Appendix A. Literature Search Strategies and Yields

Published Literature

Table A1. PubMed search, 10/14/16. Limited to date range of 1/1/1995 – present.

Search	Query	Items found
#1	Search "Depression"[Mesh] OR "Depressive Disorder"[Mesh]	173285
#5	Search "Depression"[Mesh] OR "Depressive Disorder"[Mesh] Filters: Publication date from 1995/01/01; Humans; English; Adult: 19+ years	78019
#6	Search ((("Drug Resistance"[Mesh] OR refractory[tw] OR resistant[tw] OR augment OR switch)) OR (Non-remitting OR Unremitted OR "Inadequate response" OR Refractory OR Resist* OR "Fail respon*" OR Augment OR Switch OR "Drug Resistance" OR "Treatment Failure" OR Retreatment)) OR (adjunctive OR "second step" OR second-step)	1168596
#7	Search (#5 AND #6)	3308
#8	Search (#5 AND #6) Filters: Systematic Reviews	94
#9	Search ((("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Single-Blind Method"[Mesh] OR "Double-Blind Method"[Mesh] OR "Random Allocation"[Mesh]	616555
#10	Search ((("Longitudinal Studies"[Mesh] OR "Comparative Study "[Publication Type]) OR "Cohort Studies"[Mesh] OR "observational studies"[tw]) OR "Historically Controlled Study"[Mesh] OR "Interrupted Time Series Analysis"[Mesh])	
#14	Search "Guideline" [Publication Type]	28297
#16	Search "Consensus Development Conference, NIH" [Publication Type] OR "Consensus Development Conference" [Publication Type]	10182
#17	Search (#9 OR #10 OR #14 OR #16)	3436652
#18	Search (#7 AND #17)	1656
#19	Search (#8 OR #18)	1692

NIH = National Institutes of Health

Table A2. PubMed update search, 8/18/17. Limited to date range of 6/1/2015 – present.

Search	Query	Items found
#1	Search "Depression"[Mesh] OR "Depressive Disorder"[Mesh] Sort by: Relevance	181030
#5	Search "Depression"[Mesh] OR "Depressive Disorder"[Mesh] Sort by: RelevanceFilters: Publication date from 2015/06/01; Humans; English; Adult: 19+ years	9384
#6	Search ((("Drug Resistance"[Mesh] OR refractory[tw] OR resistant[tw] OR augment OR switch)) OR (Non-remitting OR Unremitted OR "Inadequate response" OR Refractory OR Resist* OR "Fail respon*" OR Augment OR Switch OR "Drug Resistance" OR "Treatment Failure" OR Retreatment)) OR (adjunctive OR "second step" OR second-step) Sort by: Relevance	1232463
#7	Search (#5 AND #6) Sort by: Relevance	411
#8	Search (#5 AND #6) Sort by: Relevance Filters: Systematic Reviews	913
#9	Search ((("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Single-Blind Method"[Mesh] OR "Double-Blind Method"[Mesh] OR "Random Allocation"[Mesh] Sort by: Relevance	645671
#10	Search ((("Longitudinal Studies"[Mesh] OR "Comparative Study "[Publication Type]) OR "Cohort Studies"[Mesh] OR "observational studies"[tw]) OR "Historically Controlled Study"[Mesh] OR "Interrupted Time Series Analysis"[Mesh]) Sort by: Relevance	3147788
#11	Search "Guideline" [Publication Type] Sort by: Relevance	29604
#12	Search "Consensus Development Conference, NIH" [Publication Type] OR "Consensus Development Conference" [Publication Type] Sort by: Relevance	10634
#13	Search (#9 OR #10 OR #11 OR #12) Sort by: Relevance	3571868
#14	Search (#7 AND #13) Sort by: Relevance	202
#16	Search (#8 OR #14) Sort by: Relevance	208

NIH = National Institutes of Health

Table A3. Databases searched for "Treatment Resistant Depression", 10/14/16. Limited to date range of 1/1/1995 – present.

Database	Hits
Cochrane Database of Systematic Reviews	4
Cochrane DARE	13
Cochrane CCTR	189
EMBASE	200
PsychInfo	361

CCTR = Central Register of Controlled Trials; DARE = Database of Abstracts of Reviews of Effects; EMBASE = Excerpta Medica Database; PsychInfo = Psychological Information Database

Table A4. Update databases searched for "Treatment Resistant Depression," 8/18/17. Limited to date range of 6/1/2015 – present.

Database	Hits
Cochrane Database of Systematic Reviews	0
Cochrane DARE	0
Cochrane CCTR	74
EMBASE	45
PsychInfo	33

CCTR = Central Register of Controlled Trials; DARE = Database of Abstracts of Reviews of Effects; EMBASE = Excerpta Medica Database; PsychInfo = Psychological Information Database

Gray Literature

Table A5. ClinicalTrials.gov, 8/24/16. Limited to date range of 1/1/1995 – present.

ID	Search	Hits
#1	"Treatment resistant depression"*	178

*A search for "Treatment-resistant depression" did not result in additional hits

Table A6. Update, ClinicalTrials.gov, 8/18/17. Limited to date range of 6/1/2015 – present.

ID	Search	Hits
#1	"Treatment resistant depression"*	13

*A search for "Treatment-resistant depression" did not result in additional hits

Table A7. Health Services Research Projects in Progress (HSRProj), 8/24/16. Limited to date range of 1/1/1995 – present.

ID	Search	Hits
#1	"Treatment resistant depression"*	2

*A search for "Treatment-resistant depression" did not result in additional hits; an updated search on 8/18/17 did not result in any additional hits

Table A8. National Guideline Clearinghouse, 10/20/16. Limited to date range of 1/1/1995 – present.

ID	Search	Hits
#1	"Treatment resistant depression"	30
#2	"Treatment-resistant depression"	1

*An updated search on 8/18/17 did not result in any additional hits

Table A9. Non-Database Sources and Search Dates

Name	Source	Search Date (s)
NIMH	www.nimh.nih.gov	First search: 9/30/16 Second search: 12/6/16 Updated search:8/18/17
UpToDate	www.uptodate.com	First search: 1/10/17 Updated search: 8/18/17
EHC Website	www.effectivehealthcare.ahrq.gov	First search: 11/8/16 Updated search: 8/18/17
SAMHSA	www.samhsa.gov	First search: 12/6/16 Updated search: 8/18/17
FDA	www.fda.gov	First search: Drugs: 1/10/17–2/9/17 Devices: 12/21/16–1/6/17 Updated search: 8/18/17

EHC = Effective Health Care; FDA = Food and Drug Administration; NIMH = National Institute of Mental Health; SAMHSA = Substance Abuse Mental Health Services Administration

Table A10. Additional Sources

Name	Source	Details
MEDCAC Panel Proceedings	https://www.cms.gov/	On 12/6/16 MEDCAC panel proceeding documents from April 2016 were searched
Proposal/Protocol Only References	EndNote Database (provided by librarian, 10/13/16)	References from the TRD proposal and protocol were screened for relevancy on 1/20/17

MEDCAC = Medicare Evidence Development and Coverage Advisory; TRD = Treatment Resistant Depression

Appendix B. Excluded Studies

Exclusions:

- X1: Ineligible publication type
- X2: Ineligible populations
- X3: Ineligible or no interventions
- X4: Ineligible or no comparators
- X5: Ineligible or no outcomes
- X6: Wrong country
- X7: Ineligible study design
- X8: Does not answer a KQ of the review
- X9: Abstract-only record (otherwise eligible)
- X10: Irretrievable
- X11: SR Published prior to 2006
- X12: Duplicate
- X13: Exclude due to new 2005 criteria
- X14: Exclude, updated publication found
- X15: Excluded primary or companion, to be cited in review
- X16: Excluded for not meeting Systematic Review (SR) quality criteria

1. Vagus nerve stimulation for treatment-resistance depression. *Technol Eval Cent Assess Program Exec Summ*. 2005 Aug;20(8):1-2. PMID: 16156089. Exclusion Code: X10.
2. Transcranial magnetic stimulation: Potential new treatment for resistant depression. *J Clin Psychiatry*. 2007;68(2):315-30. doi: 10.4088/JCP.v68n0219. PMID: 2007-07426-019. Exclusion Code: X1.
3. FDA Executive Summary: Prepared for the January 2728, 2011 meeting of the Neurological Devices Panel. Meeting to Discuss the Classification of Electroconvulsive Therapy Devices (ECT). Silver Spring, MD: United States Food and Drug Administration; 2011. https://wayback.archive-it.org/7993/20170114044018/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/UCM240933.pdf. Accessed 31 Jan, 2017. Exclusion Code: X1.
4. Abdallah CG, Fasula M, Kelmendi B, et al. Rapid antidepressant effect of ketamine in the electroconvulsive therapy setting. *J ECT*. 2012 Sep;28(3):157-61. doi: 10.1097/YCT.0b013e31824f8296 [doi]. PMID: 22847373. Exclusion Code: X2.
5. Agency for Healthcare Research and Quality. Surveillance Report: Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults Comparative Effectiveness Review No. 33. (Prepared by RTI International-University of North Carolina under Contract No. 290-02-0016I, TO #2.) AHRQ Publication No. 11-EHC056-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2016. https://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1545 Exclusion Code: X7.
6. Ahmad H, Soldani F. Risk-benefit & decision analyses of electroconvulsive therapy (ECT) in treatment refractory depression. *Bipolar Disorders*. 2013;15((Ahmad H.; Soldani F.) US Food and Drug Administration (FDA), Silver Spring, United States):102-3. Exclusion Code: X9.
7. Aiyer R, Joffe RT. Deep brain stimulation in treatment resistant depression: A systematic review. *Current Psychopharmacology*. 2015;4(1):10-6. Exclusion Code: X1.

8. Alexopoulos GS, Reynolds CF, 3rd, Bruce ML, et al. Reducing suicidal ideation and depression in older primary care patients: 24-month outcomes of the PROSPECT study. *Am J Psychiatry*. 2009 Aug;166(8):882-90. doi: 10.1176/appi.ajp.2009.08121779. PMID: 19528195. Exclusion Code: X2.

9. Amital D, Fostick L, Silberman A, et al. Serious life events among resistant and non-resistant MDD patients. *J Affect Disord*. 2008 Oct;110(3):260-4. doi: 10.1016/j.jad.2008.01.006. PMID: 18262654. Exclusion Code: X2.

10. Amsterdam JD, Garcia-Espana F, Rosenzweig M. Clomipramine augmentation in treatment-resistant depression. *Depress Anxiety*. 1997;5(2):84-90. doi: 10.1002/(SICI)1520-6394(1997)5:2<84::AID-DA4>3.0.CO;2-5 [pii]. PMID: 9262938. Exclusion Code: X13.

11. Amsterdam JD, Lorenzo-Luaces L, DeRubeis RJ. Step-wise loss of antidepressant effectiveness with repeated antidepressant trials in bipolar II depression. *Bipolar disorders*. 2016 Nov 2;18(7):563-70. doi: 10.1111/bdi.12442. PMID: CN-01288389. Exclusion Code: X2.

12. Amsterdam JD, Shults J. Does tachyphylaxis occur after repeated antidepressant exposure in patients with Bipolar II major depressive episode? *J Affect Disord*. 2009 May;115(1-2):234-40. doi: S0165-0327(08)00291-7 [pii]; 10.1016/j.jad.2008.07.007 [doi]. PMID: 18694599. Exclusion Code: X2.

13. Anderson IM, Delvai NA, Ashim B, et al. Adjunctive fast repetitive transcranial magnetic stimulation in depression. *Br J Psychiatry*. 2007 Jun;190:533-4. doi: 190/6/533 [pii]; 10.1192/bjp.bp.106.028019 [doi]. PMID: 17541116. Exclusion Code: X2.

14. Anderson IM, Ferrier IN, Baldwin RC, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2000 British Association for Psychopharmacology guidelines. *J Psychopharmacol*. 2008 Jun;22(4):343-96. doi: 10.1177/0269881107088441. PMID: 18413657. Exclusion Code:

15. Appelberg BG, Syvalahti EK, Koskinen TE, et al. Patients with severe depression may benefit from buspirone augmentation of selective serotonin reuptake inhibitors: results from a placebo-controlled, randomized, double-blind, placebo wash-in study. *J Clin Psychiatry*. 2001 Jun;62(6):448-52. PMID: 11465522. Exclusion Code: X13.

16. Aronson R, Offman HJ, Joffe RT, et al. Triiodothyronine augmentation in the treatment of refractory depression. A meta-analysis. *Arch Gen Psychiatry*. 1996 Sep;53(9):842-8. PMID: 8792761. Exclusion Code: X11.

17. Association AP. Practice guideline for the treatment of patients with major depressive disorder. 2 ed: American Psychiatric Association; 2000. Exclusion Code: X14.

18. Avery DH, Claypoole K, Robinson L, et al. Repetitive transcranial magnetic stimulation in the treatment of medication-resistant depression: preliminary data. *J Nerv Ment Dis*. 1999 Feb;187(2):114-7. PMID: 10067953. Exclusion Code: X13.

19. Avery DH, Holtzheimer PE, 3rd, Fawaz W, et al. Transcranial magnetic stimulation reduces pain in patients with major depression: a sham-controlled study. *J Nerv Ment Dis*. 2007 May;195(5):378-81. doi: 10.1097/NMD.0b013e31802f58d1 [doi]; 00005053-200705000-00003 [pii]. PMID: 17502802. Exclusion Code: X5.

20. Baeken C, Duprat R, Wu GR, et al. Subgenual Anterior Cingulate-Medial Orbitofrontal Functional Connectivity in Medication-Resistant Major Depression: A Neurobiological Marker for Accelerated Intermittent Theta Burst Stimulation Treatment? *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2017((Baeken C., cbaeken@hotmail.com; Duprat R.; Wu G.-R.; van Heeringen K.) Department of Psychiatry and Medical Psychology, Ghent University, Ghent)doi: 10.1016/j.bpsc.2017.01.001. Exclusion Code: X4.

21. Bahk WM, Woo YS, Seo HJ, et al. Nicotinic acetylcholine receptor antagonists for treatment-resistant depression: A meta-analysis. *Eur Psychiatry*. 2016;33((Bahk W.M.; Woo Y.S.; Seo H.J.; Wang H.R.) Yeouido St. Mary's Hospital, Psychiatry, Seoul, South Korea):S226. Exclusion Code: X3.

22. Ballard ED, Ionescu DF, Vande Voort JL, et al. Improvement in suicidal ideation after ketamine infusion: relationship to reductions in depression and anxiety. *J Psychiatr Res*. 2014 Nov;58:161-6. doi: 10.1016/j.jpsychires.2014.07.027. PMID: 25169854. Exclusion Code: X4.

23. Barbosa L, Berk M, Vorster M. A double-blind, randomized, placebo-controlled trial of augmentation with lamotrigine or placebo in patients concomitantly treated with fluoxetine for resistant major depressive episodes. *J Clin Psychiatry*. 2003 Apr;64(4):403-7. PMID: 12716240. Exclusion Code: X13.

24. Barbui C, Butler R, Cipriani A, et al. Depression in adults: drug and physical treatments. *BMJ Clin Evid*. 2007;2007doi: 1003 [pii]. PMID: 19454086. Exclusion Code: X8.

25. Barowsky J, Schwartz TL. An evidence-based approach to augmentation and combination strategies for treatment-resistant depression. *Psychiatry*. 2006 Jul;3(7):42-59. PMID: 2007-02351-004. Exclusion Code: X1.

26. Bauer M, Demyttenaere K, El-Khalili N, et al. Pooled analysis of adjunct extended-release quetiapine fumarate in patients with major depressive disorder according to ongoing SSRI or SNRI treatment. *Int Clin Psychopharmacol*. 2014 Jan;29(1):16-25. doi: 10.1097/YIC.0000000000000011 [doi]. PMID: 24108148. Exclusion Code: X7.

27. Bauer M, Dopfmer S. Lithium augmentation in treatment-resistant-depression: meta-analysis of placebo-controlled studies (Structured abstract). *J Clin Psychopharmacol*. 1999;19(5):427-34. PMID: DARE-11999001921. Exclusion Code: X11.

28. Bauer M, El-Khalili N, Datto C, et al. A pooled analysis of two randomised, placebo-controlled studies of extended release quetiapine fumarate adjunctive to antidepressant therapy in patients with major depressive disorder. *J Affect Disord*. 2010 Dec;127(1-3):19-30. doi: S0165-0327(10)00568-9 [pii]; 10.1016/j.jad.2010.08.032 [doi]. PMID: 20884063. Exclusion Code: X7.

