

Summary of published studies for the rTMS antidepressant studies: study type and grading of strength of evidence.

Study citation (chronological listing within category)	Study type	Sample size	Level of evidence	Comments
O'Reardon J.P., Solvason H.B., Janicak P.G., Sampson S., Isenberg K.E., Nahas Z., McDonald W.M., Avery D., Fitzgerald P.B., Loo C., Demitrack M.A., George M.S., Sackeim H.A. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. <i>Biol Psychiatry</i> 2007;62:1208–16 [6].	RCT	TMS (N = 155) Sham (N = 146)	Level 1b – individual RCT	Unique multisite RCT, sponsored by industry (Neuronetics Inc) Basis of initial FDA clearance for TMS device
George M.S., Lisanby S.H., Avery D., McDonald W.M., Durkalski V., Pavlicova M., Anderson B., Nahas Z., Bulow P., Zarkowski P., Holtzheimer P., Schwartz T., Sackeim H.A. Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. <i>Arch Gen Psychiatry</i> 2010;67(5):507–16 [7].	RCT	TMS (N = 92) Sham (N = 98)	Level 1b – individual RCT	Unique multisite RCT, sponsored by US federal NIMH Independent of industry
Levkovitz Y., Isserles M., Padberg F., Lisanby S.H., Bystritsky A., Xia G., Tendler A., Daskalakis Z.J., Winston J.L., Dannon P., Hafez H.M., Reti I.M., Morales O.G., Schlaepfer T.E., Hollander E., Berman J.A., Husain M.M., Sofer U., Stein A., Adler S., Deutsch L., Deutsch F., Roth Y., George M.S., Zangen A. Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. <i>World Psychiatry</i> 2015;14(1):64–73. [8].	RCT	TMS (N = 101) Sham (N = 111)	Level 1b – individual RCT	Unique multisite RCT, sponsored by industry (Brainsway) Basis of FDA clearance for Deep TMS device

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Avery D.H., Isenberg K.E., Sampson S.M., Janicak P.G., Lisanby S.H., Maixner D.F., Loo C., Thase M.E., Demitrack M.A., George M.S. Transcranial magnetic stimulation in the acute treatment of major depressive disorder: clinical response in an open-label extension trial. J Clin Psychiatry 2008;69(3):441–51 [9].	OL	TMS (N = 158)	Level 2b – individual OL study	Open label follow-on acute efficacy and safety study of subset cohort from O'Reardon et al. [6]
Demitrack M.A., Thase M.E. Clinical significance of transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant depression: synthesis of recent data. Psychopharmacol Bull 2009;42(2):5–38 [10].	RCT	TMS (N = 88) Sham (N = 76)	Level 1b – individual RCT	RCT subset analysis of ATHF = 1 cohort from O'Reardon et al. [6]
Lisanby S.H., Husain M.M., Rosenquist P.B., Maixner D., Gutierrez R., Krystal A., Gilmer W., Marangell L., Aaronson S., Daskalakis Z.J., Canterbury R., Richelson E., Sackeim H.A., George M.S. Transcranial Magnetic Stimulation (TMS) in the acute treatment of major depression: clinical predictors of outcome in a multisite, randomized controlled clinical trial. Neuropsychopharmacology 2009;34:522–34 [11].	RCT	TMS (N = 155) Sham (N = 146)	Level 1b – individual RCT	RCT subset analysis of predictors of outcome during acute treatment from O'Reardon et al. [6]
Janicak P.G., O'Reardon J.P., Sampson S.M., Husain M.M., Lisanby S.H., Rado J.T., Demitrack M.A. Transcranial Magnetic Stimulation (TMS) in the treatment of major depressive disorder: a comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction	RCT	TMS (N = 165) Sham (N = 160)	Level 1b – individual RCT (safety)	Comprehensive safety and tolerability analysis of population included in O'Reardon et al. [6] Includes 6 month longer term follow up phase

