensure feasibility within the project timeline and to maintain relevance, this evidence scan aimed to review between five and ten studies.

Information sources and search strategy

The search strategy was developed by combining key terms related to the population, intervention, outcome, and setting of interest. This approach aimed to capture relevant literature on rTMS implementation and effectiveness for depression.

Searches were conducted in April 2025 using the following databases: PubMed, PsycINFO, and Google Scholar. Boolean operators (AND, OR, NOT) were used to structure the search. The syntax was adapted as needed for each database. See Table 1 for a detailed description of the search strategy.

Table 1: Search strategy

Criteria	Search Terms
Intervention	(rtms OR repetitive transcranial magnetic stimulation OR tms OR transcranial magnetic stimulation OR intermittent theta-burst stimulation OR iTBS) AND
Condition	(depression OR depressive disorder OR depressive symptoms OR major depressive disorder) AND
Study Design / Context	(retrospective OR real world experience OR real world OR observational OR process evaluation OR implementation evaluation OR evaluation OR assessment) AND
Outcomes	(treatment outcomes OR Safety OR efficacy OR effectiveness OR patient outcome OR cost-effectiveness OR patient experience OR service delivery) AND
Geographic focus	(Canada OR Canadian OR Canadians OR in Canada) NOT
Population	(children OR adolescents OR youth OR child OR teenager OR pediatric OR paediatric) NOT
Study type	(randomized controlled trials OR "randomised non-inferiority trial" OR RCT OR clinical trial)

Selection process

Following the initial database search, retrieved articles were screened in three stages. First, duplicate entries were identified and removed. Second, titles, abstracts, and methods sections were reviewed to identify potentially eligible studies. Studies that did not meet the inclusion criteria were excluded at this stage. Attention was also given to screening for geographical focus. Finally, full-text reviews were conducted for studies that passed the initial screening. At this stage, articles were assessed more thoroughly against the inclusion and exclusion criteria through full text reviews.

Data extraction and synthesis

For each study included, the following data were extracted where applicable: authors, title, publication year, study aim, geographical region, programme characteristics (name, delivery method, funding, evaluation period, number of sessions), type and scope of evaluation, indicators and methods used, and key findings.

Due to the heterogeneity in study contexts and programme characteristics, findings were synthesised narratively. To facilitate direct comparisons between studies, summary tables were developed to provide an overview of treatment protocols and their main results.