29. Bauer M, Forsthoff A, Baethge C, et al. Lithium augmentation therapy in refractory depression-update 2002. *Eur Arch Psychiatry Clin Neurosci*. 2003 Jun;253(3):132-9. doi: 10.1007/s00406-003-0430-9 [doi]. PMID: 12904977. Exclusion Code: X11.

30. Bauer M, Pretorius HW, Constant EL, et al. Extended-release quetiapine as adjunct to an antidepressant in patients with major depressive disorder: results of a randomized, placebo-controlled, double-blind study. *J Clin Psychiatry*. 2009 Apr;70(4):540-9. PMID: 19358791. Exclusion Code: X6.

31. Bauer M, Tharmanathan P, Volz HP, et al. The effect of venlafaxine compared with other antidepressants and placebo in the treatment of major depression: a meta-analysis. *Eur Arch Psychiatry Clin Neurosci*. 2009 Apr;259(3):172-85. doi: 10.1007/s00406-008-0849-0 [doi]. PMID: 19165525. Exclusion Code: X2.

32. Bauer M, Thase ME, Liu S, et al. Analysis of potentially predictive factors of efficacy of adjunct extended-release quetiapine fumarate in patients with major depressive disorder. *J Psychopharmacol*. 2015 May;29(5):565-74. doi: 0269881114552715 [pii]; 10.1177/0269881114552715 [doi]. PMID: 25257148. Exclusion Code: X7.

33. Baumann P, Nil R, Souche A, et al. A double-blind, placebo-controlled study of citalopram with and without lithium in the treatment of therapy-resistant depressive patients: a clinical, pharmacokinetic, and pharmacogenetic investigation. *J Clin Psychopharmacol*. 1996 Aug;16(4):307-14. PMID: 8835706. Exclusion Code: X13.

34. Bech P, Lunde M, Lauritzen L, et al. The Diagnostic Apathia Scale predicts a dose-remission relationship of T-PEMF in treatment-resistant depression. *Acta neuropsychiatrica*. 2015(1):1-7. doi: 10.1017/neu.2014.26. PMID: CN-01113381. Exclusion Code: X8.

35. Bedson E, Bell D, Carr D, et al. Folate Augmentation of Treatment--Evaluation for Depression (FolATED): randomised trial and economic evaluation. *Health Technol Assess*. 2014 Jul;18(48):vii-viii, 1-159. doi: 10.3310/hta18480 [doi]. PMID: 25052890. Exclusion Code: X2.

36. Belmaker B, Fitzgerald P, George MS, et al. Managing the risks of repetitive transcranial stimulation. *CNS Spectrums*. 2003 July;8(7):489. Exclusion Code: X2.

37. Benadhira R, Saba G, Samaan A, et al. Transcranial magnetic stimulation for refractory depression. *Am J Psychiatry*. 2005 Jan;162(1):193. doi: 162/1/193 [pii]; 10.1176/appi.ajp.162.1.193 [doi]. PMID: 15625226. Exclusion Code: X4.

38. Bergfeld IO, Denys D. Deep brain stimulation as a treatment for treatment-resistant depression. *Tijdschrift voor psychiatrie*. 2016(12):897. PMID: CN-01331852. Exclusion Code: X1.

39. . A randomized, crossover trial of deep brain stimulation of the ventral anterior limb of the internal capsule in depression. European neuropsychopharmacology. Conference: 29th european college of neuropsychopharmacology congress, ECNP 2016. Austria. Conference start: 20160917. Conference end: 20160920; 2016. Exclusion Code: X9.

40. Berlim MT, Broadbent HJ, Van den Eynde F. Blinding integrity in randomized sham-controlled trials of repetitive transcranial magnetic stimulation for major depression: a systematic review and meta-analysis. *Int J Neuropsychopharmacol*. 2013 Feb 11:1-9. doi: S1461145712001691 [pii]; 10.1017/S1461145712001691. PMID: 23399312. Exclusion Code: X2.

41. Berlim MT, Fleck MP, Turecki G. Current trends in the assessment and somatic treatment of resistant/refractory major depression: an overview. *Ann Med*. 2008;40(2):149-59. PMID: 18293145. Exclusion Code: X1.

42. Berlim MT, McGirr A, Eynde F, et al. Effectiveness and acceptability of deep brain stimulation (DBS) of the subgenual cingulate cortex for treatment-resistant depression: a systematic review and exploratory meta-analysis *J Affect Disord*. 2014 20 April;159(2):31-8. PMID: DARE-12014020668. Exclusion Code: X7.

43. Berlim MT, Van den Eynde F, Daskalakis ZJ. A systematic review and meta-analysis on the efficacy and acceptability of bilateral repetitive transcranial magnetic stimulation (rTMS) for treating major depression. *Psychol Med*. 2012 Dec 3:1-10. doi: S0033291712002802 [pii]; 10.1017/S0033291712002802. PMID: 23200131. Exclusion Code: X2.

44. Berlim MT, Van den Eynde F, Daskalakis ZJ. A systematic review and meta-analysis on the efficacy and acceptability of bilateral repetitive transcranial magnetic stimulation (rTMS) for treating major depression. *Psychol Med*. 2013 Nov;43(11):2245-54. doi: 10.1017/S0033291712002802. PMID: 23200131. Exclusion Code: X2.

45. Berlim MT, Van den Eynde F, Jeff Daskalakis Z. Clinically Meaningful Efficacy and Acceptability of Low-Frequency Repetitive Transcranial Magnetic Stimulation (rTMS) for Treating Primary Major Depression: A Meta-Analysis of Randomized, Double-Blind and Sham-Controlled Trials. *Neuropsychopharmacology*. 2013 Mar;38(4):543-51. doi: 10.1038/npp.2012.237; npp2012237 [pii]. PMID: 23249815. Exclusion Code: X2.

46. Berlim MT, van den Eynde F, Tovar-Perdomo S, et al. 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. *Psychol Med*. 2013 Mar 18:1-15. doi: S0033291713000512 [pii]; 10.1017/S0033291713000512. PMID: 23507264. Exclusion Code: X2.

47. Berman RM, Narasimhan M, Sanacora G, et al. A randomized clinical trial of repetitive transcranial magnetic stimulation in the treatment of major depression. *Biol Psychiatry*. 2000 Feb 2000;47(4):332-7. PMID: 2000-07308-008. Exclusion Code: X13.

48. Berry SM, Broglio K, Bunker M, et al. A patient-level meta-analysis of studies evaluating vagus nerve stimulation therapy for treatment-resistant depression. *Medical Devices: Evidence and Research*. 2013;6(1):17-35. Exclusion Code: X7.

49. Bhagwagar Z, Torbeyns A, Hennicken D, et al. Assessment of the Efficacy and Safety of BMS-820836 in Patients With Treatment-Resistant Major Depression: Results From 2 Randomized, Double-Blind Studies. *J Clin Psychopharmacol*. 2015 Aug;35(4):454-9. doi: 10.1097/JCP.0000000000000335 [doi]. PMID: 25961781. Exclusion Code: X3.

50. Bird D, Haddad PM, Dursun SM. An Overview of The Definition and Management of Treatment-Resistant Depression. *Klinik Psikofarmakoloji Bülteni*. 2002;12(2):92-101. Exclusion Code: X1.

51. Birkenhager TK, van den Broek WW, Mulder PG, et al. Efficacy and tolerability of tranylcypromine versus phenelzine: a double-blind study in antidepressant-refractory depressed inpatients. *J Clin Psychiatry*. 2004 Nov;65(11):1505-10. PMID: 15554763. Exclusion Code: X13.

52. Birkenhager TK, van den Broek WW, Wijkstra J, et al. Treatment of unipolar psychotic depression: an open study of lithium addition in refractory psychotic depression. *J Clin Psychopharmacol*. 2009 Oct;29(5):513-5. doi: 10.1097/JCP.0b013e3181b6744e [doi]; 00004714-200910000-00025 [pii]. PMID: 19745662. Exclusion Code: X4.

53. Blier P, Ward HE, Tremblay P, et al. Combination of antidepressant medications from treatment initiation for major depressive disorder: a double-blind randomized study. *Am J Psychiatry*. 2010 Mar;167(3):281-8. doi: 10.1176/appi.ajp.2009.09020186. PMID: 20008946. Exclusion Code: X2.

54. Blumberger DM, Maller JJ, Thomson L, et al. A randomized controlled comparison of neuro-navigated unilateral vs sequential bilateral rTMS for treatment resistant depression. *Brain Stimulation*. 2015(2):365. PMID: CN-01100736. Exclusion Code: X9.

55. Blumberger DM, Mulsant BH, Emeremni C, et al. Impact of prior pharmacotherapy on remission of psychotic depression in a randomized controlled trial. *J Psychiatr Res*. 2011 Jul;45(7):896-901. doi: S0022-3956(11)00004-5 [pii]; 10.1016/j.jpsychires.2011.01.003 [doi]. PMID: 21300377. Exclusion Code: X2.

56. Blumberger DM, Vila-Rodriguez F, Dunlop K, et al. Intermittent theta-burst versus 10 Hz left dorsolateral prefrontal rTMS for treatment resistant depression: Preliminary results from a two-site, randomized, single blind noninferiority trial. *Brain Stimulation*. 2015(2):329. PMID: CN-01100751. Exclusion Code: X9.

57. Bocchio-Chiavetto L, Miniussi C, Zanardini R, et al. 5-HTTLPR and BDNF Val66Met polymorphisms and response to rTMS treatment in drug resistant depression. *Neurosci Lett*. 2008 May 30;437(2):130-4. PMID: 18450378. Exclusion Code: X4.

58. Bond DJ, Hadjipavlou G, Lam RW, et al. The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid attention-deficit/hyperactivity disorder. *Ann Clin Psychiatry*. 2012 Feb;24(1):23-37. doi: acp_2401d [pii]. PMID: 22303520. Exclusion Code: X2.

59. Bondolfi G, Aubry JM, Golaz J, et al. A stepwise drug treatment algorithm to obtain complete remission in depression: a Geneva study. *Swiss Med Wkly*. 2006 Feb 04;136(5-6):78-85. doi: 2006/05/smw-11267. PMID: 16633950. Exclusion Code: X4.

60. Borckardt JJ, Nahas ZH, Teal J, et al. The painfulness of active, but not sham, transcranial magnetic stimulation decreases rapidly over time: results from the double-blind phase of the OPT-TMS Trial. *Brain Stimul*. 2013 Nov;6(6):925-8. doi: 10.1016/j.brs.2013.04.009. PMID: 23769413. Exclusion Code: X2.

61. Bortnick B, El-Khalili N, Banov M, et al. Efficacy and tolerability of extended release quetiapine fumarate (quetiapine XR) monotherapy in major depressive disorder: a placebo-controlled, randomized study. *J Affect Disord*. 2011 Jan;128(1-2):83-94. doi: 10.1016/j.jad.2010.06.031. PMID: 20691481. Exclusion Code: X2.

62. Boutros NN, Gueorguieva R, Hoffman RE, et al. Lack of a therapeutic effect of a 2-week sub-threshold transcranial magnetic stimulation course for treatment-resistant depression. *Psychiatry Res*. 2002 Dec 2002;113(3):245-54. PMID: 2003-01501-006. Exclusion Code: X13.

63. Bowie CR, Gupta M, Holshausen K, et al. Cognitive remediation for treatment-resistant depression: effects on cognition and functioning and the role of online homework. *J Nerv Ment Dis*. 2013 Aug;201(8):680-5. doi: 10.1097/NMD.0b013e31829c5030 [doi]; 00005053-201308000-00006 [pii]. PMID: 23896849. Exclusion Code: X3.

64. Bozkurt A. Transcranial magnetic stimulation in treatment resistant depression: The Turkish experience. *World Psychiatric Association, International Congress 2006; July 12 - 16 2006; Istanbul, Turkey*. 2006:137-8. PMID: CN-00595853. Exclusion Code: X10.

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Appendix C. Evidence Tables

Table C1. Eligible and reported patient characteristics from key question 6

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Aaronson, 2013[140] NA	NM	MDD Unipolar and Bipolar	Inclusion: Chronic Exclusion: Psychotic	Moderate	No	No	Ideation: Exclusion criteria Attempts: Just reported
Aaronson, 2017[50] NA	NM	MDD Unipolar and Bipolar	Inclusion: Chronic Exclusion: Psychotic	NA	Yes	No	Ideation: Not considered Attempts: Not considered
Aguirre, 2011[141] NA	NM	MDD Unipolar	None	NR	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Allen, 2015[142] NA	NR	MDD Unipolar	Just reported: Melancholic	NR	Yes	No	Ideation: Just reported Attempts: Just reported
Altamura, 2008[143] NA	NR	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Amsterdam, 2009[144] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Avery, 2006[145] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Baeken, 2013[146] NA	NR	MDD Unipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Exclusion criteria
Baeken, 2014[147] NA	NR	MDD Unipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Exclusion criteria
Baldomero, 2005[148] ARGOS Study	NM	MDD Unipolar	Just reported: Chronic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Barak, 2011[149] NA	NM	MDD Unipolar	None	NR	No	No	Ideation: Not considered Attempts: Just reported

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Barbee, 2011[150] NA	65	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical, Melancholic	Moderate	Yes	No	Ideation: Just reported Attempts: Not considered
Bares, 2009[151] NA	65	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Bares, 2009[152] NA	NR	MDD Unipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Bares, 2013[153] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Bauer, 2013[154] RUBY	65	MDD Unipolar	None	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria
Bauer, 2016[155] NA	65	Bipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Not considered Attempts: Not considered
Bennabi, 2015[156] NA	NR	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Bergfeld, 2016[157] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Bergfeld, 2017[158] NA	65	Bipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Not considered Attempts: Not considered
Berman, 2007[159] NA	65	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Berman, 2009[160] NA	65	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Blumberger, 2012[161] NA	85	MDD Unipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Blumberger, 2016[162] NA	85	MDD Unipolar	Just reported: Melancholic	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Bortolomasi, 2007[163] NA	NR	MDD Unipolar and Bipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Bretlau, 2008[164] NA	75	MDD Unipolar and Bipolar	Exclusion: Psychotic, Chronic	NR	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Brunelin, 2014[165] NA	NM	MDD Unipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Butler, 2011[166] Holt, 2011[167] NA	NR	MDD Unipolar	Just reported: Psychotic, Chronic, Melancholic, Catatonic, Postpartum	NR	No	No	Ideation: Just reported Attempts: Not considered
Chaput, 2008[168] NA	NM	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Chiesa, 2015[169] NA	65	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Mild	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Concerto, 2015[170] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Corya, 2006[171] NA	NM	MDD Unipolar	Exclusion: Psychotic	NA	Yes	No	Ideation: Not considered Attempts: Not considered
Cusin, 2013[172] NA	75	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Dell'Osso, 2015[173] NA	NR	MDD Unipolar and Bipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Diazgranados, 2010[174] NA	65	Bipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Exclusion criteria Attempts: Just reported
Doree, 2007[175] NA	65	MDD Unipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Dougherty, 2015[176] Kubu, 2017[177] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Exclusion criteria Attempts: Not considered
Dunner, 2007[178] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Duprat, 2016[179] NA	NR	MDD Unipolar	Exclusion: Psychotic Just reported: Melancholic	NR	Yes	No	Ideation: Not considered Attempts: Exclusion criteria
Durgam, 2016[180] NA	65	MDD Unipolar	Exclusion: Psychotic, Catatonic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Eche, 2012[181] NA	65	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Eisendrath, 2016[182] PATH-D	NM	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Just reported
El-Khalili, 2010[183] NA	65	MDD Unipolar	None	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria
Eschweiler, 2007[184] NA	NR	MDD Unipolar and Bipolar	Just reported: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Fava, 2006[185] STAR*D	75	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical, Chronic, Melancholic	Mild	Yes	No	Ideation: Not considered Attempts: Just reported