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treatment. J Clin Psychiatry 2008;69(2):222–32 [12]. Carpenter L.L., Janicak P.G., Aaronson S.T., Boyadjis T., Brock D.G., Cook I.A., Dunner D.L., Lanocha K., Solvason H.B., Demitrack M.A. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. Depress Anxiety 2012;29(7):587–96 [13].	Cohort	TMS (N = 307)	Level 2b – individual cohort study	Unique, cohort study of patients treated in routine, real-world clinical practice settings in the United States
Janicak P.G., Dunner D.L., Aaronson S.T., Carpenter L.L., Boyadjis T.A., Brock D.G., Cook I.A., Lanocha K., Solvason H.B., Bonneh-Barkay D., Demitrack M.A. Transcranial Magnetic Stimulation (TMS) for major depression: a multisite, naturalistic, observational study of quality of life outcome measures in clinical practice. CNS Spectr 2013;18:322–32 [14].	Cohort	TMS (N = 307)	Level 2b – individual cohort study	Cohort study of patients treated in routine, real-world clinical practice settings in the United States Quality of life outcomes based on Carpenter et al. [13]
McDonald W.M., Durkalski V., Ball E.R., Holtzheimer P.E., Pavlicova M., Lisanby S.H., Avery D., Anderson B.S., Nahas Z., Zarkowski P., Sackeim H.A., George M.S. Improving the antidepressant efficacy of transcranial magnetic stimulation: maximizing the number of stimulations and treatment location in treatment-resistant depression. Depress Anxiety 2011;28(11):973–80 [15].	OL	TMS (N = 141)	Level 2b – individual OL study	Open label follow-on acute efficacy and safety study of subset cohort from George et al. [7]
Janicak P.G., Nahas Z., Lisanby S.H., Solvason H.B., Sampson S.M., McDonald W.M., Marangell L.B., Rosenquist P.B., McCall W.V., Kimball J., O'Reardon J.,	OL	TMS (N = 99) Sham (N = 21)	Level 2b – individual OL study	Open label follow-on long term efficacy study of subset cohort from O'Reardon et al. [6]

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Loo C., Husain M.H., Krystal A., Gilmer W., Dowd S.M., Demitrack M.A., Schatzberg A.F. Durability of clinical benefit with transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant major depression: assessment of relapse during a 6-month, multisite, open-label study. <i>Brain Stimul</i> 2010;3:187–99 [16].				
Mantovani A., Pavlicova M., Avery D., Nahas Z., McDonald W.M., Wajdik C.D., Holtzheimer P.E., George M.S., Sackeim H.A., Lisanby S.H. Long-term efficacy of repeated daily prefrontal transcranial magnetic stimulation (TMS) in treatment-resistant depression. <i>Depress Anxiety</i> 2012;29:883–90 [17].	OL	TMS (N = 50)	Level 2b – individual OL study	Open label follow-on long term efficacy study of subset cohort from George et al. [7]
Levkovitz Y., Harel E.V., Roth Y., Braw Y., Most D., Katz L.N., Sheer A., Gersner R., Zangen A. Deep transcranial magnetic stimulation over the prefrontal cortex: evaluation of antidepressant and cognitive effects in depressive patients. <i>Brain Stimul</i> 2009;2:188–200 [18].	RCT	TMS (N = 65)	Level 2b – randomized feasibility study	Feasibility efficacy study randomized groups between various deep TMS coils and in intensities
Isserles M., Rosenberg O., Dannon P., Levkovitz Y., Kotler M., Deutsch F., Lerer B., Zangen A. Cognitive-emotional reactivation during deep transcranial magnetic stimulation over the prefrontal cortex of depressive patients affects antidepressant outcome. <i>J Affect Disord</i> 2011;128:235–42 [19].	OL	TMS (N = 57)	Level 2b – individual OL study	Open label efficacy study of deep TMS as add on to antidepressant medications
Harel E.V., Rabany L., Deutsch L., Bloch Y., Zangen A., Levkovitz Y. H-coil repetitive transcranial magnetic stimulation for treatment	OL	TMS (N = 29)	Level 2b – individual OL study	Open label long term efficacy study of deep TMS