Results

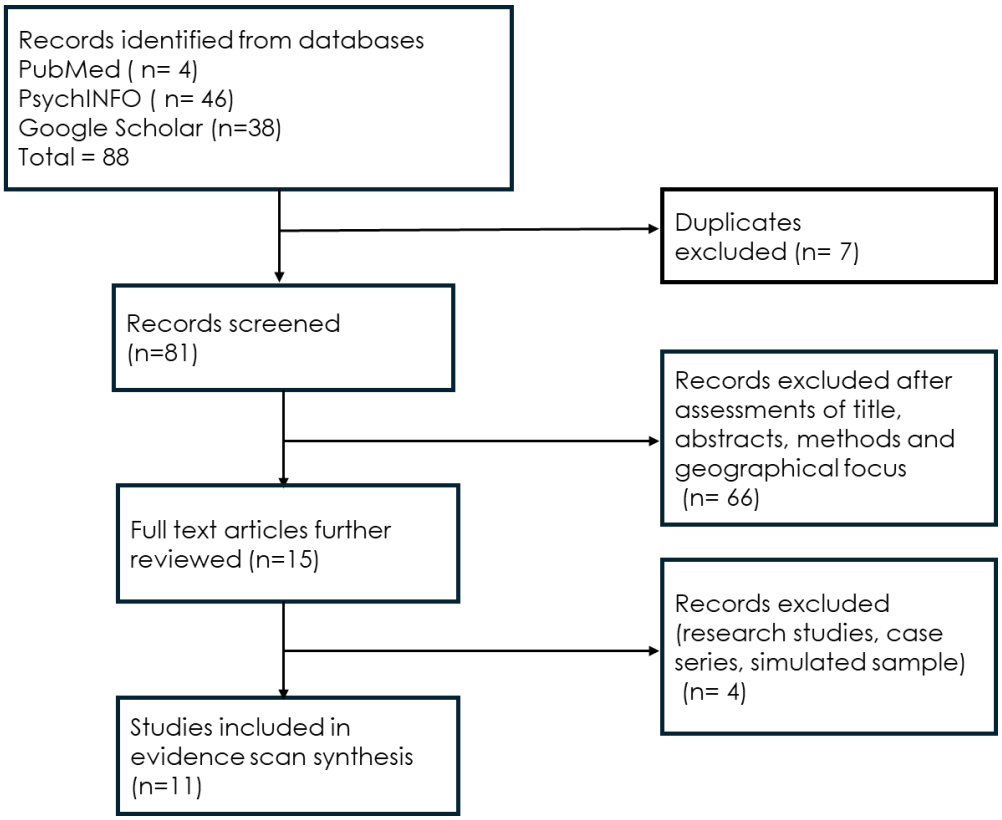
Study selection

The database search retrieved 88 records. After duplicates were removed (n = 7), 70 unique articles were excluded based on the inclusion and exclusion criteria. Reasons for exclusion included study designs such as RCTs, meta-analyses, research protocols, reviews, theoretical or simulated samples, and case reports; studies focusing on non-target conditions (e.g., traumatic brain injury, chronic vagus nerve stimulation, OCD); formats that typically provide limited methodological detail (e.g., conference abstracts, posters); and populations outside the scope of interest, such as children or adolescents.

In total, 11 articles were included in the synthesis. Given that a sufficient number of relevant Canadian evaluations were identified, international articles were not included, in keeping with the project's scope. See Figure 1 for a flow diagram outlining the article selection process.

In line with the inclusion and exclusion criteria, Health Technology Assessments were excluded, as evidence on effectiveness and cost-effectiveness in these documents was primarily synthesised from clinical trials, meta-analyses, or simulated models.

Figure 1: Study selection flow chart



Study characteristics

All included studies were naturalistic retrospective chart reviews based on routinely collected clinical data from various hospitals and rTMS clinics in Canada. These included sites in Ontario (n=6), Manitoba (n=2) Quebec (n= 2), and British Columbia (n=1) (see Appendix A for more details on study sites). Publication years ranged from 2015 to 2024. However, primary data were collected over a much broader timeframe; some studies used data collected as early as 2012.

All studies focused on treatment outcomes, including response and remission rates, as well as adverse effects. Four studies focused primarily on patients receiving rTMS for unipolar depression (also referred to in some studies as MDD),[13–16] and seven studies included individuals with either unipolar or bipolar depression.[17–23]

Patients were typically referred for rTMS treatment following an inadequate response to pharmacological therapy. Definitions of TRD generally required failure of at least two antidepressant trials, though two studies applied a one-trial threshold.[15,21] See Table 2 below for more details on study characteristics.

Sample sizes in the studies ranged from 36 to 208 participants and included both single-site and multi-site settings. This synthesis includes samples sizes as reported by each study. In some studies, participants were excluded due to missing demographic or treatment data, a primary diagnosis other than unipolar or bipolar depression, use of non-standard TMS systems, or failure to meet study-specific inclusion criteria.

Treatment protocols

rTMS was delivered using various treatment protocols that differed in frequency, duration, and technical setup. Protocol variations were observed between and within studies. Stimulation parameters varied, particularly in terms of:

- **Number of sessions:** Settings offered 20 to 32 treatment sessions, with some programmes providing daily sessions and others providing accelerated or twice-daily sessions.
- **Number of pulses per session:** The number of pulses per session ranged from 360 to 6000.
- **Stimulation region:** Stimulation targeted different brain regions, most commonly the left dorsolateral prefrontal cortex (DLPFC), but also the dorsomedial (DMPFC) and orbitofrontal (OFC) cortices.
- **Stimulation frequency:** Frequencies ranged from 1 Hz to 50 Hz, with the most common being 10 Hz for left DLPFC.

- **Use of neuronavigation:** Neuronavigation was used in three studies. One study used a heuristically guided targeting method, initially validated against magnetic resonance imaging (MRI)-based neuronavigation.[22]

In studies that used multiple treatment protocols, treatment parameters were often interrelated, with each influencing the others. For example, treatment protocols such as iTBS, cTBS (continuous theta burst stimulation), dTMS (deep transcranial magnetic stimulation), and standard rTMS usually involved different stimulation frequencies and number of pulses. Some studies also reported using combinations of these treatment protocols on the same patients.[15,18,20]

The number of pulses delivered was influenced by the stimulation site (unilateral vs. bilateral), with bilateral protocols typically requiring more pulses.[18,20] In other words, stimulating both hemispheres usually required delivering more pulses than when only one side was stimulated. At the same time, the stimulation frequency varied depending on the specific protocol used (e.g., cTBS, iTBS) Overall, treatment settings were interconnected, with changes in one aspect of the protocol often linked to changes in others, rather than being chosen separately.