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	65	MDD Unipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Fitzgerald, 2003[189] NA	NR	MDD Unipolar and Bipolar	None	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2006[190] NA	NR	MDD Unipolar and Bipolar	Just reported: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2006[191] NA	NR	MDD Unipolar and Bipolar	Exclusion: Atypical Just reported: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2007[192] NA	NR	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2008[193] NA	NR	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2008[194] NA	70	MDD Unipolar and Bipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2009[195] NA	70	MDD Unipolar	Just reported: Chronic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2009[196] NA	NR	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2011[197] NA	NR	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2012[198] NA	NR	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Fitzgerald, 2013[199] NA	NR	MDD Unipolar and Bipolar	Just reported: Psychotic, Melancholic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Fitzgerald, 2016[200] NA	70	MDD Unipolar and Bipolar	Just reported: Melancholic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Fonagy, 2015[201] TADS	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Just reported
Fornaro, 2014[202] NA	65	MDD Unipolar	Inclusion: Atypical Just reported: Postpartum	Moderate	No	No	Ideation: Just reported Attempts: Not considered
Fujita, 2006[203] NA	NM	MDD Unipolar and Bipolar	Exclusion: Rapid-cycling bipolar illness	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Garcia-Toro, 2006[204] NA	NM	MDD Unipolar	None	NR	No	No	Ideation: Exclusion criteria Attempts: Not considered
George, 2010[205] McDonald, 2011[206] NA	70	MDD Unipolar and Bipolar	None	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
George, 2017[207] NA	NM	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Exclusion criteria Attempts: Not considered
Girlanda, 2014[208] NA	NM	MDD Unipolar	Exclusion: Postpartum	NR	Yes	No	Ideation: Not considered Attempts: Inclusion criteria
Harley, 2008[209] Feldman, 2009[210] NA	65	MDD Unipolar	Exclusion: Chronic	NR	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Holtzheimer, 2012[129] NA	70	MDD Unipolar and Bipolar	None	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Jarventausta, 2013[211] NA	80	MDD Unipolar	Inclusion: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Joffe, 2006[212] NA	NR	MDD Unipolar	Exclusion: Psychotic	NR	No	No	Ideation: Not considered Attempts: Not considered
Kamijima, 2013[213] Ozaki, 2015[214] NA	65	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Kayser, 2011[215] NA	65	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Just reported
Keitner, 2009[216] NA	65	MDD Unipolar	Exclusion: Psychotic	Mild	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	75	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Just reported
Kok, 2007[220] NA	NM	MDD Unipolar	Just reported: Psychotic, Melancholic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Kopecek, 2007[221] NA	NR	MDD Unipolar and Bipolar	Just reported: Psychotic	NR	No	No	Ideation: Not considered Attempts: Not considered
Kranaster, 2011[222] NA	NR	MDD Unipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Lally, 2014[223] NA	65	Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Lapidus, 2014[224] NA	80	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic Just reported: Melancholic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Lenox-Smith, 2008[225] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Lenze, 2015[226] Kaneriya, 2016[227] NA	NM	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Mild	Yes	No	Ideation: Just reported Attempts: Not considered
Lenze, 2016[228] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Levkovitz, 2009[229] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Levkovitz, 2015[230] NA	NR	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria
Loo, 2016[231] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Not considered Attempts: Not considered
Mahmoud, 2007[232] NA	65	MDD Unipolar and Bipolar	None	NA	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Marcus, 2008[95] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria
Martinot, 2010[233] NA	65	MDD Unipolar and Bipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Martiny, 2010[234] NA	NM	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Mazeh, 2007[235] NA	NM	MDD Unipolar	None	Moderate	No	No	Ideation: Not considered Attempts: Not considered
McDonald, 2006[236] NA	70	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
McGrath, 2006[237] STAR*D	75	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical, Chronic, Melancholic	Mild	Yes	No	Ideation: Not considered Attempts: Just reported
Miniussi, 2005[238] NA	NR	MDD Unipolar and Bipolar	Just reported: Psychotic, Chronic	Mild	No	No	Ideation: Not considered Attempts: Not considered
Mischoulon, 2015[239] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria
Mogg, 2008[240] NA	NM	MDD Unipolar and Bipolar	Just reported: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Mohamed, 2017[241] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Exclusion criteria Attempts: Not considered
Moller, 2006[242] NA	NR	MDD Unipolar and Bipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Mota-Pereira, 2011[243] NA	60	MDD Unipolar	Exclusion: Psychotic	NR	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Muller, 2013[244] NA	NR	MDD Unipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Murphy, 2014[245] NA	65	Bipolar	None	Mild	Yes	No	Ideation: Not considered Attempts: Not considered
Murrough, 2013[246] Murrough, 2015[247] NA	80	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Nasr, 2014[248] NA	NR	MDD Unipolar	None	NR	No	No	Ideation: Just reported Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Nierenberg, 2006[249] STAR*D	75	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical, Chronic, Melancholic	Mild	Yes	No	Ideation: Not considered Attempts: Just reported
Nierenberg, 2006[250] STEP-BD	NM	Bipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Okamoto, 2010[251] NA	NM	MDD Unipolar	None	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Olin, 2012[252] NA	NR	MDD Unipolar and Bipolar	Exclusion: Psychotic	NA	Yes	No	Ideation: Not considered Attempts: Not considered
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	70	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Paillere Martinot, 2010[257] NA	65	MDD Unipolar and Bipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Pallanti, 2010[258] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Just reported
Palm, 2012[259] Palm, 2013[260] NA	NR	MDD Unipolar and Bipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Papakostas, 2005[261] NA	NM	MDD Unipolar	Exclusion: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Papakostas, 2010[262] NA	80	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Papakostas, 2012[263] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Papakostas, 2015[264] Mischoulon, 2017[265] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Exclusion criteria Attempts: Not considered
Patkar, 2006[266] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Exclusion criteria Attempts: Not considered
Perahia, 2008[267] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Philip, 2016[268] NA	70	MDD Unipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Pilu, 2007[269] Carta, 2008[270] NA	60	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Price, 2010[271] NA	NR	MDD Unipolar	None	Mild	No	No	Ideation: Not considered Attempts: Not considered
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	70	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Quante, 2011[274] NA	85	MDD Unipolar and Bipolar	Just reported: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	85	MDD Unipolar	Just reported: Psychotic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Ravindran, 2008[277] Rizvi, 2014[278] NA	65	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical, Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Reynolds, 2010[279] Greenlee, 2010[280] NA	NM	MDD Unipolar	Exclusion: Psychotic Just reported: Chronic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Rossini, 2005[281] NA	75	MDD Unipolar and Bipolar	Exclusion: Psychotic	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Rosso, 2012[282] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Ruhe, 2009[283] NA	70	MDD Unipolar	Exclusion: Psychotic Just reported: Melancholic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	80	MDD Unipolar and Bipolar	Exclusion: Psychotic, Atypical	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Rush, 2006[287] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] Rush, 2004[294] STAR*D	75	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Just reported
Rybakowski, 2016[295] NA	75	Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Sackeim, 2009[296] NA	NR	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Schindler, 2007[297] NA	NR	MDD Unipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Schoeyen, 2015[298] Kessler, 2014[299] NA	NM	Bipolar	Just reported: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Schulze, 2017[300] NA	NR	MDD Unipolar and Bipolar	Exclusion: Psychotic	NA	Yes	Yes	Ideation: Not considered Attempts: Not considered
Schulze-Rauschenbach, 2005[301] NA	NM	MDD Unipolar	Exclusion: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Sharma, 2017[302] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	Yes	Ideation: Not considered Attempts: Not considered
Shelton, 2005[303] NA	65	MDD Unipolar and Bipolar	Exclusion: Psychotic	Moderate	No	No	Ideation: Not considered Attempts: Not considered
Sienaert, 2009[304] Sienaert, 2010[305] NA	NM	MDD Unipolar and Bipolar	Just reported: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Singh, 2015[306] NA	65	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Singh, 2016[307] NA	65	MDD Unipolar	Exclusion: Psychotic, Postpartum	Severe	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Souery, 2011[308] NA	NM	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Souery, 2011[309] NA	NR	MDD Unipolar	Just reported: Melancholic	NR	No	No	Ideation: Just reported Attempts: Not considered
Speer, 2009[310] NA	NR	MDD Unipolar and Bipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Speer, 2014[311] NA	NR	MDD Unipolar and Bipolar	None	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Sperling, 2009[312] NA	NR	MDD Unipolar	None	NR	No	No	Ideation: Not considered Attempts: Not considered
Stalsett, 2012[313] NA	NR	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Exclusion criteria
Straaso, 2014[314] NA	NM	MDD Unipolar	Exclusion: Psychotic Just reported: Melancholic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Thase, 2006[315] NA	NM	MDD Unipolar	None	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Thase, 2007[316] NA	65	MDD Unipolar	Exclusion: Psychotic, Atypical, Postpartum	Severe	Yes	No	Ideation: Not considered Attempts: Not considered
Theleritis, 2017[317] NA	60	MDD Unipolar and Bipolar	Exclusion: Psychotic	NA	Yes	Yes	Ideation: Not considered Attempts: Not considered
Town, 2017[318] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Not considered
Triggs, 2010[319] NA	75	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Exclusion criteria

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Trivedi, 2006[320] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] Rush, 2004[294] STAR*D	75	MDD Unipolar	Exclusion: Psychotic Just reported: Atypical	Moderate	Yes	No	Ideation: Exclusion criteria Attempts: Just reported
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	70	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Trojak, 2014[325] NA	NM	MDD Unipolar	None	Severe	Yes	No	Ideation: Not considered Attempts: Just reported
Turnier-Shea, 2006[326] NA	65	MDD Unipolar and Bipolar	None	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
van den Broek, 2006[327] NA	65	MDD Unipolar	Just reported: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Watkins, 2011[328] NA	NM	MDD Unipolar	Inclusion: Chronic Exclusion: Psychotic	Mild	Yes	No	Ideation: Not considered Attempts: Not considered
Wiles, 2008[329] NA	65	MDD Unipolar	Exclusion: Chronic, Psychotic	Mild	Yes	No	Ideation: Not considered Attempts: Not considered

Table C1. Eligible and reported patient characteristics from key question 6 (continued)

Author, Year Study Name	Maximum Age for Study Enrollment	Eligible Type of Depressive Disorder	Type of Depressive Episode Considered	Mean Baseline Depressive Severity	Any General or Specific Psychiatric Comorbidity Exclusion?	Any General or Specific Medical Comorbidity Exclusion?	Consideration of Suicidal Ideation and Prior Attempts
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	75	MDD Unipolar	Exclusion: Psychotic	Mild	Yes	No	Ideation: Not considered Attempts: Not considered
Xu, 2015[334] NA	NM	Bipolar	Exclusion: Psychotic	NR	Yes	No	Ideation: Not considered Attempts: Not considered
Zarate, 2006[335] NA	65	MDD Unipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered
Zarate, 2012[336] NA	65	Bipolar	Exclusion: Psychotic	Moderate	Yes	No	Ideation: Not considered Attempts: Not considered

MDD = Major Depressive Disorder; NA = Not Applicable; NM = No Maximum; NR = Not Reported; PATH-D = Practicing Alternative Techniques to Heal From Depression**;** REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; TADS = Tavistock Adult Depression Study;

Table C2. Eligible and reported prior treatment characteristics from key question 6

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Aaronson, 2013[140] NA	Inclusion criteria: Adequate	Inclusion criteria	4	None	None	None	Not considered	Just reported	Not considered
Aaronson, 2017[50] NA	Inclusion criteria: 4 weeks	Not considered	4	None	None	None	Not considered	Not considered	Not considered
Aguirre, 2011[141] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Allen, 2015[142] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	SSRI; SNRI; TCA	Just reported	Not considered	Not considered
Altamura, 2008[143] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI	None	Mood stabilizers	Not considered	Exclusion criteria	Not considered
Amsterdam, 2009[144] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	SSRI	None	SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Avery, 2006[145] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Baeken, 2013[146] NA	Inclusion criteria: Adequate	Inclusion criteria	3	TCA	None	None	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Baeken, 2014[147] NA	Inclusion criteria: 6 weeks	Inclusion criteria	3	SSRI; SNRI; TCA	None	None	Not considered	Not considered	Not considered
Baldomero, 2005[148] ARGOS Study	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	MAOI; Atypical antipsychotics	None	Not considered	Exclusion criteria	Not considered
Barak, 2011[149] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Not considered	Not considered
Barbee, 2011[150] NA	Inclusion criteria: 8 weeks	Inclusion criteria	2	None	SSRI	None	Not considered	Exclusion criteria	Just reported
Bares, 2009[151] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	SSRI; SNRI	None	Not considered	Not considered	Not considered
Bares, 2009[152] NA	Inclusion criteria: Adequate	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; Atypical antipsychotics	Not considered	Not considered	Not considered
Bares, 2013[153] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	SSRI; SNRI; NDRI; TCA	Not considered	Not considered	Exclusion criteria
Bauer, 2013[154] RUBY	Inclusion criteria: Adequate	Inclusion criteria	1	SSRI; SNRI	None	None	Not considered	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Bauer, 2016[155] NA	Inclusion criteria; 5-7 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Antagonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Bennabi, 2015[156] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Exclusion criteria	Exclusion criteria	Not considered
Bergfeld, 2016[157] NA	Not considered	Not considered	4	SSRI; SNRI; TCA; MAOI	None	None	Inclusion criteria	Inclusion criteria	Not considered
Bergfeld, 2017[158] NA	Not considered	Not considered	5	SSRI; SNRI; TCA; MAOI; Mood stabilizers	None	None	Inclusion criteria	Inclusion criteria	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Berman, 2007[159] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	MAOI; Atypical antipsychotics	None	Exclusion criteria	Exclusion criteria	Not considered
Berman, 2009[160] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Blumberger, 2012[161] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	MAOI	None	Not considered	Not considered	Not considered
Blumberger, 2016[162] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; TCA	Not considered	Just reported	Not considered
Bortolomasi, 2007[163] NA	Not considered	Not considered	1	None	None	SSRI; TCA	Not considered	Not considered	Not considered
Bretlau, 2008[164] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	Atypical antipsychotics	None	Not considered	Not considered	Not considered
Brunelin, 2014[165] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Butler, 2011[166] Holt, 2011[167] NA	Not considered	Not considered	2	SSRI; SNRI	None	None	Not considered	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Chaput, 2008[168] NA	Inclusion criteria: 8 weeks	Inclusion criteria	2	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist	Mood stabilizers	None	Just reported	Not considered	Exclusion criteria
Chiesa, 2015[169] NA	Inclusion criteria: 8 weeks	Not considered	1	None	None	SSRI; SNRI	Not considered	Not considered	Not considered
Concerto, 2015[170] NA	Just reported	Just reported	3	None	None	SSRI; SNRI; TCA; Atypical antipsychotics	Inclusion criteria	Not considered	Not considered
Corya, 2006[171] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	SSRI	None	None	Not considered	Not considered	Not considered
Cusin, 2013[172] NA	Inclusion criteria: Adequate	Inclusion criteria	1	SSRI; SNRI	Atypical antipsychotics	None	Not considered	Not considered	Not considered
Dell'Osso, 2015[173] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
[174] NA	Inclusion criteria: Adequate	Inclusion criteria	1	Anticonvulsants; Mood stabilizers	NMDA	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Antagonist; Atypical antipsychotics; Psychostimulants	Just reported	Just reported	Exclusion criteria

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Doree, 2007[175] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; 5-HT Receptor Agonist	Not considered	Not considered	Not considered
Dougherty, 2015[176] Kubu, 2017[177] NA	Inclusion criteria: 4 weeks	Inclusion criteria	4	None	None	None	Inclusion criteria	Just reported	Inclusion criteria
Dunner, 2007[178] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Exclusion criteria	Not considered
Duprat, 2016[179] NA	Not considered	Inclusion criteria	1	SSRI; SNRI	None	None	Not considered	Exclusion criteria	Not considered
Durgam, 2016[180] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	Atypical antipsychotics; Anticonvulsants; Psychostimulants; Mood stabilizers	SSRI; SNRI	Exclusion criteria	Not considered	Exclusion criteria
Eche, 2012[181] NA	Inclusion criteria: 12 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Eisendrath, 2016[182] PATH-D	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Exclusion criteria
El-Khalili, 2010[183] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI; SNRI; NDRI; TCA	None	None	Not considered	Not considered	Exclusion criteria