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resistant major depressive disorder: an 18-week continuation safety and feasibility study. World J Biol Psychiatry 2014;15:298–306 [20]. Rosenquist P.B., Krystal A., Heart K.L., Demitrack M.A., McCall W.V. Left dorsolateral prefrontal transcranial magnetic stimulation (TMS): sleep factor changes during treatment in patients with pharmacoresistant major depressive disorder. Psychiatry Res 2013;205(1–2):67–73 [21].	RCT	TMS (N = 155) Sham (N = 146)	Level 1b – individual RCT	RCT subset analysis of sleep outcomes from O'Reardon et al. [6]
Simpson K.N., Welch M.J., Kozel F.A., Demitrack M.A., Nahas Z. Cost-effectiveness of transcranial magnetic stimulation in the treatment of major depression: a health economics analysis. Adv Ther 2009;26(3):346–68 [22].	RCT	TMS (N = 155) Sham (N = 146)	Level 2b – economic/decision analysis study	Health economic decision analysis study based on data from O'Reardon et al. [6] Comparative health economic cost analysis with next-choice pharmacotherapy
Agency for Healthcare Research and Quality, Effective Health Care Program, Comparative Effectiveness Review Number 33, “Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults”. 2012	SR	Total active TMS sample examined for SR (N = 497) Includes TMS study data: (N = 247)	Level 1a – systematic review	Independent, US government funded systematic review
Allan C.L., Herrmann L.L., Ebmeier K.P. Transcranial magnetic stimulation in the management of mood disorders. Neuropsychobiology 2011;64:163–9 [23].	SR	Total sample for SR (N = 1531)	Level 1a – systematic review (with minor heterogeneity)	Independent, academic-based systematic review Modest, clinically non-significant heterogeneity in outcome reported
Schutter D.J. Antidepressant efficacy of high-frequency transcranial magnetic stimulation	SR	Total sample for	Level 1a – systematic review	Independent, academic-based systematic review

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over the left dorsolateral prefrontal cortex in double-blind sham-controlled designs: a meta-analysis. <i>Psychol Med</i> 2009;39:65–75 [24].		SR (N = 1164)		
Slotema C.W., Blom J.D., Hoek H.W., Sommer I.E. Should we expand the toolbox of psychiatric treatment methods to include repetitive transcranial magnetic stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. <i>J Clin Psychiatry</i> 2010;71(7):873–84 [25].	SR	Total sample for SR (N = 1383)	Level 1a – systematic review	Independent, academic-based systematic review
Berlim M.T., van den Eynde F., Tovar-Perdomo S., Daskalakis Z.J. Response, remission and drop-out rates following high-frequency repetitive transcranial magnetic stimulation (rTMS) for treating major depression: a systematic review and meta-analysis of randomized, double-blind and sham-controlled trials. <i>Psychol Med</i> 2014;44(2):225–39 [26].	SR	Total sample for SR (N = 1371)	Level 1a – systematic review	Independent, academic-based systematic review
Solvason H.B., Husain M., Fitzgerald P.B., Rosenquist P., McCall W.V., Kimball J., Gilmer W., Demitrack M.A., Lisanby S.H. Improvement in quality of life with left prefrontal transcranial magnetic stimulation in patients with pharmacoresistant major depression: acute and six month outcomes. <i>Brain Stimul</i> 2014;7:219–25 [27].	SR		Level 1b – systematic review	Independent, academic-based systematic review
Dunner D.L., Aaronson S.T., Sackeim H.A., Janicak P.G., Carpenter L.L., Boyadjis T., Brock D.G., Bonneh-Barkay D., Cook I.A., Lanocha K., Solvason H.B., Demitrack M.A. A multisite,				

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<p>naturalistic, observational study of transcranial magnetic stimulation for patients with pharmacoresistant major depressive disorder: durability of benefit over a 1-year follow-up period. J Clin Psychiatry 2014;75(12):1394–401 [28].</p>				