Table 2: Study characteristics and treatment details

Data collection period; sample size	TRD Definition & Type of Depression	Depression Scale(s)	Frequency	Total Number of Sessions*; Daily sessions	Total Number of Pulses	Equipment & Neuro-navigation
Bakker et al., 2015						
2011-2014; n=185	≥2 AD; Unipolar or bipolar	HAM-D-17, BDI-II	10 Hz and iTBS of the DMPFC	Mean (SD): 21.4 ± 4.7; 1 session/ day	1200 (iTBS), 6000 (rTMS)	MagPro R30 device (MagVenture, Farum, Denmark); Nav: Yes
Modirrousta et al., 2018						
2012-2016; n=36	Not specified; MDD	BDI-II, BAI, PHQ-9, SDS, HAM-D-17	10Hz left DLPFC	30; 1–2 sessions/ day	3000	Magstim Rapid2 rTMS (Magstim Co. Ltd., Whitland, UK); Nav: Yes
Feffer et al., 2018						
2015-2017; n=42	≥2 AD; Unipolar	BDI-II	1 Hz right OFC	20-30; 1 session/ day	360	MagPro R30 device (MagVenture, Farum, Denmark); Nav: No

Data collection period; sample size	TRD Definition & Type of Depression	Depression Scale(s)	Frequency	Total Number of Sessions*; Daily sessions	Total Number of Pulses	Equipment & Neuro-navigation
Schulze et al., 2018						
N/A; n=130	≥2 AD; Unipolar or bipolar	BDI-II	10 HZ bilateral DMPFC, 20HZ bilateral DMPFC	22.2 ± 4.5; 1–2 sessions/ day	6000	MagPro R30 device (MagVenture, Farum, Denmark); Nav: Heuristically guided (validated by MRI)
Jodoin et al., 2019						
2013-2018; n=73	≥2 AD; Unipolar or bipolar	MADRS, HAM-A,	20 Hz left DLPFC,	Unipolar: 28.8 ± 7.8, Bipolar: 29.9 ± 8.5; 2 sessions/ day	3000	MagPro X100 device (MagVenture, Farum, Denmark); Nav: No
Yang et al., 2020						
2012-2016; n=76	Response failure; Unipolar and bipolar	HRDS-21	10 HZ left DLPFC	Unipolar: 28.7 ± 0.66, Bipolar: 26.2 ± 1.95; 1 session/ day	3000	Magstim Super Rapid 2 (Magstim Co. Ltd, TM., UK); Nav: No
Abo Aoun et al., 2023						
2013-2019; n=196	Not specified; MDD	HAM-D-17, BAI, SDS	10 Hz left DLPFC, 1 Hz right DLPFC, iTBS left DLPFC	30; 1–2 sessions/ day	ITBS: 600 I Hz: 1200 10 Hz: 3000	Magstim Rapid2 rTMS (Magstim Co. Ltd., Whitland, UK); Nav: Yes
Lee et al., 2023						
2014-2019; n=40	≥1 AD; Unipolar	PHQ-9, QIDS-SR16	iTBS left DLPFC, cTBS right DLPFC + iTBS left DLPFC	23.1 ±5.9; N/A	600 – 1200 (600 per hemisphere for cTBS/iTBS)	MagPro X100 stimulator (MagVenture, Denmark); Nav: No

Data collection period; sample size	TRD Definition & Type of Depression	Depression Scale(s)	Frequency	Total Number of Sessions*; Daily sessions	Total Number of Pulses	Equipment & Neuro-navigation
Massé-Leblanc et al., 2024						
2012-2022; n=147	≥2 AD; Unipolar or bipolar	MADRS, BDI-II, HAM-A, BAI	1-2 Hz right DLPFC, 10-20 Hz left DLPFC, iTBS left DLPFC, 20 Hz left DLPFC + cTBS right DLPFC, iTBS left DLPFC + cTBS right DLPFC + 20 Hz left DLPFC, 20 Hz left + 1 Hz right DLPFC	32.9 ±5.3; Mean 2.7 sessions/ day	RH: 648 ± 166.1, LH: 2761.8 ± 841.4, Unilateral protocols: 2597.4 ± 759.2	MagPro R30/X100 device (MagVenture, Farum, Denmark); Nav: No
Mollica et al., 2024						
2019-2023; n=208	≥1 AD; MDD or bipolar	HAM-D-17, SETS	iTBS left DLPFC, 18Hz dTMS left DLPFC	20 - 30; 1 session/ day	600 (iTBS) 1980 (dTMS)	MagStim Horizon system (Wales, UK); Nav: No
Elnazali et al., 2024						
2015-2020; n=161	≥2 AD; MDD, PDD, and bipolar	CGI-I, PHQ-9, GAD-7, HAM-D-17	40 to 50HZ Bilateral: rcTBS right DLPFC+liTBS left DLPFC, Unilateral: iTBS left DLPFC	Unilateral: 29 ±2.80, bilateral: 27 ±4.55; N/A	600 per site	TMS Magstim Super Rapid 2 (Magstim Co. Ltd, TM., UK); Nav: No