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Eschweiler, 2007[184] NA	Inclusion criteria: 3 weeks	Inclusion criteria	2	None	Anticonvulsants; Mood stabilizers	SNRI; NDRI; TCA; 5-HT Receptor Agonist	Not considered	Exclusion criteria	Not considered
Fava, 2006[185] STAR*D	Inclusion criteria: 12 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	SSRI; SNRI	Atypical antipsychotics	None	Not considered	Exclusion criteria	Exclusion criteria
Fitzgerald, 2003[189] NA	Inclusion criteria: 6 weeks	Not considered	2	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimu-lants; Mood stabilizers	Not considered	Just reported	Not considered
Fitzgerald, 2006[190] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Fitzgerald, 2006[191] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	SSRI; SNRI; TCA	None	None	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Fitzgerald, 2007[192] NA	Inclusion criteria: 6 weeks	Not considered	2	None	None	None	Not considered	Not considered	Not considered
Fitzgerald, 2008[193] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	SSRI; SNRI; TCA; Atypical antipsychotics; Mood stabilizers	Not considered	Not considered	Not considered
Fitzgerald, 2008[194] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Fitzgerald, 2009[195] NA	Inclusion criteria: 6 weeks	Not considered	2	None	None	SSRI; SNRI; TCA	Not considered	Not considered	Not considered
Fitzgerald, 2009[196] NA	Inclusion criteria: 6 weeks	Not considered	2	None	None	SSRI; SNRI; TCA; MAOI	Just reported	Just reported	Not considered
Fitzgerald, 2011[197] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Fitzgerald, 2012[198] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Fitzgerald, 2013[199] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	Mood stabilizers	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Fitzgerald, 2016[200] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	Atypical antipsychotics; Mood stabilizers	Not considered	Not considered	Not considered
Fonagy, 2015[201] TADS	Not considered	Not considered	2	None	None	None	Not considered	Not considered	Exclusion criteria
Fornaro, 2014[202] NA	Inclusion criteria: Adequate	Inclusion criteria	1	SSRI	None	None	Not considered	Exclusion criteria	Exclusion criteria
Fujita, 2006[203] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	Anticonvulsants; Mood stabilizers	None	Not considered	Exclusion criteria	Not considered
Garcia-Toro, 2006[204] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
George, 2010[205] McDonald, 2011[206] NA	Inclusion criteria: Adequate	Inclusion criteria	1	None	None	None	Not considered	Exclusion criteria	Not considered
George, 2017[207] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Girlanda, 2014[208] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Harley, 2008[209] Feldman, 2009[210] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Exclusion criteria
Holtzheimer, 2012[129] NA	Inclusion criteria: 4 weeks	Inclusion criteria	4	None	None	None	Not considered	Inclusion criteria	Not considered
Jarventausta, 2013[211] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Joffe, 2006[212] NA	Inclusion criteria: 5 weeks	Inclusion criteria	1	None	None	SSRI	Not considered	Not considered	Not considered
Kamijima, 2013[213] Ozaki, 2015[214] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	MAOI; Atypical antipsychotics; Psychostimulants	None	Not considered	Exclusion criteria	Not considered
Kayser, 2011[215] NA	Not considered	Not considered	2	None	None	None	Not considered	Not considered	Just reported

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Keitner, 2009[216] NA	Inclusion criteria: 5 weeks	Inclusion criteria	1	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	None	Not considered	Exclusion criteria	Exclusion criteria
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	Inclusion criteria: 12 weeks	Not considered	1	SSRI; SNRI; NDRI; Mood stabilizers	None	None	Not considered	Not considered	Exclusion criteria
Kok, 2007[220] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	SNRI; TCA	MAOI; Mood stabilizers	None	Not considered	Not considered	Not considered
Kopecek, 2007[221] NA	Inclusion criteria: 3 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; TCA; 5-HT Receptor Agonist; Atypical antipsychotics; Anticonvulsants; Mood stabilizers	Just reported	Not considered	Not considered
Kranaster, 2011[222] NA	Not considered	Not considered	Not considered	None	None	None	Not considered	Exclusion criteria	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Lally, 2014[223] NA	Inclusion criteria: Adequate	Inclusion criteria	1	Anticonvulsants; Mood stabilizers	NMDA	None	Not considered	Not considered	Exclusion criteria
Lapidus, 2014[224] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	None	Not considered	Just reported	Not considered
Lenox-Smith, 2008[225] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	SSRI	MAOI	None	Not considered	Exclusion criteria	Just reported
Lenze, 2015[226] Kaneriya, 2016[227] NA	Inclusion criteria: 12 weeks	Inclusion criteria	1	SNRI	None	None	Not considered	Not considered	Not considered
Lenze, 2016[228] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	just reported	not considered	not considered
Levkovitz, 2009[229] NA	Not considered	Not considered	2	None	None	None	Not considered	Exclusion criteria	Not considered
Levkovitz, 2015[230] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Loo, 2016[231] NA	Inclusion criteria: 5-7 weeks	Inclusion criteria	1	None	None	None	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Mahmoud, 2007[232] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	TCA; MAOI; Mood stabilizers	None	Not considered	Not considered	Not considered
Marcus, 2008[95] NA	Inclusion criteria: 6 weeks	Not considered	1	None	None	None	Not considered	Exclusion criteria	Not considered
Martinot, 2010[233] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	SSRI; TCA; Atypical antipsychotics; Mood stabilizers	Not considered	Exclusion criteria	Not considered
Martiny, 2010[234] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; TCA; MAOI; Atypical antipsychotics; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Mazeh, 2007[235] NA	Inclusion criteria: 8 weeks	Inclusion criteria	2	SSRI; TCA	None	None	Not considered	Not considered	Not considered
McDonald, 2006[236] NA	Inclusion criteria: 6 weeks	Inclusion criteria	3	None	None	None	Not considered	Not considered	Not considered
McGrath, 2006[237] STAR*D	Inclusion criteria: Adequate	Inclusion criteria	3	None	None	None	Not considered	Not considered	Not considered
Miniussi, 2005[238] NA	Not considered	Not considered	2	None	None	SSRI; SNRI	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Mischoulon, 2015[239] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Anticonvulsants; Psychostimulants; Mood stabilizers	Just reported	Exclusion criteria	Not considered
Mogg, 2008[240] NA	Not considered	Not considered	Not considered	None	None	SSRI; SNRI; TCA; MAOI; Mood stabilizers	Not considered	Not considered	Not considered
Mohamed, 2017[241] NA	Inclusion criteria: 5-7 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Moller, 2006[242] NA	Not considered	Not considered	1	None	None	SNRI; TCA; Anticonvulsants	Not considered	Not considered	Not considered
Mota-Pereira, 2011[243] NA	Inclusion criteria: 36 weeks	Inclusion criteria	2	None	None	None	Inclusion criteria	Not considered	Exclusion criteria
Muller, 2013[244] NA	Not considered	Not considered	Not considered	None	None	None	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

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Murphy, 2014[245] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Murrough, 2013[246] Murrough, 2015[247] NA	Inclusion criteria: Adequate	Inclusion criteria	3	None	None	None	Not considered	Not considered	Not considered
Nasr, 2014[248] NA	Not considered	Not considered	1	None	None	None	Not considered	Not considered	Not considered
Nierenberg, 2006[249] STAR*D	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Nierenberg, 2006[250] STEP-BD	Not considered	Not considered	2	Mood stabilizers	None	None	Not considered	Not considered	Not considered
Okamoto, 2010[251] NA	Not considered	Not considered	2	None	None	None	Not considered	Not considered	Not considered
Olin, 2012[252] NA	Not considered	Not considered	4	None	None	None	Not considered	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	Inclusion criteria: 7 weeks	Inclusion criteria	1	None	None	None	Not considered	Exclusion criteria	Not considered
Paillere Martinot, 2010[257] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	SSRI; TCA; Atypical antipsychotics; Mood stabilizers	Not considered	Exclusion criteria	Not considered
Pallanti, 2010[258] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Palm, 2012[259] Palm, 2013[260] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	SSRI; SNRI; NDRI; TCA; MAOI; ; Atypical antipsychotics; Anticonvulsants; Mood stabilizers	Just reported	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Papakostas, 2005[261] NA	Just reported	Not considered	1	None	None	SSRI; SNRI; NDRI; TCA; 5-HT Receptor Agonist	Not considered	Not considered	Not considered
Papakostas, 2010[262] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Not considered	Not considered
Papakostas, 2012[263] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Not considered	Not considered
Papakostas, 2015[264] Mischoulon, 2017[265] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	None	Atypical antipsychotics	None	Not considered	Not considered	Not considered
Patkar, 2006[266] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI; SNRI; NDRI; TCA; 5-HT Receptor Agonist	MAOI; Atypical antipsychotics; Anticonvulsants	None	Not considered	Not considered	Not considered
Perahia, 2008[267] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Not considered	Not considered
Philip, 2016[268] NA	Inclusion criteria: Adequate	Inclusion criteria	1	None	None	None	Not considered	Exclusion criteria	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Pilu, 2007[269] Carta, 2008[270] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; NDRI; TCA	Not considered	Not considered	Not considered
Price, 2010[271] NA	Not considered	Not considered	1	None	None	None	Not considered	Not considered	Not considered
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	Inclusion criteria: Adequate	Inclusion criteria	4	TCA; 5-HT Receptor Agonist	None	None	Not considered	Inclusion criteria	Not considered
Quante, 2011[274] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Not considered	Exclusion criteria	Not considered
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Ravindran, 2008[277] Rizvi, 2014[278] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	TCA; MAOI; Atypical antipsychotics; Anticonvulsants	None	Inclusion criteria	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Reynolds, 2010[279] Greenlee, 2010[280] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Not considered	Not considered
Rossini, 2005[281] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	SSRI; SNRI; TCA	None	None	Not considered	Just reported	Not considered
Rosso, 2012[282] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	SSRI	None	None	Not considered	Not considered	Exclusion criteria
Ruhe, 2009[283] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	None	Not considered	Just reported	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Rush, 2006[287] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] Rush, 2004[294] STAR*D	Inclusion criteria: Just reported	Inclusion criteria	1	SSRI	None	SNRI; NDRI	Just reported	Not considered	Just reported
Rybakowski, 2016[295] NA	Not considered	Not considered	2	None	None	None	Not considered	Not considered	Not considered
Sackeim, 2009[296] NA	Inclusion criteria: 4 weeks	Inclusion criteria	Not considered	None	None	None	Not considered	Exclusion criteria	Not considered
Schindler, 2007[297] NA	Inclusion criteria: 6 weeks	Not considered	2	None	None	MAOI; Atypical antipsychotics	Just reported	Just reported	Not considered
Schoeyen, 2015[298] Kessler, 2014[299] NA	Inclusion criteria: Not considered	Inclusion criteria	2	None	None	None	Not considered	Exclusion criteria	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Schulze, 2017[300] NA	Not considered	Not considered	2	None	None	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Not considered
Schulze-Rauschenbach, 2005[301] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Just reported	Exclusion criteria	Not considered
Sharma, 2017[302] NA	Not considered	Not considered	Not considered	None	None	None	Not considered	Not considered	Exclusion criteria
Shelton, 2005[303] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	SSRI	None	None	Not considered	Exclusion criteria	Not considered
Sienaert, 2009[304] Sienaert, 2010[305] NA	Not considered	Not considered	Not considered	None	None	None	Not considered	Exclusion criteria	Not considered
Singh, 2015[306] NA	Inclusion criteria: Adequate	Inclusion criteria	2	None	None	SSRI; SNRI; NDRI; TCA	not considered	not considered	not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Singh, 2016[307] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Souery, 2011[308] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	Atypical antipsychotics; Anticonvulsants; Mood stabilizers	SSRI; SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist	Not considered	Exclusion criteria	Just reported
Souery, 2011[309] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	SNRI	SSRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist	Not considered	Just reported	Just reported
Speer, 2009[310] NA	Not considered	Not considered	1	None	None	None	Not considered	Not considered	Not considered
Speer, 2014[311] NA	Not considered	Not considered	2	None	None	None	Not considered	Exclusion criteria	Not considered
Sperling, 2009[312] NA	Not considered	Not considered	Not considered	None	None	SSRI; TCA; Atypical antipsychotics	Just reported	Just reported	Not considered
Stalsett, 2012[313] NA	Not considered	Not considered	1	None	None	None	Not considered	Not considered	Inclusion criteria
Straaso, 2014[314] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	SSRI; SNRI; TCA; Atypical antipsychotics	Not considered	Not considered	Not considered
Thase, 2006[315] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	SSRI	MAOI; Atypical antipsychotics	None	Not considered	Exclusion criteria	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Thase, 2007[316] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Theleritis, 2017[317] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Town, 2017[318] NA	Inclusion criteria: 5-7 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Triggs, 2010[319] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	SSRI	Anticonvulsants; Mood stabilizers	None	Not considered	Not considered	Not considered
Trivedi, 2006[320] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] Rush, 2004[294] STAR*D	Inclusion criteria: Just reported	Inclusion criteria	1	SSRI	None	SNRI; NDRI	Just reported	Not considered	Not considered
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	Inclusion criteria: 8 weeks	Inclusion criteria	2	SSRI	SNRI; NDRI; TCA; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	None	Not considered	Not considered	Not considered

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Trojak, 2014[325] NA	Inclusion criteria: 6 weeks	Inclusion criteria	2	None	None	None	Not considered	Just reported	Exclusion criteria
Turnier-Shea, 2006[326] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Not considered	Just reported	Not considered
van den Broek, 2006[327] NA	Just reported	Not considered	1	TCA; MAOI	None	Mood stabilizers	Inclusion criteria	Inclusion criteria	Not considered
Watkins, 2011[328] NA	Inclusion criteria: 8 weeks	Inclusion criteria	1	TCA	None	SSRI; SNRI; NDRI; MAOI; 5-HT Receptor Agonist; Atypical antipsychotics; NMDA; Anticonvulsants; Psychostimulants; Mood stabilizers	Not considered	Not considered	Exclusion criteria
Wiles, 2008[329] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	SSRI	Not considered	Not considered	Exclusion criteria
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	Inclusion criteria: 6 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Exclusion criteria

Table C2. Eligible and reported prior treatment characteristics from key question 6 (continued)

Author, Year Study Name	Inclusion Criteria Concerning Reported Duration of Prior Treatment Attempts and Minimum Required Duration	Inclusion Criteria Concerning Adequacy of Prior Treatment Dosage	Minimum # of Prior Failed Treatment Attempts for Study Inclusion	Classes of Prior AD Treatment Attempts: Study Inclusion Criteria	Classes of prior AD Treatment Attempts: Study Exclusion Criteria	Classes of Prior AD Treatment Attempts: Just Reported	Prior Use of Augmentation and Combination Pharmacological Therapies	Prior use of ECT:	Prior Use of Psychotherapy:
Xu, 2015[334] NA	Inclusion criteria: 4 weeks	Inclusion criteria	1	None	None	None	Not considered	Not considered	Not considered
Zarate, 2006[335] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	None	None	None	Not considered	Not considered	Not considered
Zarate, 2012[336] NA	Inclusion criteria: 4 weeks	Inclusion criteria	2	Mood stabilizers	None	None	Not considered	Not considered	Not considered

AD = Antidepressant; MAOI = Monoamine Oxidase Inhibitors; NDRI = Norepinephrine-Dopamine Reuptake Inhibitors; NMDA = N-Methyl D-Aspartate; REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; SNRI: Serotonin and Norepinephrine Reuptake Inhibitor; SSRI: Selective Serotonin Reuptake Inhibitor; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; TADS = Tavistock Adult Depression Study; TCA = Tricyclic Antidepressants; 5-HT = 5-Hydroxytryptamine

Table C3. Eligible and reported diagnostic characteristics from key question 6

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Aaronson, 2013[140] NA	MADRS	MINI	Inpatient + any outpatient clinic
Aaronson, 2017[50] NA	NST	MINI	Unspecified outpatient clinic
Aguirre, 2011[141] NA	NST	Unstructured clinical assessment	Unspecified outpatient clinic
Allen, 2015[142] NA	NST	MINI	Psychiatric clinic
Altamura, 2008[143] NA	HAM-D-21	SCID	Psychiatric clinic
Amsterdam, 2009[144] NA	HAM-D-17	SCID	Setting not reported
Avery, 2006[145] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Baeken, 2013[146] NA	NST	MINI	Setting not reported
Baeken, 2014[147] NA	NST	MINI	Setting not reported
Baldomero, 2005[148] ARGOS Study	HAM-D-17	Unstructured clinical assessment	Psychiatric clinic
Barak, 2011[149] NA	NST	Unstructured clinical assessment	Inpatient setting
Barbee, 2011[150] NA	HAM-D-21	MINI	Unspecified outpatient clinic
Bares, 2009[151] NA	MADRS	MINI	Inpatient setting