** Sessions delivered unless otherwise specified.*

Abbreviations:
AD – Antidepressants
BAI – Beck Anxiety Inventory
BDI-II – Beck Depression Inventory (Second Edition)
CGI-I – Clinical Global Impression Scale
cTBS – continuous theta-burst stimulation
DLPFC – Dorsolateral Prefrontal Cortex
DMPFC – Dorsomedial Prefrontal Cortex
MADRS – Montgomery-Åsberg Depression Rating Scale
MDD – Major Depressive Disorder
MRI – Magnetic Resonance Imaging
NAV – Neuronavigated
OFC – Orbitofrontal Cortex
PDD – Persistent Depressive Disorder
PHQ-9 – Patient Health Questionnaire–9

Data collection period; sample size	TRD Definition & Type of Depression	Depression Scale(s)	Frequency	Total Number of Sessions*; Daily sessions	Total Number of Pulses	Equipment & Neuro-navigation

dTMS – Deep Transcranial Magnetic Stimulation
GAD-7 – Generalized Anxiety Disorder scale (7-item)
HAM-A – Hamilton Anxiety Rating Scale
HAM-D-17 – Hamilton Rating Scale for Depression (17-item)
HRDS-21 – Hamilton Rating Scale for Depression (21-item)
iTBS – Intermittent Theta-Burst Stimulation
LH – Left Hemisphere
liTBS – Low Intensity Theta-Burst Stimulation
QIDS-SR16 – Quick Inventory of Depressive Symptomatology- Self Report (16-item)
rcTBS – Repeated Continuous Theta-burst Stimulation
RH – Right Hemisphere
rTMS – Repetitive Transcranial Magnetic Stimulation
SDS – Sheehan Disability Scale
SETS – Stanford Expectancy of Treatment Scale
TRD – Treatment Resistant Depression.

Studies comparing standard and accelerated protocols often maintained consistency in certain parameters. For instance, in one study, patients received the same total number of sessions and pulses by the end of treatment, regardless of the number of sessions delivered per day.[16] Similarly, another study reported that the total number of daily pulses remained consistent for standard and accelerated protocols.[22]

All studies mentioned or made references to procedures for motor threshold measurements, which guided the determination of the amount of energy required by the brain for treatment. Other factors that influenced the assignment of patients to particular treatment protocols included current medication,[13] treatment slot or machine availability,[16,21,22] study design,[19,20] patient preference and availability,[17,21,22] and patient factors.[21,23]

As shown in Table 2 above, two main equipment types were reported: Magstim and MagPro devices, both manufactured internationally (Magstim Co. Ltd., Whitland, UK, and the MagVenture, Farum, Denmark, respectively).

Indicators evaluated and key findings

Indicators and measures

Most studies assessed depressive symptoms using a combination of clinician-rated and self-reported measures, while only a few studies relied on a single type of assessment. The Hamilton Depression Rating Scale, either the 17-item version (HAM-D-17) or the 21-item version (HRSD-21), was used in 6 of the 11 studies, making it the most frequently applied clinician-rated tool for assessing depressive symptoms. The Beck Depression Inventory-II (BDI-II) was the self-reported measure most commonly used in the studies.

In summary, outcome measures included:

- **Clinician-rated:** HAM-D-17/ HRSD-21, Montgomery–Åsberg Depression Rating Scale (MADRS), Clinical Global Impression - Improvement scale (CGI-I).

- **Self-reported:** BDI-II, Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder scale (GAD-7), Beck Anxiety Inventory (BAI), Quick Inventory of Depressive Symptomatology – Self-Report (QIDS-SR16), Sheehan Disability Scale (SDS), and Stanford Expectations of Treatment Scale (SETS).

The number of assessments conducted to monitor clinical outcomes during the treatment varied across studies. All studies included baseline and post-treatment assessments, and some also incorporated intermediate measurements. For instance, every 5 sessions,[14] every 5 days,[22] every 2 weeks[21] and every 10 sessions.[13] A few studies noted that follow-up assessments were conducted with patients between 1 week and 6 months after treatment completion.

In addition to clinical outcomes, studies also reported documenting patient demographics (e.g., age, sex); medical history (e.g., number of failed medication trials, episode length, previous rTMS treatment response); diagnosis type (e.g., unipolar depression or bipolar depression); and treatment procedures (e.g., unilateral or bilateral stimulation, brain region stimulated, stimulation frequency and intensity, etc.). See Appendix B for a summary of these indicators.

Moreover, the majority of the studies compared rTMS response, remission, and changes in depressive symptoms (i.e., depression scores) among different patient groups (e.g., unipolar vs. bipolar depression, previous responders vs. non-responders); treatment protocols (e.g., once-daily vs. twice-daily, standard rTMS vs. iTBS, high-frequency vs. low-frequency); and assessment methods. While all studies defined response as a ≥50% reduction in depressive symptoms, remission criteria varied slightly. This disparity was due to the different assessment scales used: HAMD-17 ≤7, HAM-D-17 <8, MADRS ≤10, or BDI-II ≤12.

Some studies had predefined discontinuation criteria, such as no change or worsening of the HAM-D-17 score from baseline after 20 sessions.[13,16] Others indicated that additional sessions were provided only to patients who showed response but not remission after 20 sessions.[14,22] It is unclear whether the number of sessions was chosen arbitrarily or based on clinical judgement and experience, as no scientific evidence was provided to support these discontinuation criteria. Most of the studies generally monitored and documented reasons for discontinuation. Similarly, to measure safety and tolerability of rTMS treatment, all studies documented observed adverse effects.

Outcomes: Key findings

Response rates ranged from approximately 8% to over 80%, and remission rates ranged from 20% to 65%. The variation in these figures reflects the variability in patient populations. Twice-daily protocols tended to show faster symptom improvement and, in some cases, higher response and remission rates. However, statistically significant differences between the protocols were not consistently observed, and final outcomes were generally similar across groups.[16,22]

Regarding patient age, mixed associations were reported. While one study reported higher response rates among younger participants,[13] other studies reported significantly greater improvements in depression and anxiety scores among older adults.[19,20] Yet, others reported that age had no significant impacts in the response rate.[14,16–18] Additionally, greater baseline

depression severity was associated with lower odds of remission in one study,[21] and another found that lower baseline depression and anxiety scores were linked to better outcomes.[19]

In relation to other potential predictors, inconsistent associations were reported for diagnosis type. For example, one study found that patients with bipolar depression showed significantly lower response rates,[23] while others reported that diagnosis type was not a significant predictor.[17,19]

Regarding neuronavigation, one study compared outcomes between patients who received neuronavigation-guided stimulation and those who did not, reporting significant differences in treatment response.[16] See Table 3 below for more details on treatment outcomes.

Although direct comparisons were generally not available for most studies, one study reported a discrepancy between clinician-rated and self-rated measures, with self-reported scores (BDI-II) indicating higher perceived severity of depression compared to the clinician-rated assessment (HAM-D-17).[16] In another study, the clinician-rated measure (MADRS) reported more significant improvements in depressive symptoms compared to the self-rated measure (BDI-II).[20]

In general, the studies that tracked adverse events reported high tolerability of rTMS treatment. The most commonly noted side effects were mild headaches, local discomfort, and fatigue. No serious adverse events were reported, and treatment discontinuation due to adverse effects did not occur.

Discontinuation rates were generally low, with the highest rate stated at 25%.[20] When discontinuation occurred, it was either related to:

- Lack of response,
- Logistical challenges (e.g., commuting burden),
- Hypomanic switch, or
- Suicidal crisis/ hostile thoughts.

In one study, 69% of treatment responders did not require further intervention (e.g., new medication or second rTMS course) at 6-month follow-up. However, 31% needed additional treatment, indicating varied durability of treatment effects.[18]

Study-reported limitations

All studies acknowledged limitations associated with their retrospective design. Commonly cited limitations included the lack of randomisation and blinding, which could introduce bias and affect internal validity. Some studies also noted heterogeneity in navigation methods, as not all sessions were neuronavigated. Missing data, particularly on demographics and baseline measurements, limited the accuracy of effect size estimations. Small sample sizes and lack of control groups were mentioned as limiting the ability to make strong causal inferences. In addition, differences in medication types and duration may have introduced confounding

effects, potentially influencing treatment response. Finally, the absence of clinician-rated measures and sham controls in some studies was cited as potentially limiting the validity of symptom assessments.