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Bares, 2009[152] NA	NST	MINI	Inpatient setting
Bares, 2013[153] NA	MADRS; CGI-I	MINI	Inpatient setting
Bauer, 2013[154] RUBY	MADRS	MINI	Inpatient + any outpatient clinic
Bauer, 2016[155] NA	HAM-D-17	Unstructured clinical assessment	Setting not reported
Bennabi, 2015[156] NA	MADRS	Unstructured clinical assessment	Inpatient setting
Bergfeld, 2016[157] NA	HAM-D-17; GAF	Unstructured clinical assessment	Inpatient setting
Bergfeld, 2017[158] NA	HAM-D-17	Unstructured clinical assessment	Unspecified outpatient clinic
Berman, 2007[159] NA	HAM-D-17	Unstructured clinical assessment	Unspecified outpatient clinic
Berman, 2009[160] NA	HAM-D-17; CGI-I	Unstructured clinical assessment	Setting not reported
Blumberger, 2012[161] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Blumberger, 2016[162] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Bortolomasi, 2007[163] NA	NST	Unstructured clinical assessment	Unspecified outpatient clinic
Bretlau, 2008[164] NA	NST	MINI	Unspecified outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Brunelin, 2014[165] NA	HAM-D-17	MINI	Psychiatric clinic
Butler, 2011[166] Holt, 2011[167] NA	NST	Unstructured clinical assessment	Unspecified outpatient clinic
Chaput, 2008[168] NA	HAM-D-21; CGI-S	Unstructured clinical assessment	Primary Care + psychiatric clinics
Chiesa, 2015[169] NA	HAM-D-21	MINI	Primary Care + psychiatric clinics
Concerto, 2015[170] NA	HAM-D-21	Unstructured clinical assessment	Unspecified outpatient clinic
Corya, 2006[171] NA	CGI-S	Unstructured clinical assessment	Unspecified outpatient clinic
Cusin, 2013[172] NA	MADRS	SCID	Psychiatric clinic
Dell'Osso, 2015[173] NA	NST	SCID	Inpatient + any outpatient clinic
[174] NA	MADRS	SCID	Inpatient setting
Doree, 2007[175] NA	HAM-D-17	MINI	Unspecified outpatient clinic
Dougherty, 2015[176] Kubu, 2017[177] NA	MADRS	Unstructured clinical assessment	Psychiatric clinic
Dunner, 2007[178] NA	MADRS	Unstructured clinical assessment	Unspecified outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Duprat, 2016[179] NA	NST	MINI	Inpatient + any outpatient clinic
Durgam, 2016[180] NA	MADRS	SCID	Unspecified outpatient clinic
Eche, 2012[181] NA	HAM-D-21; MADRS	MINI	Inpatient + any outpatient clinic
Eisendrath, 2016[182] PATH-D	HAM-D-17	SCID	Primary Care + psychiatric clinics
El-Khalili, 2010[183] NA	HAM-D-17	MINI	Unspecified outpatient clinic
Eschweiler, 2007[184] NA	HAM-D-21	Unstructured clinical assessment	Unspecified outpatient clinic
Fava, 2006[185] STAR*D	QIDS-CR-16	Structured DSM Checklist	Primary Care + psychiatric clinics
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	HAM-D-17; QIDS-SR16	SCID	Unspecified outpatient clinic
Fitzgerald, 2003[189] NA	MADRS	Unstructured clinical assessment	Unspecified outpatient clinic
Fitzgerald, 2006[190] NA	HAM-D-17	MINI	Inpatient setting
Fitzgerald, 2006[191] NA	MADRS	Unstructured clinical assessment	Unspecified outpatient clinic
Fitzgerald, 2007[192] NA	MADRS	Unstructured clinical assessment	Psychiatric clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Fitzgerald, 2008[193] NA	MADRS	Unstructured clinical assessment	Primary Care + psychiatric clinics
Fitzgerald, 2008[194] NA	MADRS	MINI	Psychiatric clinic
Fitzgerald, 2009[195] NA	MADRS	MINI	Psychiatric clinic
Fitzgerald, 2009[196] NA	MADRS	MINI	Psychiatric clinic
Fitzgerald, 2011[197] NA	HAM-D-17	MINI	Inpatient setting
Fitzgerald, 2012[198] NA	HAM-D-17	MINI	Unspecified outpatient clinic
Fitzgerald, 2013[199] NA	HAM-D-17	MINI	Inpatient setting
Fitzgerald, 2016[200] NA	HAM-D-17	MINI	Unspecified outpatient clinic
Fonagy, 2015[201] TADS	HAM-D-17; BDI	SCID	Primary care clinic
Fornaro, 2014[202] NA	HAM-D-21	SCID	Unspecified outpatient clinic
Fujita, 2006[203] NA	NST	Unstructured clinical assessment	Inpatient setting
Garcia-Toro, 2006[204] NA	NST	Unstructured clinical assessment	Psychiatric clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
George, 2010[205] McDonald, 2011[206] NA	HAM-D-24	Unstructured clinical assessment	Unspecified outpatient clinic
George, 2017[207] NA	MADRS	SCID	Unspecified outpatient clinic
Girlanda, 2014[208] NA	NST	Unstructured clinical assessment	Setting not reported
Harley, 2008[209] Feldman, 2009[210] NA	NST	SCID	Psychiatric clinic
Holtzheimer, 2012[129] NA	HAM-D-17; GAF	SCID	Psychiatric clinic
Jarventausta, 2013[211] NA	NST	Unstructured clinical assessment	Setting not reported
Joffe, 2006[212] NA	NST	Unstructured clinical assessment	Psychiatric clinic
Kamijima, 2013[213] Ozaki, 2015[214] NA	HAM-D-17	Unstructured clinical assessment	Unspecified outpatient clinic
Kayser, 2011[215] NA	HAM-D-28	SCID	Unspecified outpatient clinic
Keitner, 2009[216] NA	MADRS	SCID	Unspecified outpatient clinic
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	HAMD-21; CGI-S	SCID	Unspecified outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Kok, 2007[220] NA	MADRS	Structured DSM Checklist	Inpatient setting
Kopecek, 2007[221] NA	NST	Unstructured clinical assessment	Inpatient setting
Kranaster, 2011[222] NA	NST	Unstructured clinical assessment	Inpatient + any outpatient clinic
Lally, 2014[223] NA	MADRS	SCID	Inpatient setting
Lapidus, 2014[224] NA	IDS-CR-30	SCID	Psychiatric clinic
Lenox-Smith, 2008[225] NA	HAM-D-21	Unstructured clinical assessment	Inpatient + any outpatient clinic
Lenze, 2015[226] Kaneriya, 2016[227] NA	MADRS	SCID	Psychiatric clinic
Lenze, 2016[228] NA	MADRS	Unstructured clinical assessment	Setting not reported
Levkovitz, 2009[229] NA	HAM-D-24; CGI-S	SCID	Psychiatric clinic
Levkovitz, 2015[230] NA	HAM-D-21; CGI-S	Unstructured clinical assessment	Unspecified outpatient clinic
Loo, 2016[231] NA	MADRS	SCID	Unspecified outpatient clinic
Mahmoud, 2007[232] NA	CGI-S; CRS-40	Unstructured clinical assessment	Primary Care + psychiatric clinics

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Marcus, 2008[95] NA	HAM-D-17;CGI-I	Unstructured clinical assessment	Unspecified outpatient clinic
Martinot, 2010[233] NA	HAM-D-21	MINI	Inpatient setting
Martiny, 2010[234] NA	HAM-D-17	Unstructured clinical assessment	Psychiatric clinic
Mazeh, 2007[235] NA	HAM-D-21	Unstructured clinical assessment	Inpatient setting
McDonald, 2006[236] NA	HAM-D-21	SCID	Setting not reported
McGrath, 2006[237] STAR*D	QIDS-CR-16	Structured DSM Checklist	Primary Care + psychiatric clinics
Miniussi, 2005[238] NA	HAM-D-21	Unstructured clinical assessment	Inpatient setting
Mischoulon, 2015[239] NA	HAM-D-17	SCID	Psychiatric clinic
Mogg, 2008[240] NA	NST	SCID	Setting not reported
Mohamed, 2017[241] NA	QIDS-CR16	Unstructured clinical assessment and PHQ-5	Unspecified outpatient clinic
Moller, 2006[242] NA	NST	Unstructured clinical assessment	Setting not reported
Mota-Pereira, 2011[243] NA	NST	Unstructured clinical assessment	Psychiatric clinic
Muller, 2013[244] NA	NST	Unstructured clinical assessment	Setting not reported

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Murphy, 2014[245] NA	MADRS	Unstructured clinical assessment	Unspecified outpatient clinic
Murrough, 2013[246] Murrough, 2015[247] NA	IDS-CR-30	SCID	Unspecified outpatient clinic
Nasr, 2014[248] NA	NST	Unstructured clinical assessment	Inpatient + any outpatient clinic
Nierenberg, 2006[249] STAR*D	QIDS-CR-16	Structured DSM Checklist	Primary Care + psychiatric clinics
Nierenberg, 2006[250] STEP-BD	NST	MINI	Unspecified outpatient clinic
Okamoto, 2010[251] NA	HAM-D-17	SCID	Inpatient setting
Olin, 2012[252] NA	CGI-S	Unstructured clinical assessment	Inpatient + any outpatient clinic
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	HAM-D-17; CGI-S	Unstructured clinical assessment	Unspecified outpatient clinic
Paillere Martinot, 2010[257] NA	NST	MINI	Inpatient + any outpatient clinic
Pallanti, 2010[258] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Palm, 2012[259] Palm, 2013[260] NA	NST	Unstructured clinical assessment	Inpatient + any outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Papakostas, 2005[261] NA	NST	Unstructured clinical assessment	Psychiatric clinic
Papakostas, 2010[262] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Papakostas, 2012[263] NA	QIDS-SR-16	SCID	Unspecified outpatient clinic
Papakostas, 2015[264] Mischoulon, 2017[265] NA	QIDS-CR-16	SCID	Inpatient + any outpatient clinic
Patkar, 2006[266] NA	HAM-D-21	MINI	Psychiatric clinic
Perahia, 2008[267] NA	HAM-D-17; CGI-S	Unstructured clinical assessment	Psychiatric clinic
Philip, 2016[268] NA	HAM-D-17; CGI-S	Unstructured clinical assessment	Unspecified outpatient clinic
Pilu, 2007[269] Carta, 2008[270] NA	HAM-D-17	SCID	Psychiatric clinic
Price, 2010[271] NA	HAM-D-21	Unstructured clinical assessment	Unspecified outpatient clinic
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	HAM-D-17	SCID	Psychiatric clinic
Quante, 2011[274] NA	NST	Unstructured clinical assessment	Inpatient setting
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	HAM-D-17	Unstructured clinical assessment	Inpatient + any outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Ravindran, 2008[277] Rizvi, 2014[278] NA	MADRS; CGI-S	MINI	Unspecified outpatient clinic
Reynolds, 2010[279] Greenlee, 2010[280] NA	HAM-D-17	SCID	Primary Care + psychiatric clinics
Rossini, 2005[281] NA	HAM-D-21	Unstructured clinical assessment	Psychiatric clinic
Rosso, 2012[282] NA	HAM-D-17	SCID	Psychiatric clinic
Ruhe, 2009[283] NA	HAM-D-17	SCID	Primary Care + psychiatric clinics
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	HAM-D-17	Unstructured clinical assessment	Unspecified outpatient clinic
Rush, 2006[287] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] Rush, 2004[294] STAR*D	HAM-D-17; QIDS-SR16	Structured DSM Checklist	Primary Care + psychiatric clinics
Rybakowski, 2016[295] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Sackeim, 2009[296] NA	HAM-D-24	SCID	Primary Care + psychiatric clinics

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Schindler, 2007[297] NA	HAM-D-17	Unstructured clinical assessment	Inpatient setting
Schoeyen, 2015[298] Kessler, 2014[299] NA	MADRS	MINI	Inpatient + any outpatient clinic
Schulze, 2017[300] NA	NST	Unstructured clinical assessment	Unspecified outpatient clinic
Schulze-Rauschenbach, 2005[301] NA	NST	Unstructured clinical assessment	Setting not reported
Sharma, 2017[302] NA	HAMD-17	Unstructured clinical assessment	Psychiatric clinic
Shelton, 2005[303] NA	MADRS	Unstructured clinical assessment	Setting not reported
Sienaert, 2009[304] Sienaert, 2010[305] NA	HAM-D-17	Unstructured clinical assessment	Unspecified outpatient clinic
Singh, 2015[306] NA	IDS-CR-30	MINI	Setting not reported
Singh, 2016[307] NA	IDS-CR-30	MINI	Inpatient + any outpatient clinic
Souery, 2011[308] NA	HAM-D-17	MINI	Inpatient + any outpatient clinic
Souery, 2011[309] NA	NST	MINI	Inpatient + any outpatient clinic
Speer, 2009[310] NA	NST	Unstructured clinical assessment	Unspecified outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Speer, 2014[311] NA	NST	SCID	Inpatient + any outpatient clinic
Sperling, 2009[312] NA	NST	Unstructured clinical assessment	Inpatient setting
Stalsett, 2012[313] NA	GAF	Unstructured clinical assessment	Inpatient setting
Straaso, 2014[314] NA	HAM-D-17	Unstructured clinical assessment	Psychiatric clinic
Thase, 2006[315] NA	HAM-D-21	SCID	Unspecified outpatient clinic
Thase, 2007[316] NA	HAM-D-17	SCID	Unspecified outpatient clinic
Theleritis, 2017[317] NA	NST	MINI and SCID	Unspecified outpatient clinic
Town, 2017[318] NA	HAMD-17	MINI	Unspecified outpatient clinic
Triggs, 2010[319] NA	HAM-D-24	SCID	Unspecified outpatient clinic
Trivedi, 2006[320] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] Rush, 2004[294] STAR*D	HAM-D-17; QIDS-SR16	Structured DSM Checklist	Primary Care + psychiatric clinics
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	HAM-D-17	SCID	Unspecified outpatient clinic

Table C3. Eligible and reported diagnostic characteristics from key question 6 (continued)

Author, Year Study Name	Screening Tools Used to Diagnose Depression and Rate Severity	Tools Used to Make or Confirm Depression Diagnosis	Clinical Setting in which Patients Enrolled or Treated
Trojak, 2014[325] NA	HAM-D-21	Unstructured clinical assessment	Inpatient + any outpatient clinic
Turnier-Shea, 2006[326] NA	HAM-D-17	Unstructured clinical assessment	Inpatient + any outpatient clinic
van den Broek, 2006[327] NA	NST	Unstructured clinical assessment	Inpatient setting
Watkins, 2011[328] NA	HAM-D-17; BDI	Unstructured clinical assessment	Unspecified outpatient clinic
Wiles, 2008[329] NA	BDI	Unstructured clinical assessment	Primary care clinic
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	BDI	Unstructured clinical assessment	Primary care
Xu, 2015[334] NA	NST	SCID	Inpatient setting
Zarate, 2006[335] NA	HAM-D-21	SCID	Inpatient setting
Zarate, 2012[336] NA	MADRS	SCID	Inpatient setting

BDI = Beck Depression Inventory; CGI = Clinical Global Impressions Scale (S= severity, I = improvement); CRS = Carroll Rating Scale (40 item); DSM = Diagnostic Statistical Manual; GAF = Global Assessment of Functioning Scale; HAM-D = Hamilton Rating Scale for Depression (12, 17, 24, and 28 item); IDS = Inventory of Depressive Symptomatology (C = clinician rated, SR = self-rated, 30 = 30 item); MADRS = Montgomery–Åsberg Depression Rating Scale; MINI = Mini International Neuropsychiatric Interview; NST = Nondirective Supportive Therapy; PATH-D = Practicing Alternative Techniques to Heal From Depression**;** QIDS = Quick Inventory of Depressive Symptomatology (CR = clinician rated, SR = self-rated, 16 = 16 item); REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; SCID = Structured Clinical Interview for DSM-IV; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; TADS = Tavistock Adult Depression Study