Strengths and limitations of the evidence scan

The focus of this scan on real-world evidence is a key strength, as this enhances relevance to clinical practice and service planning. The use of pre-defined eligibility criteria and a systematic search strategy ensure methodological rigour. Moreover, limiting the scope to Canadian studies increases contextual applicability.

However, the exclusion of international literature may limit the scope of practices in rTMS delivery and evaluation. Finally, we relied on published data only, which may have excluded relevant insights from unpublished evaluations or internal health authority reports.

Table 3: Outcome measurement and key findings

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings
Bakker et al., 2015			

rTMS vs iTBS	Baseline & Post treatment (2 to 6 weeks post treatment);
	
	Not specified
		Response: ≥50% symptom reduction from baseline
		
		Remission: HAM-D-17 < 7; BDI-II ≤ 12
			• No difference between 10Hz and iTBS groups in response and remission
			• HAM-D-17 Response= 49.7%; Remission= 33.5%
			• BDI-II Response= 41.8%; Remission= 30.1%
			• No significant predictors of % improvement
			• Discontinuations:
			  ○ 10Hz: 6/98 (6.1%)
			  ○ iTBS: 12/87 (13.8%)
			• Reasons for discontinuation:
			  ○ 10Hz: headaches (1), lack of response (4), commute (1)
			  ○ iTBS: headaches (2), vertigo (1), hostile thoughts (1), lack of response (2), commute (3), satisfactory results (2), unspecified (1)
			• No serious adverse effects recorded

Modirrousta et al., 2018			
Once daily (OD) vs twice daily (TD)	1 week before the first session & every 10 sessions;	Response: >50% reduction in HAM-D-17	• Response Rates: OD= 52.6%, TD= 82.4% • Remission Rates: OD= 36.8%, TD= 64.7% • Differences between OD and TD were not statistically significant.

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings

	No change or worsening of HAM-D score from baseline after 20 sessions	Remission: HAM-D-17 <7 + clinical interview	• Baseline age, sex & depression severity were not predictors of response
			• Treatment Trajectory:
			  ○ Groups showed a similar improvement pattern every 10 sessions.
			  ○ TD responders achieved improvement in half the time due to the accelerated treatment schedule.
			• Clinician- vs. Self-rated Scores:
			  ○ Discrepancy noted between clinician-rated (HAM-D-17) and self-rated (BDI-II) depression severity at baseline.
			• Discontinuations:
			  ○ 3/36 patients discontinued after 20 sessions due to non-response, while 2/36 discontinued for personal reasons.
			• Use of a neuronavigator did not influence treatment outcomes.

Feffer et al., 2018			
None	Every 5 sessions during treatment & 1-3 weeks for follow-ups; No clinical improvement after 20 sessions	Response: ≥ 50% reduction in BDI-II Remission: BDI-II≤ 12	• Response rate = 35.7% Remission rate = 23.8% • Predictors of outcome: No significant predictors identified (e.g., sex, age, pre-treatment BDI-II, number of failed medication trials, episode length) • No patients discontinued due to adverse effects No serious adverse events occurred All sessions (n = 882) were well tolerated
Schulze et al., 2018			
OD vs TD	Baseline & every 5 days. Follow-up (interval not specified);	Response: ≥ 50% reduction in BDI-II Remission: BDI-II≤ 12	• Response Rates: OD= 35.4%, TD= 41.5% Remission Rates: OD= 33.8%, TD= 35.4% • No significant difference in final BDI-II scores between groups. • Treatment Duration: TD group completed treatment in about half the number of days compared to OD

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings
	No clinical improvement after 20 sessions		• Faster improvement observed with TD (significant group-by-time interaction) • Pace of improvement was related to number of sessions, not cumulative pulses • No serious or treatment-limiting adverse events in either group. • All patients tolerated the treatment; common sensations included transient, painful but tolerable facial/scalp sensations.
Jodoin et al., 2019			
<60 years vs ≥60 years Unipolar vs Bipolar	Baseline & 7 days post treatment; Not specified	Response: ≥50% reduction in MADRS score Remission: MADRS score ≤10	• Response rate: <60 years = 35.2%, ≥60 years = 73.7% • Remission rate: <60 years = 33.3%, ≥60 years = 63.2% • Response and remission rates significantly higher in the older group • Patients with lower baseline depression and anxiety scores were more likely to respond. • No significant differences in treatment response or remission rates between unipolar vs bipolar depression. • Discontinuations: 4 patients <60 years; 2 patients ≥60 years. Reasons included hypomanic episode, local sensitivity, and tremor. • Common adverse events: Headaches, local sensitivity, fatigue, and nausea.
Yang et al., 2020			
Unipolar vs Bipolar	Baseline & treatment completion; N/A	Response: ≥50% reduction in HDRS-21 Remission: N/A	• Response: MDD = 39.3%; Bipolar depression = 7.7% (significantly lower in Bipolar depression, p = 0.029) • Remission: Not reported. • Discontinuations: 2 patients with MDD discontinued treatment. No discontinuations were due to adverse effects.