Table C4. Characteristics of systematic review studies from key question 8

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Aaronson, 2013[140] NA	RCT - Double-Blind 50 wks N = 331	CNS	G1: VNS low (0.25 mA current, 130 ms pulse width) G2: VNS medium (0.5e1.0 mA, 250 ms) G3: VNS high (1.25e1.5 mA, 250 ms)	NR
Aaronson, 2017[50] NA	Prospective controlled cohort study 260 wks N = 795	CNS	G1: VNS G2: TAU	NR
Aguirre, 2011[141] NA	RCT - Double-blind 8 wks N = 34	CNS	G1: Active right rTMS G2: sham rTMS	NR
Allen, 2015[142] NA	Non-randomized Controlled Study NA N = 35	Pharmacotherapy	G1: Ketamine 0.5 mg/kg G2: Brief-pulse bilateral ECT @ 1.5x seizure threshold	NR
Altamura, 2008[143] NA	RCT - Single-blind 1 wk N = 36	Pharmacotherapy	G1: Citalopram 10 mg i.v. augmentation + prior oral SSRIs G2: Placebo i.v. augmentation + prior oral SSRIs	NR
Amsterdam, 2009[144] NA	RCT - Double-blind 14 wks N = 146	Pharmacotherapy	G1: Sertraline plus atomoxetine G2: Sertraline plus placebo	Run-in: 8, Active Treatment Wash-out: NR
Avery, 2006[145] NA	RCT - Double-blind 26 wks N = 68	CNS	G1: HF rTMS to the left DLPFC G2: Sham rTMS	Run-in: NR Wash-out: 2, Medication Free
Baeken, 2013[146] NA	RCT - Single-blind 2 wks N = 20	CNS	G1: HF-rTMS G2: Sham rTMS	Run-in: NR Wash-out: 2, Medication Free
Baeken, 2014[147] NA	RCT - Single-blind 2 wks N = 20	CNS	G1: rTMS G2: Sham rTMS	Run-in: NR Wash-out: 2, Medication Free
Baldomero, 2005[148] ARGOS Study	RCT - Open Label 24 wks N = 3,502	Pharmacotherapy	G1: Venlafaxine ER G2: Conventional antidepressant monotherapy	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Barak, 2011[149] NA	Retrospective controlled Cohort Study NA N = 232	Pharmacotherapy	G1: Venlafaxine G2: Switch to a second SSRI	NR
Barbee, 2011[150] NA	RCT - Double-blind 10 wks N = 96	Pharmacotherapy	G1: Lamotrigine 400 mg/d G2: Placebo	NR
Bares, 2009[151] NA	RCT - Double-blind 4 wks N = 60	CNS	G1: rTMS + placebo G2: Venlafaxine ER + sham rTMS	Run-in: NR Wash-out: 1, Medication Free
Bares, 2009[152] NA	Retrospective Controlled Cohort Study NR N = 49	Pharmacotherapy	G1: Antidepressant monotherapy G2: Combination of antidepressants and/or various augmentations	NR
Bares, 2013[153] NA	RCT - Opel Label 14 wks N = 60	Pharmacotherapy	G1: Antidepressant combination using different drug classes than were previously ineffective, flexibly dosed G2: Antidepressant monotherapy switch, flexibly dosed	Run-in: NR Wash-out: 1, Medication Free
Bauer, 2013[154] RUBY	RCT - Opel Label 6 wks N = 688	Pharmacotherapy	G1: Quetiapine XR add-on, 300 mg/d target dose + Prior antidepressant G2: Lithium carbonate add-on, 0.6-1.2 mmol/L target plasma level + Prior antidepressant G3: Quetiapine XR monotherapy, 300 mg/d target dose	Run-in: NR Wash-out: 1, Medication Free
Bauer, 2016[155] NA	RCT – Double-blind 6 wks N = 25	Pharmacotherapy	G1: Levothyroxine G2: Placebo	NR
Bennabi, 2015[156] NA	RCT - Double-blind 9 wks N = 24	CNS	G1: Active left prefrontal cortex tDCS G2: Sham anodal tDCS	Run-in: 4, Active Treatment Wash-out: NR
Bergfeld, 2016[157] NA	RCT - Double-blind 64 wks N = 16	CNS	G1: First active DBS, then sham G2: First sham, then active DBS	Run-in: NR Wash-out: NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Bergfeld, 2017[158] NA	RCT – Double-blind 110 wks N = 39	CNS	G1: DBS G2: ECT	NR
Berman, 2007[159] NA	RCT - Double-blind 6 wks N = 362	Pharmacotherapy	G1: Adjunctive aripiprazole G2: Adjunctive placebo	Run-in: 8, Active Treatment Wash-out: 1, Medication Free
Berman, 2009[160] NA	RCT - Double-blind 14 wks N = 349	Pharmacotherapy	G1: Adjunctive aripiprazole G2: Adjunctive placebo	Run-in: 8, Active Treatment Wash-out: 4, Taper
Blumberger, 2012[161] NA	RCT - Double-blind 6 wks N = 74	CNS	G1: Bilateral rTMS G2: Unilateral rTMS G3: Sham rTMS	NR
Blumberger, 2016[162] NA	RCT - Double-blind 6 wks N = 121	CNS	G1: Bilateral rTMS G2: Unilateral rTMS G3: Sham control	NR
Bortolomasi, 2007[163] NA	RCT - Single-blind 13 wks N = 19	CNS	G1: Active rTMS G2: Sham rTMS	NR
Bretlau, 2008[164] NA	RCT - Double-Blind 21 wks N = 49	CNS	G1: rTMS with escitalopram G2: Sham-rTMS with escitalopram	NR
Brunelin, 2014[165] NA	RCT - Double-blind 10 wks N = 170	CNS	G1: Active left dorsolateral prefrontal rTMS @ 20 Hz G2: Venlafaxine 75-225 mg/d G3: Active left dorsolateral prefrontal rTMS + venlafaxine 75-225 mg/d	Run-in: NR Wash-out: 2, Taper
Butler, 2011[166] Holt, 2011[167] NA	Retrospective Controlled Cohort Study NR N = 75	Pharmacotherapy	G1: Mirtazepine + Prior SSRI or SNRI G2: Atypical antipsychotics + Prior SSRI or SNRI G3: Mirtazepine and atypical antipsychotics + Prior SSRI or SNRI	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Chaput, 2008[168] NA	RCT - Double-Blind 12 wks N = 22	Psychotherapy	G1: Quetiapine w/ CBT G2: Placebo w/ CBT	Run-In: 3 wks, Active Treatment Wash-out: 1 wk, Taper
Chiesa, 2015[169] NA	RCT - Single-Blind 26 wks N = 50	Psychotherapy	G1: MBCT G2: Psych-education	NR
Concerto, 2015[170] NA	RCT - Opel Label 26 wks N = 30	CNS	G1: rTMS G2: Sham rTMS	NR
Corya, 2006[171] NA	RCT - Double-blind 12 wks N = 483	Pharmacotherapy	G1: Olanzapine G2: Fluoxetine G3: Olanzapine/Fluoxetine combination G4: Velafaxine	Run-in: 7, Active Treatment Wash-out: 1, Taper
Cusin, 2013[172] NA	RCT - Double-blind 14 wks N = 60	Pharmacotherapy	G1: Pramipexole 0.25-1.5 mg BID + Prior antidepressant G2: Placebo + Prior antidepressant	Run-in: 6, Active Treatment Wash-out: NR
Dell'Osso, 2015[173] NA	RCT - Single-blind 4 wks N = 33	CNS	G1: Low frequency rTMS 430 stimuli/day G2: Low frequency rTMS 900 stimuli/day G3: High frequency rTMS 750 stimuli/day	NR
Diazgranados, 2010[174] NA	RCT - Double-blind 10 wks N = 18	Pharmacotherapy	G1: Ketamine 0.5 mg/kg, single infusion G2: Placebo, single infusion	Run-in: 4, Active Treatment Wash-out: 2, Medication Free
Doree, 2007[175] NA	RCT - Open Label 8 wks N = 20	Pharmacotherapy	G1: Continuation therapy + quetiapine G2: Continuation therapy + lithium	NR
Dougherty, 2015[176] Kubu, 2017[177] NA	RCT - Double-Blind 16 wks N = 30	CNS	G1: VC/VS DBS G2: Sham DBS	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Dunner, 2007[178] NA	RCT - Open Label 8 wks N = 64	Pharmacotherapy	G1: Sertraline 100-200 mg/day G2: Sertraline 100-200 mg/day + ziprasidone 80 mg/day G3: Sertraline 100-200 mg/day + ziprasidone 160 mg/day	Run-in: 6, Active Treatment Wash-out: NR
Duprat, 2016[179] NA	RCT - Double-Blind 2 wks N = 50	CNS	G1: 1 week of 20 real iTBS sessions followed by one week of sham iTBS sessions G2: 1 week of sham iTBS sessions followed by 1 wk of 20 real iTBS sessions	Run-in: NR Wash-out: 2, Medication Free
Durgam, 2016[180] NA	RCT - Double-blind 8 wks N = 819	Pharmacotherapy	G1: Cariprazine 2-4.5 mg/d + Prior antidepressant G2: Cariprazine 1-2 mg/d + Prior antidepressant G3: Placebo	NR
Eche, 2012[181] NA	RCT - Single-blind 4 wks N = 14	CNS	G1: 10 Hz rTMS w/ venlafaxine G2: 1 Hz rTMS w/ venlafaxine	Run-in: 1, Active Treatment Wash-out: 2, Medication Free
Eisendrath, 2016[182] PATH-D	RCT - Single-Blind 8 wks N = 173	Psychotherapy	G1: MBCT + pharmacotherapy G2: HEP + pharmacotherapy	Run-In: 2 wks, Stable Medication Wash-out: NR
El-Khalili, 2010[183] NA	RCT - Double-blind 8 wks N = 446	Pharmacotherapy	G1: Quetiapine XR 150mg G2: Quetiapine XR 300mg G3: Placebo	Run-in: NR Wash-out: 2, Taper
Eschweiler, 2007[184] NA	RCT - Double-Blind 3 wks N = 92	CNS	G1: Right unilateral ECT G2: Bifrontal ECT	NR
Fava, 2006[185] STAR*D	RCT - Single-Blind 14 wks N = 235	Pharmacotherapy	G1: Mirtazapine G2: Nortriptyline	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	RCT - Double-blind 9 wks N = 225	Pharmacotherapy	G1: Aripiprazole augmentation in both phases G2: Placebo augmentation in both phases G3: Placebo augmentation in phase 1 (first 30-days) and aripiprazole augmentation in phase 2 (second 30-days)	Run-in: 4, No Treatment Wash-out: NR
Fitzgerald, 2003[189] NA	RCT - Double-blind 4 wks N = 60	CNS	G1: HF-rTMS, left-sided G2: LF- rTMS, right-sided G3: Sham rTMS	NR
Fitzgerald, 2006[190] NA	RCT - Double-blind 2 wks N = 130	CNS	Initial treatment: G1: 1-Hz rTMS over the right PFC G2: 2-Hz rTMS over the right PFC Non-responders randomized to either: G1: 5-Hz left PFC rTMS G2: 10-Hz right PFC rTMS	NR
Fitzgerald, 2006[191] NA	RCT - Double-blind 6 wks N = 50	CNS	G1: Active rTMS G2: Sham rTMS	NR
Fitzgerald, 2007[192] NA	RCT - Double-blind 3 wks N = 26	CNS	G1: LF-rTMS to the right dorsolateral PFC G2: HF-rTMS to the left dorsolateral PFC	NR
Fitzgerald, 2008[193] NA	RCT - Double-blind 6 wks N = 50	CNS	G1: rTMS G2: Sham rTMS	Run-in: 4, Stable Medication Wash-out: NR
Fitzgerald, 2008[194] NA	RCT - Double-blind 4 wks N = 60	CNS	G1: Priming stimulation + right 1-Hz rTMS G2: Sham stimulation + right 1-Hz rTMS	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Fitzgerald, 2009[195] NA	RCT - Double-blind 4 wks N = 51	CNS	G1: rTMS targeted with standard 5 cm technique (standard localization procedure) G2: rTMS using a neuro-navigational approach	NR
Fitzgerald, 2009[196] NA	RCT - Double-blind 4 wks N = 27	CNS	G1: HF-rTMS to the left PFC G2: LF-rTMS to the right PFC	NR
Fitzgerald, 2011[197] NA	RCT - Double-blind 4 wks N = 219	CNS	G1: LF right, HF left rTMS G2: Bilateral LF-rTMS G3: Right unilateral rTMS	NR
Fitzgerald, 2012[198] NA	RCT - Double-blind 6 wks N = 66	CNS	G1: Left Side HF rTMS G2: Right HF Left LF Sequential Bilateral rTMS G3: Sham rTMS	NR
Fitzgerald, 2013[199] NA	RCT - Double-blind 4 wks N = 179	CNS	G1: Sequential bilateral rTMS G2: Right sided unilateral rTMS using priming protocol	NR
Fitzgerald, 2016[200] NA	RCT - Double-blind 4 wks N = 46	CNS	G1: Bilateral rTMS G2: Sham rTMS	NR
Fonagy, 2015[201] TADS	RCT - Single-Blind 168 wks N = 129	Psychotherapy	G1: LTPP + TAU G2: TAU	NR
Fornaro, 2014[202] NA	RCT - Double-blind 8 wks N = 48	Pharmacotherapy	G1: Bupropion SR 150 mg/d or 300 mg/d + Duloxetine 60-120 mg/d G2: Placebo + Duloxetine 60-120 mg/d	Run-in: NR Wash-out: 12, Medication Free
Fujita, 2006[203] NA	Non-randomized Controlled Study NA N = 18	CNS	G1: Sine wave bitemporal ECT G2: Pulse wave bitemporal ECT	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Garcia-Toro, 2006[204] NA	RCT - Double-blind NA N = 30	CNS	G1: Active rTMS to the left PFC and right PFC G2: Active rTMS to different regions of the brain after examination with SPECT G3: Sham rTMS	NR
George, 2010[205] McDonald, 2011[206] NA	RCT - Double-blind 6 wks N = 199	CNS	G1: Active rTMS G2: Sham rTMS	Run-in: NR Wash-out: 2, Medication Free
George, 2017[207] NA	RCT - Double-blind 27 wks N = 16	Pharmacotherapy	G1: Ketamine G2: Midalozam	Run-in: 4, Stable Medication Wash-out: NR
Girlanda, 2014[208] NA	RCT - Single-blind 52 wks N = 56	Pharmacotherapy	G1: Lithium + Usual Care G2: Usual Care	NR
Harley, 2008[209] Feldman, 2009[210] NA	RCT - Single-Blind 16 wks N = 24	Psychotherapy	G1: DBT-based group skills therapy G2: Waitlist	NR
Holtzheimer, 2012[129] NA	Interrupted time-series study 104 wks N = 17	CNS	G1: DBS in subcallosal cingulate	Run-in: 4, Placebo Wash-out: NR
Jarventausta, 2013[211] NA	RCT - Single-blind NA N = 34	Pharmacotherapy	G1: Ketamine + propofol + ECT G2: Saline + propofol + ECT	NR
Joffe, 2006[212] NA	RCT - Double-Blind 2 wks N = 36	Pharmacotherapy	G1: Antidepressant + T3 G2: Antidepressant + Lithium G3: Antidepressant + T3 + Lithium G4: Antidepressant + placebo	NR
Kamijima, 2013[213] Ozaki, 2015[214] NA	RCT - Double-blind 6 wks N = 586	Pharmacotherapy	G1: Flexible dose aripiprazole adjunctive G2: Fixed dose aripiprazole adjunctive G3: Placebo adjunctive	Run-in: 8, Active Treatment Wash-out: 1, Medication Free