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings
Abo Aoun et al., 2023			

High frequency (HF) vs Low frequency (LF)	Baseline, 10, 20 & 30 sessions;
	
	No change or worsening of HAM-D-17 score from baseline after 20 sessions
		Response: >50% reduction in HAM-D-17 score
		
		Remission: HAM-D-17 <7 + clinical interview
			• Response rate: 57.7% (HF=62.3%, LF=71.4%, iTBS= 49.5%)
			• Remission rate: 42.3% (HF=50.9%, LF=49.2%, iTBS= 37.6%)
			• Protocol type predicted response (but not remission).
			• Early symptom improvement (after 10–20 sessions) was a significant predictor of final response and remission.
			• Predictors: Younger patients had a higher probability of response. Sex and baseline severity were not predictors for response.
			• Medication impacts:
			  ○ Bupropion use → increased response/remission rates.
			  ○ Antipsychotics, anticonvulsants, benzodiazepines → associated with reduced likelihood of response/remission.
			  ○ SSRIs/SNRIs → no significant effect.

Lee et al., 2023			
Responders vs non-responders; Remitters vs non-remitters	Baseline & last day of treatment; Not specified	Response: ≥50% reduction in QIDS-SR16 or PHQ-9 score from baseline Remission: QIDS-SR16 <6 or PHQ-9 <5 at end of treatment	• Response rate: 30.0% • Remission rate: 20.0% • Higher response and remission rates were observed among patients who had previously responded or remitted to rTMS/TBS compared to previous non-responders. • Discontinuations: 87.5% (35/40) completed the full course, with 1 out of 5 discontinuations reporting pain at the stimulation site.
Massé-Leblanc et al., 2024			
	Baseline & last day of treatment; Not specified	Response: ≥50% improvement on the MADRS score	• Response Rate=46.3% • Remission Rate=36.1% • No Improvement=33.3% • Predictors: Higher baseline depression and anxiety severity predicted poor outcomes

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings
		Remission: MADRS score ≤10	(clinical scores), adults > 60 years showed greater symptom improvement than younger adults • Discontinuations: 25.5% of patients discontinued treatment. Reasons for discontinuation included: ○ No improvement: 13.7% ○ Hypomanic switch: 2.4% ○ Inability to tolerate stimulation: 2.0% ○ Suicidal crisis: 1.5% ○ Other reasons (e.g., COVID-19, personal commitments): 5.4% • Common adverse effects: Headaches: 37.1%, Pain at stimulation site: 32.2% and Fatigue: 22.4% • No serious adverse effects recorded.
Mollica et al., 2024			
dTMS vs iTBS	Baseline, week 2, 4 & 6; < 25% improvement by week 4	Response: ≥50% reduction in HAM-D-17 Remission: HAM-D-17 <8	• Response rate: 46.8% • Remission rate: 30.5% • Mean HAMD-17 improvement among completers: 9.7 ± 6.1 points • dTMS vs iTBS: No difference in response and remission rates • Predictors of outcome: ○ Higher positive treatment expectancy (OR = 1.5 associated with greater odds of remission ○ Greater baseline HAMD-17 and treatment resistance associated with lower odds of remission ○ Negative expectancy not associated with remission or discontinuation • Discontinuations: 10% discontinued before completing 20 treatments (dTMS: 6.2%, iTBS: 12.5%). • No serious adverse events reported.
Elnazali et al., 2024			
Unilateral vs bilateral	Baseline, treatment completion & 6	Response: ≥50%	• Response rate: 42.7% • Remission rate: 31.2%

Group Comparison	Assessment timepoints; Discontinuation criteria	Response/ remission definitions	Key findings

	months after completion;
	
	N/A
		reduction in HAM-D-17
		
		Remission: HAM-D-17 < 7
			• No significant differences in response or remission between iTBS groups.
			• Symptom changes:
			  ○ No significant difference in post-treatment HAM-D-17 or PHQ-9 scores between groups.
			  ○ Significant difference in GAD-7 scores (unilateral > bilateral).
			• No significant predictors of treatment outcome identified e.g. baseline factors, age.
			• Adverse effects:
			  ○ Unilateral iTBS associated with significantly more post-treatment headache and pain/discomfort than bilateral.
			  ○ No difference in serious side effects (seizures)or other physiological changes (heart rate and blood pressure changes).
			• Follow-up at 6 months (among responders):
			  ○ 69% did not require additional treatment or medication change.
			  ○ 31% required further intervention (e.g., second TBS course, ECT, or medication change).
			• No difference in maintenance of response between unilateral and bilateral groups at 6 months.