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Kayser, 2011[215] NA	RCT - Double-blind 6 wks N = 20	CNS	G1: Magnetic seizure therapy @ 100 Hz (about 3x seizure threshold in ECT) G2: Right unilateral ECT (about 3x seizure threshold)	NR
Keitner, 2009[216] NA	RCT - Double-blind 4 wks N = 97	Pharmacotherapy	G1: Antidepressant monotherapy + Risperidone G2: Antidepressant monotherapy + Placebo	Run-in: 6, Active Treatment Wash-out: NR
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	RCT - Single-Blind 12 wks N = 491	Psychotherapy	G1: CBASP + Continued pharmacotherapy G2: BSP + Continued pharmacotherapy G3: Continued pharmacotherapy alone	Run-In: 12 wks, Active Treatment Wash-out: NR
Kok, 2007[220] NA	RCT - Open Label 6 wks N = 29	Pharmacotherapy	G1: Lithium G2: Phenelzine	NR
Kopecek, 2007[221] NA	Retrospective Controlled Cohort Study NA N = 44	CNS	G1: Bitemporal ECT G2: Venlafaxine ≥150 mg	NR
Kranaster, 2011[222] NA	Retrospective controlled cohort study NA N = 42	Pharmacotherapy	G1: Ketamine + ECT G2: Thiopental + ECT	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Lally, 2014[223] NA	RCT - Double-blind 4 wks N = 36	Pharmacotherapy	G1: Ketamine 0.5 mg/kg G2: Placebo	NR
Lapidus, 2014[224] NA	RCT - Double-Blind 1 wk N = 20	Pharmacotherapy	G1: Ketamine G2 Placebo	Run-In: NR Wash-out: 7, Medication Free
Lenox-Smith, 2008[225] NA	RCT - Double-blind 14 wks N = 406	Pharmacotherapy	G1: Venlafaxine ER 75-300 mg/d switch G2: Citalopram 20-60 mg/d switch	Run-in: 1, No Treatment Wash-out: 1, Medication Free
Lenze, 2015[226] Kaneriya, 2016[227] NA	RCT - Double-blind 12 wks N = 181	Pharmacotherapy	G1: Aripipraxole augmentation G2: Placebo augmentation	Run-in: 12, Active Treatment Wash-out: NR
Lenze, 2016[228] NA	RCT - Double-blind 8 wks N = 20	Pharmacotherapy	G1: Saline only for 95 hours and 20 minutes and then 40 minutes of ketamine G2: 96 hours of ketamine	Run-in: 1, Active Treatment Wash-out: NR
Levkovitz, 2009[229] NA	RCT - Double-blind 4 wks N = 65	CNS	G1: rTMS H-coil 1 - 120% G2: rTMS H-coil 2 - 120% G3: rTMS H-coil 1L - 120% G4: rTMS H-coil 1L - 110%	Run-in: NR Wash-out: 2, Taper
Levkovitz, 2015[230] NA	RCT - Double-blind 16 wks N = 181	CNS	G1: dTMS G2: Sham dTMS	Run-in: NR Wash-out: 2, Medication Free
Loo, 2016[231] NA	RCT - Double-blind 2 wks N = 15	Pharmacotherapy	G1: Ketamine G2: Midalozam	Run-in: 4, Stable Medication Wash-out: NR
Mahmoud, 2007[232] NA	RCT - Double-blind 6 wks N = 274	Pharmacotherapy	G1: Risperidone G2: Placebo	Run-in: 4, Active Treatment Wash-out: NR
Marcus, 2008[95] NA	RCT - Double-blind 14 wks N = 381	Pharmacotherapy	G1: Physician chosen AD + aripiprazole G2: Physician chosen AD	Run-in: 8, Active Treatment Wash-out: 4, Taper

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Martinot, 2010[233] NA	RCT - Double-blind 2 wks N = 50	CNS	G1: PET-Guided active TMS G2: Sham TMS G3: Standard active TMS	NR
Martiny, 2010[234] NA	RCT - Double-Blind 5 wks N = 50	CNS	G1: T-PEMF G2: Sham T-PEMF	NR
Mazeh, 2007[235] NA	RCT - Single-Blind 8 wks N = 30	Pharmacotherapy	G1: Venlafaxine G2: Paroxetine	NR
McDonald, 2006[236] NA	RCT - Double-blind 2 wks N = 62	CNS	G1: Fast Left (10 Hz) rTMS followed by Slow Right (1Hz) DLPFC rTMS G2: Slow Right followed by Fast Left rTMS G3: Sham TMS	NR
McGrath, 2006[237] STAR*D	RCT - Single-Blind 12 wks N = 109	Pharmacotherapy	G1: Tranylcypromine G2: Venlafaxine ER + mirtazapine	NR
Miniussi, 2005[238] NA	RCT - Double-blind First experiment: 1 wk N = 20 Second experiment: 10 wksN = 51	CNS	First experiment: G1: HF-rTMS, 17 Hz G2: LF-rTMS, 1 Hz Second experiment: G1: Real 1-Hz TMS followed by a second block of sham 1Hz-TMS G2: Sham 1Hz-TMS followed by real 1Hz-TMS G3: Real 17Hz-TMS followed by a second block of sham 17Hz-TMS G4: Sham 17Hz-TMS followed by real 17Hz-TMS	NR
Mischoulon, 2015[239] NA	RCT - Double-Blind 3 wks N = 30	CNS	G1: CES to left and right dorsolateral prefrontal cortex G2: Sham CES	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Mogg, 2008[240] NA	RCT - Double-blind 4 wks N = 59	CNS	G1: rTMS DLPFC G2: Sham rTMS	NR
Mohamed, 2017[241] NA	RCT - Single-Blind 12 wks N = 1522	Pharmacotherapy	G1: Bupropion Switch G2: Bupropion Augment G3: Aripiprazole Augment	NR
Moller, 2006[242] NA	RCT - Double-blind 6 wks N = 10	CNS	G1: rTMS G2: Sham rTMS	NR
Mota-Pereira, 2011[243] NA	RCT - Single-Blind 12 wks N = 33	Other	G1: Pharmacotherapy plus aerobic exercise G2: Pharmacotherapy	NR
Muller, 2013[244] NA	Case Control Study NR N = 20	CNS	G1: Low Frequency/High Strength VNS G2: High Frequency/Low Strength VNS	NR
Murphy, 2014[245] NA	RCT - Double-Blind 6 wks N = 20	Other	G1: SAMe + existing medication G2: Placebo + existing medication	NR
Murrough, 2013[246] Murrough, 2015[247] NA	RCT - Double-Blind 1 wk N = 73	Pharmacotherapy	G1: Ketamine G2: Midazolam	Run-In: NR Wash-out: 1, Medication Free
Nasr, 2014[248] NA	Retrospective controlled Cohort Study NA N = 153	Pharmacotherapy	G1: Aripiprazole augmentation G2: Buproprion augmentation	NR
Nierenberg, 2006[250] STEP-BD	RCT - Open Label 16 wks N = 66	Pharmacotherapy	G1: Lamotrigine augmentation G2: Inositol augmentation G3: Risperidone augmentation	NR
Nierenberg, 2006[249] STAR*D	RCT - Single-Blind 14 wks N = 142	Pharmacotherapy	G1: Lithium augmentation G2: T3 augmentation	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Okamoto, 2010[251] NA	Non-Randomized Controlled Study 4 wks N = 31	Pharmacotherapy	G1:Ketamine anesthesia plus ECT G2: Propofol anesthesia plus ECT	NR
Olin, 2012[252] NA	Prospective controlled cohort study 240 wks N = 636	CNS	G1: Treatment as usual + VNS G2: Treatment as usual	NR
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	RCT - Double-blind 10 wks N = 325	CNS	G1: Active TMS @ 120% resting MT with tapered introduction of medication G2: Sham TMS with tapered introduction of medication	Run-in: 1, No Treatment Wash-out: NR
Paillere Martinot, 2010[257] NA	RCT - Double-blind 2 wks N = 48	CNS	G1: Standard rTMS G2: PET-guided rTMS G3: Sham rTMS	NR
Pallanti, 2010[258] NA	RCT - Double-blind 3 wks N = 60	CNS	G1: Unilateral rTMS G2: Bilateral rTMS G3: Sham rTMS	NR
Palm, 2012[259] Palm, 2013[260] NA	RCT - Double-blind 7 wks N = 22	CNS	G1: Active tDCS, then sham G2: Sham tDCS, then active	NR
Papakostas, 2005[261] NA	Retrospective Controlled Cohort Study NA N = 85	Pharmacotherapy	G1: Augmentation G2: Switch	NR
Papakostas, 2010[262] NA	RCT - Double-blind 6 wks N = 73	Other	G1: SAMe augmentation G2: placebo augmentation	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Papakostas, 2012[263] NA	RCT - Double-blind 9 wks First trial N = 148 Second trial N = 75	Other	First trial: G1: 7.5-15mg l-methylfolate G2: Placebo Second trial: G1: 15mg l-methylfolate G2: Placebo	NR
Papakostas, 2015[264] Mischoulon, 2017[265] NA	RCT - Double-blind 8 wks N = 139	Pharmacotherapy	G1: Escitalopram + Ziprasidone G2: Escitalopram + placebo	NR
Patkar, 2006[266] NA	RCT - Double-Blind 4 wks N = 60	Pharmacotherapy	G1: Antidepressant + methylphenidate augmentation G2: Antidepressant + placebo augmentation	NR
Perahia, 2008[267] NA	RCT - Open Label 10 wks N = 368	Pharmacotherapy	G1: Abrupt SSRI discontinuation with immediate duloxetine initiation (DS) G2: Tapered SSRI discontinuation and simultaneous duloxetine admin (STS)	NR
Philip, 2016[268] NA	RCT - Open Label 6 wks N = 49	CNS	G1: Scheduled TMS G2: Observation	Run-in: 6, Active Treatment Wash-out: 3, Taper
Pilu, 2007[269] Carta, 2008[270] NA	RCT - Open-label 32 wks N = 30	Other	G1: Pharmacotherapy + physical activity G2: Pharmacotherapy alone	NR
Price, 2010[271] NA	RCT - Double-blind 4 wks N = 44	CNS	G1: Left dorsolateral rTMS + stimulus timing G2: Left dorsolateral rTMS only	NR
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	RCT - Double-blind 26 wks N = 5	CNS	G1: Sham DBS 3 months active DBS 3 months G2. active DBS 3 months sham DBS 3 months	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Quante, 2011[274] NA	RCT - Double-blind 3 wks N = 41	CNS	G1: High-dose right unilateral ECT @ 4x seizure threshold G2: High-dose right unilateral ECT @ 7x seizure threshold G3: High-dose right unilateral ECT @ 10x seizure threshold	NR
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	RCT - Double-blind 24 wks N = 243	Pharmacotherapy	G1: Risperidone Augmentation G2: Placebo Augmentation	NR
Ravindran, 2008[277] Rizvi, 2014[278] NA	RCT - Double-blind 5 wks N = 145	Pharmacotherapy	G1: OROS methylphenidate augmentation G2: Placebo augmentation	NR
Reynolds, 2010[279] Greenlee, 2010[280] NA	RCT - Single Blind 16 wks N = 124	Pharmacotherapy	G1: Escitalopram + DCM + IPT G2: Escitalopram + DCM	NR
Rossini, 2005[281] NA	RCT - Double-blind 5 wks N = 54	CNS	G1: rTMS at 80% of MT stimulation G2: rTMS at 100% of MT stimulation G3: Sham rTMS	NR
Rosso, 2012[282] NA	RCT - Single-blind 8 wks N = 49	Pharmacotherapy	G1: Duloxetine 120 mg/d + previous SSRI G2: Bupropion XR 300 mg/d + previous SSRI	Run-in: NR Wash-out: 2, Medication Free

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Ruhe, 2009[283] NA	RCT - Double-blind 6 wks N = 60	Pharmacotherapy	G1: Paroxetine dose escalation G2: Placebo dose escalation (paroxetine + placebo)	NR
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	RCT - Double-blind 10 wks 235	CNS	G1: Active VNS G2: Sham VNS	Run-in: 4, Stable Medication Wash-out: NR
Rush, 2006[287] Rush, 2004[294] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] STAR*D	RCT - Open Label 12 wks N = 727	Pharmacotherapy	G1: SR bupropion G2: Sertraline G3: ER venlafaxine	Run-in: NR Wash-out: 0, Immediate Discontinuation
Rybakowski, 2016[295] NA	RCT - Double-blind NA N = 30	CNS	G1: ECT + Ketamine anesthesia for 2nd and 3rd ECT sessions (thiopental for all other sessions) G2: ECT + Ketamine anesthesia for 2nd, 4th, 8th, and 10th ECT sessions (thiopental for all other sessions)	NR
Sackeim, 2009[296] NA	RCT - Double-blind 208 wks N = 319	CNS	G1: ECT plus Nortriptyline G2: ECT plus Venlafaxine G3: ECT plus Placebo	NR
Schindler, 2007[297] NA	RCT - Open Label 8 wks N = 34	Pharmacotherapy	G1: Continuation therapy + lamotrigine G2: Continuation therapy + lithium	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Schoeyen, 2015[298] Kessler, 2014[299] NA	RCT - Single-blind 6 wks N = 73	CNS	G1: Right unilateral brief-pulse ECT G2: Algorithm-based pharmacologic treatment	NR
Schulze, 2017[300] NA	Retrospective controlled cohort study NA N = 105	Pharmacotherapy	G1: TBS + antipsychotics G2: TBS	Run-in: 4, Stable Medication Wash-out: NA Run-in: 4, Stable Medication Wash-out: NR
Schulze-Rauschenbach, 2005[301] NA	Non-randomized Controlled Study NA N = 30	CNS	G1: Right unilateral ECT at 2 to 2.5x seizure threshold G2: Left dorsolateral prefrontal rTMS at 10 Hz	NR
Sharma, 2017[302] NA	RCT - Single-blind 8 wks N = 25	Other	G1: Meditation (yoga) G2: Waitlist (control)	Run-in: 8, Stable Medication Wash-out: NR
Shelton, 2005[303] NA	RCT - Double-Blind 8 wks N = 500	Pharmacotherapy	G1: Olanzapine G2: Fluoxetine G3: Combination olanzapine/fluoxetine G4: Notriptyline	Run-in: 7, Active Treatment Wash-out: 7, Medication Free
Sienaert, 2009[304] Sienaert, 2010[305] NA	RCT - Single-blind NR N = 81	CNS	G1: Unilateral ECT G2: Bilateral ECT	NR
Singh, 2015[306] NA	RCT - Double-blind 1 wk N = 30	Pharmacotherapy	G1: Placebo G2: .20 mg/kg ketamine G3: .40 mg/kg ketamine on day 1. Second randomization on day 4 depending on response	NR
Singh, 2016[307] NA	RCT - Double-Blind 4 wks N = 68	Pharmacotherapy	G1: IV ketamine 2x per week G2: IV ketamine 3x per week G3: Placebo 2x per week G4: Placebo 3x per week	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Souery, 2011[308] NA	RCT - Opel Label NR N = 189	Pharmacotherapy	G1: Citalopram switch (≥40 mg/d for ages ≤65, or ≤40 mg/d for ages >65) to desipramine (≥200 mg/d for ages ≤65, or ≤200 mg/d for ages >65) G2: Desipramine switch (≥200 mg/d for ages ≤65, or ≤200 mg/d for ages >65) to citalopram (≥40 mg/d for ages ≤65, or ≤40 mg/d for ages >65) G3: Citalopram continuation (≥40 mg/d for ages ≤65, or ≤40 mg/d for ages >65) after non-response in first 4 weeks G4: Desipramine continuation (≥200 mg/d for ages ≤65, or ≤200 mg/d for ages >65) after non-response in first 4 weeks	NR
Souery, 2011[309] NA	Retrospective Controlled Cohort Study 4 wks N = 340	Pharmacotherapy	G1: Across-class switch following prior antidepressant treatment failure G2: Within-class switch following prior antidepressant treatment failure	NR
Speer, 2009[310] NA	RCT - Double-blind 4 wks N = 22	CNS	Crossover design: G1: First two weeks of active rTMS followed by 2 weeks of sham rTMS conditions G2: First two weeks of sham rTMS conditions followed by 2 weeks of active rTMS	NR
Speer, 2014[311] NA	RCT - Double-blind 3 wks N = 24	CNS	G1: 1 Hz rTMS G2: 20 Hz rTMS G3: Sham rTMS	Run-in: NR Wash-out: 2, Medication Free
Sperling, 2009[312] NA	Case-control study 52 wks N = 18	CNS	G1: VNS G2: Age & sex-matched control	NR