Abbreviations:
BDI-II – Beck Depression Inventory (Second Edition)
dTMS – Deep Transcranial magnetic Stimulation
ECT – Electroconvulsive Therapy
GAD-7 – Generalized Anxiety Disorder scale (7-item)
HAM-A – Hamilton Anxiety Rating Scale
HAM-D-17 – Hamilton Rating Scale for Depression (17-item)
HDRS-21 – Hamilton Depression Rating Scale (21-item)
iTBS – Intermittent theta-burst stimulation
MADRS – Montgomery-Åsberg Depression Rating Scale
MDD – Major Depressive Disorder
PHQ-9– Patient Health Questionnaire–9
QIDS-SR16 – Quick Inventory of Depressive Symptomatology – Self Report (16-item)
rTMS – Repetitive Transcranial Magnetic Stimulation
SNRIs – Serotonin-Norepinephrine Reuptake Inhibitors
SSRIs – Selective Serotonin Reuptake Inhibitors
TBS – Theta-Burst Stimulation

Conclusions

This evidence scan aimed to identify and synthesise evaluations of rTMS programmes, with a focus on Canadian studies. Although the scan sought both outcome and process evaluations, all identified studies focused exclusively on clinical outcomes, primarily response, remission, safety, and tolerability. No studies reported on implementation processes, service quality, or patient and provider experiences.

Variation in symptom rating tools, timing of assessments, and treatment protocols limited comparability between studies. Reported outcomes ranged from modest to substantial improvements in depressive symptoms, reflecting the diversity of clinical contexts and treatment protocols. This heterogeneity likely reflects the absence of standardised evaluation frameworks or benchmarks within routine rTMS service delivery.

> **Nonetheless, the evidence consistently supported the effectiveness and safety of rTMS in routine clinical practice; however, important gaps remain**.

While retrospective designs are useful for assessing clinical outcomes in routine care, they rarely capture how programmes are implemented or experienced. As such, they provide limited insight into implementation processes, service quality, or the perspectives of patients and providers.

Future evaluations should incorporate standardised outcome measures alongside qualitative and mixed-methods approaches to examine implementation, service quality, and the experience of providers and patients. Strengthening the evidence base in these areas will better inform service planning and support the effective integration of rTMS into routine mental health services.

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Appendix A: Study distribution per province

Province	Service providers (n=number of studies)
Ontario	- University Health Network (n=3) - Centre for Addiction and Mental Health (CAMH) (n=1) - Harquail Centre for Neuromodulation at Sunnybrook Health Sciences Centre(n=1) - The Saint John's Health Centre (n=1)
Manitoba	- Winnipeg Regional Authority at the St. Boniface Hospital (n= 2)
Quebec	- Centre Hospitalier de l'Université de Montréal (CHUM) (n=2)
British Columbia	- BrainStim Healthcare (n=1)

Appendix B: Summary of study indicators

Indicator category	Indicator description
Outcome measures	
Response rate	% of patients who attain rTMS response criteria (≥50% reduction in depression scores) through tracking of depressive symptoms
Remission rate	% of patients who attain rTMS remission (based on programme predefined criteria) through tracking of depressive symptoms
Relapse rate	% of patients who after achieving improvements experience a return of the original symptoms
Changes in depression scores	% change in depression scores from baseline through the treatment course
Safety	# of adverse events recorded
Acceptability/tolerability	# of patients who successfully complete treatment course # of discontinuations and reasons for treatment discontinuations
Demographics	
Age	Continuous age; <60 years, ≥60 years, etc.
Gender	Male, female
Medical history	
Diagnosis type	Unipolar, bipolar
Medication trials	# of failed medication trials
Depressive symptoms at the beginning of treatment	Depression scores at baseline
Depression symptoms duration	Depression episode length
Previous rTMS treatment response	Responder, non-responder
Other previous treatments	ECT; Ketamine
Treatment procedures	
Type of stimulation	LF, HF; Unilateral, bilateral
Brain stimulation region	left DLPFC, right DLPFC, left DMPFC, right DMPFC, left OFC, etc.
Number of daily treatments	Once daily, twice daily
Treatment protocol	Standard rTMS, iTBS, cTBS, etc.