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Stalsett, 2012[313] NA	Prospective Controlled Cohort Study 64 wks N = 100	Psychotherapy	G1: Vita (existential short-term dynamic group-oriented therapy) G2: TAU	NR
Straaso, 2014[314] NA	RCT - Double-blind 8 wks N = 65	CNS	G1: T-PEMF, 2 active doses of 50 Hz daily G2: T-PEMF, 1 active dose of 50 Hz + 1 sham dose daily	NR
Thase, 2006[315] NA	RCT - Open Label 12 wks N = 232	Pharmacotherapy	G1: Standard dose venlafaxine ER (mean dose = 148 mg/d) G2: Higher dose venlafaxine ER (mean dose = 309 mg/d)	Run-in: NR Wash-out: 2, Medication Free
Thase, 2007[316] NA	RCT - Double-blind 8 wks N = 605	Pharmacotherapy	G1: Olanzapine G2: Olanzapine/Fluoxetine combination G3: Fluoxetine	Run-in: 8, Active Treatment Wash-out: 1, Taper
Theleritis, 2017[317] NA	RCT - Double-blind 3 wks N = 98	CNS	G1: rTMS 1/day G2: rTMS 2/day G3: Sham 1/day G4: Sham 2/day	Run-in: 4, Stable Medication Wash-out: NR
Town, 2017[318] NA	RCT - Single-blind 27 wks N = 60	Psychotherapy	G1: ISTDP (Dynamic Psychotherapy) G2: TAU	Run-in: 6, Stable Medication Wash-out: NR
Triggs, 2010[319] NA	RCT - Double-blind 2 wks N = 48	CNS	G1: Right rTMS 5hz G2: Left rTMS 5hz G3: Sham right rTMS G4: Sham left rTMS	NR
Trivedi, 2006[320] Rush, 2004[294] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] STAR*D	RCT - Open Label 12 wks N = 565	Pharmacotherapy	G1: Augmentation of citalopram with SR bupropion G2: Augmentation of citalopram with buspirone	Run-in: NR Wash-out: 0, Immediate Discontinuation

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	RCT - Single-blind 12 wks N = 126	Other	G1: SSRI + 4 KKW exercise G2: SSRI + 16 KKW exercise	NR
Trojak, 2014[325] NA	RCT - Double-blind 4 wks N = 15	CNS	G1: rTMS targeting Brodmann Area 9 G2: rTMS targeting Brodmann Area 46	Run-in: NR Wash-out: 2, Taper
Turnier-Shea, 2006[326] NA	RCT - Single-blind 2 wks N = 16	CNS	G1: Daily rTMS treatment (total of 10 treatments) G2: Spaced rTMS treatment (three rTMS treatments in week one and two treatments in week two)	NR
van den Broek, 2006[327] NA	RCT - Double-Blind 24 wks N = 27	Pharmacotherapy	G1: Imipramine G2: Placebo	Run-in: NR Wash-out: 1, Medication Free
Watkins, 2011[328] NA	RCT - Open Label 12 wks N = 42	Psychotherapy	G1: RFCBT G2: TAU	NR
Wiles, 2008[329] NA	RCT - Open Label 16 wks N = 25	Psychotherapy	G1: CBT G2: Usual care	NR
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	RCT - Open Label 52 wks N = 469	Psychotherapy	G1: CBT + usual care G2: Usual care	NR
Xu, 2015[334] NA	Prospective controlled cohort study 2 wks N = 36	Pharmacotherapy	G1: Lithium + ketamine G2: Valproate + ketamine	Run-in: 4, Active treatment Wash-out: 2, Medication Free

Table C4. Characteristics of systematic review studies from key question 8 (continued)

Author, Year Study Name	Study Design Study Duration (wks) Overall Sample Size (N randomized)	Intervention Category	Active Intervention and Control Group(s)	Run-In (wks), Type Wash-out (wks), Type
Zarate, 2006[335] NA	RCT - Double-blind 2 wks/10wks N = 18	Pharmacotherapy	G1: Placebo G2: Ketamine	Run-in: NR Wash-out: 2, Medication Free
Zarate, 2012[336] NA	RCT - Double-Blind 4 wks N = 15	Pharmacotherapy	G1: Ketamine G2: Placebo	Run-in: 4, Active Treatment Wash-out: 2, Medication Free

BID = Twice a day; BSP = Brief Supportive Psychotherapy; CBASP = Cognitive Behavioral Analysis System of Psychotherapy; CBT = Cognitive Behavioral Therapy (RF = Rumination Focused); CES = Cranial Electrical Stimulation; CNS = Central Nervous System; DBS = Direct Brain Stimulation; DBT = Dialectical Behavior Therapy; DCM = Depression Care Management; DCS = Direct Current Stimulation (t = Transcranial); DLPFC = Dorsolateral Prefrontal Cortex; DS = Direct Switch; ECT = Electroconvulsive Therapy; ER = Extended-Release; HEP = Health Enhancement Program; Hz = Hertz; IPT = Interpersonal Therapy; KKW = Kcal per-kilogram per-week; LTPP = Long-Term Psychoanalytic Psychotherapy; RCT = Randomized Controlled Trial; MBCT = Mindfulness-Based Cognitive Therapy; Mg/d = Milligrams per-day; mmol = millimole; MT = Motor Threshold; NR = Not Reported; OROS = Osmotic-Release Oral System; PATH-D = Practicing Alternative Techniques to Heal From Depression; PET = Positron Emission Tomography; PFC = Pre-frontal cortex; REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; SAMe = S-adenosyl-L-methione; SPECT = Single Photon Emission Computed Tomography; SR = Sustained Release; SNRI: Serotonin and Norepinephrine Reuptake Inhibitor; SSRI: Selective Serotonin Reuptake Inhibitor; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; STS = Start-taper Switch; T3 = Triiodothyronine; TADS = Tavistock Adult Depression Study; TAU = Treatment as Usual; TBS = Theta-Burst Stimulation (i = Intermittent); TMS = Transcranial Magnetic Stimulation (r = Repetitive, d = Direct, HF = High frequency, LF = Low frequency); T-PEMF = Transcranial Pulsating ElectroMagnetic Fields; VC/VS = Ventral Capsule/Ventral Striatum; VNS = Vagus Nerve Stimulation; XR = Extended Release

Table C5. Risk factors of systematic review studies from key question 9

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Aaronson, 2013[140] NA	RCT - Double-Blind 50 wks N = 331	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	No	NA
Aaronson, 2017[50] NA	Prospective controlled cohort study 260 wks N = 795	NA	Duration of current episode Number of prior failed treatments Age Coexisting psychiatric comorbidities	Psychiatric comorbidities	NA	NA	Statistical adjustment during analysis
Aguirre, 2011[141] NA	RCT - Double-blind 8 wks N = 34	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Age	Unclear	Yes	NA
Allen, 2015[142] NA	Non-randomized Controlled Study NA N = 35	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	NA	NA	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Altamura, 2008[143] NA	RCT - Single-blind 1 wk N = 36	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Amsterdam, 2009[144] NA	RCT - Double-blind 14 wks N = 146	Y	Depressive disease severity Number of prior failed treatments Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Number of prior failed treatments	Unclear	Unclear	NA
Avery, 2006[145] NA	RCT - Double-blind 26 wks N = 68	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Baeken, 2013[146] NA	RCT - Single-blind 2 wks N = 20	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Baeken, 2014[147] NA	RCT - Single-blind 2 wks N = 20	NR	Number of prior failed treatments Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Baldomero, 2005[148] ARGOS Study	RCT - Open Label 24 wks N = 3,502	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder	None	Unclear	Yes	NA
Barak, 2011[149] NA	Retrospective controlled Cohort Study NA N = 232	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder	None	NA	NA	Statistical adjustment during analysis

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Barbee, 2011[150] NA	RCT - Double-blind 10 wks N = 96	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	No	NA
Bares, 2009[151] NA	RCT - Double-blind 4 wks N = 60	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Bares, 2009[152] NA	Retrospective Controlled Cohort Study NR N = 49	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	NA	NA	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Bares, 2013[153] NA	RCT - Opel Label 14 wks N = 60	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Number of prior failed treatments Dose of previous antidepressants	Yes	Yes	NA
Bauer, 2013[154] RUBY	RCT - Opel Label 6 wks N = 688	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity Number of prior failed treatments	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Bauer, 2016[155] NA	RCT – Double-blind 6 wks N = 25	N	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age	None	Unclear	No	NA
Bennabi, 2015[156] NA	RCT - Double-Blind 9 wks N = 24	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Depressive disease severity	Yes	Yes	NA
Bergfeld, 2016[157] NA	RCT - Double-Blind 64 wks N = 16	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Bergfeld, 2017[158] NA	RCT – Double-blind 110 wks N = 39	N	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Berman, 2007[159] NA	RCT - Double-blind 6 wks N = 362	Y	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Age Gender	Yes	Yes	NA
Berman, 2009[160] NA	RCT - Double-blind 14 wks N = 349	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Age	Age Gender	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Blumberger, 2012[161] NA	RCT - Double-blind 6 wks N = 74	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	No	NA
Blumberger, 2016[162] NA	RCT - Double-blind 6 wks N = 121	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	No	NA
Bortolomasi, 2007[163] NA	RCT - Single-blind 13 wks N = 19	NR	Number of prior failed treatments Coexisting Medical Comorbidities	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Bretlau, 2008[164] NA	RCT - Double-Blind 21 wks N = 49	NR	Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	No	NA
Brunelin, 2014[165] NA	RCT - Double-blind 10 wks N = 170	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Butler, 2011[166] Holt, 2011[167] NA	Retrospective Controlled Cohort Study NR N = 75	NR	Number of prior failed treatments Class of previous antidepressants Bipolar disorder	None	NA	NA	NR

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Chaput, 2008[168] NA	RCT - Double-Blind 12 wks N = 22	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Chiesa, 2015[169] NA	RCT - Single-Blind 26 wks N = 50	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Concerto, 2015[170] NA	RCT - Opel Label 26 wks N = 30	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Corya, 2006[171] NA	RCT - Double-blind 12 wks N = 483	Y	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Psychiatric Comorbidities	Class of previous antidepressants	Unclear	Yes	NA
Cusin, 2013[172] NA	RCT - Double-blind 14 wks N = 60	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Age Gender	Unclear	Yes	NA
Dell'Osso, 2015[173] NA	RCT - Single-blind 4 wks N = 33	NR	Duration of current episode Number of previous hospitalizations Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Gender Bipolar disorder	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Diazgranados, 2010[174] NA	RCT - Double-blind 10 wks N = 18	N	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	NA	NA
Doree, 2007[175] NA	RCT - Open Label 8 wks N = 20	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Dougherty, 2015[176] Kubu, 2017[177] NA	RCT - Double-Blind 16 wks N = 30	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Dunner, 2007[178] NA	RCT - Open Label 8 wks N = 64	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Class of previous antidepressants	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Duprat, 2016[179] NA	RCT - Double-Blind 2 wks N = 50	NR	Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity Duration of current episode Number of prior failed treatments Age Gender	Yes	Unclear	NA
Durgam, 2016[180] NA	RCT - Double-blind 8 wks N = 819	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NR

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Eche, 2012[181] NA	RCT - Single-blind 4 wks N = 14	Y	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities	None	Unclear	No	NA
Eisendrath, 2016[182] PATH-D	RCT - Single-Blind 8 wks N = 173	Y	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities MDD onset before age 20 Suicidal risk or behavior	None	Yes	Yes	NA
El-Khalili, 2010[183] NA	RCT - Double-blind 8 wks N = 446	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	No	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Eschweiler, 2007[184] NA	RCT - Double-Blind 3 wks N = 92	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Fava, 2006[185] STAR*D	RCT - Single-Blind 14 wks N = 235	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	RCT - Double-blind 9 wks N = 225	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Fitzgerald, 2003[189] NA	RCT - Double-blind 4 wks N = 60	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Fitzgerald, 2006[190] NA	RCT - Double-blind 2 wks N = 130	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Depressive disease severity Age Gender Psychiatric Comorbidities	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Fitzgerald, 2006[191] NA	RCT - Double-blind 6 wks N = 50	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Fitzgerald, 2007[192] NA	RCT - Double-blind 3 wks N = 26	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder	None	Unclear	Yes	NA
Fitzgerald, 2008[193] NA	RCT - Double-blind 6 wks N = 50	Y	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Fitzgerald, 2008[194] NA	RCT - Double-blind 4 wks N = 60	NR	Depressive disease severity Number of prior failed treatments Age	Duration of current episode Age Psychiatric Comorbidities	Yes	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Fitzgerald, 2009[195] NA	RCT - Double-blind 4 wks N = 51	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities	None	Yes	No	NA
Fitzgerald, 2009[196] NA	RCT - Double-blind 4 wks N = 27	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder	None	Yes	Yes	NA
Fitzgerald, 2011[197] NA	RCT - Double-blind 4 wks N = 219	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Age Gender	Unclear	Yes	NA
Fitzgerald, 2012[198] NA	RCT - Double-blind 6 wks N = 66	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder Coexisting Medical Comorbidities	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Fitzgerald, 2013[199] NA	RCT - Double-blind 4 wks N = 179	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Gender	Yes	Yes	NA
Fitzgerald, 2016[200] NA	RCT - Double-blind 4 wks N = 46	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Fonagy, 2015[201] The Tavistock Adult Depression Study (TADS)	RCT - Single-Blind 168 wks N = 129	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Fornaro, 2014[202] NA	RCT - Double-blind 8 wks N = 48	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities	None	Yes	No	NA
Fujita, 2006[203] NA	Non-randomized Controlled Study NA N = 18	NR	Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	NA	NA	NR
Garcia-Toro, 2006[204] NA	RCT - Double-blind NA N = 30	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
George, 2010[205] McDonald, 2011[206] NA	RCT - Double-blind 6 wks N = 199	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
George, 2017[207] NA	RCT - Double-blind 27 wks N = 16	N	Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk of behavior	None	Yes	Yes	NA
Girlanda, 2014[208] NA	RCT - Single-blind 52 wks N = 56	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Harley, 2008[209] Feldman, 2009[210] NA	RCT - Single-Blind 16 wks N = 24	NR	Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	No	NR
Holtzheimer, 2012[129] NA	Interrupted time-series study 104 wks N = 17	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Bipolar disorder	NA	NA	Statistical adjustment during analysis
Jarventausta, 2013[211] NA	RCT - Single-blind NA N = 34	NR	Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Joffe, 2006[212] NA	RCT - Double-Blind 2 wks N = 36	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder	None	Unclear	Yes	NA
Kamijima, 2013[213] Ozaki, 2015[214] NA	RCT - Double-blind 6 wks N = 586	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Kayser, 2011[215] NA	RCT - Double-blind 6 wks N = 20	NR	Depressive disease severity Number of prior failed treatments Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Keitner, 2009[216] NA	RCT - Double-blind 4 wks N = 97	Y	Depressive disease severity Number of prior failed treatments Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Age Gender Race/Ethnicity	Unclear	Yes	NA
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	RCT - Single-Blind 12 wks N = 491	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Kok, 2007[220] NA	RCT - Open Label 6 wks N = 29	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Kopecek, 2007[221] NA	Retrospective Controlled Cohort Study NA N = 44	NR	Number of prior failed treatments Dose of previous antidepressants	None	NA	NA	NR
Kranaster, 2011[222] NA	Retrospective controlled cohort study NA N = 42	NR	Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None		No	Unclear
Lally, 2014[223] NA	RCT - Double-blind 4 wks N = 36	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	NA	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Lapidus, 2014[224] NA	RCT - Double-Blind 1 wk N = 20	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	NA	NA	NA
Lenox-Smith, 2008[225] NA	RCT - Double-blind 14 wks N = 406	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Lenze, 2015[226] Kaneriya, 2016[227] NA	RCT - Double-blind 12 wks N = 181	Y	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Lenze, 2016[228] NA	RCT - Double-blind 8 wks N = 20	Y	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Levkovitz, 2009[229] NA	RCT - Double-blind 4 wks N = 65	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Number of prior failed treatments Age	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Levkovitz, 2015[230] NA	RCT - Double-blind 16 wks N = 181	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity Number of previous hospitalizations	Unclear	Yes	NA
Loo, 2016[231] NA	RCT - Double-blind 2 wks N = 15	N	Depressive disease severity Duration of current episode Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Mahmoud, 2007[232] NA	RCT - Double-blind 6 wks N = 274	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	No	NA
Marcus, 2008[95] NA	RCT - Double-blind 14 wks N = 381	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Age Gender	Unclear	Yes	NA
Martinot, 2010[233] NA	RCT - Double-blind 2 wks N = 50	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities	None	Yes	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Martiny, 2010[234] NA	RCT - Double-Blind 5 wks N = 50	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Mazeh, 2007[235] NA	RCT - Single-Blind 8 wks N = 30	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Coexisting Medical Comorbidities	None	No	Yes	NA
McDonald, 2006[236] NA	RCT - Double-blind 2 wks N = 62	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
McGrath, 2006[237] STAR*D	RCT - Single-Blind 12 wks N = 109	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Miniussi, 2005[238] NA	RCT - Double-blind First experiment: 1 wk N = 20 Second experiment: 10 wks N = 51	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities	None	Unclear	Yes	NA
Mischoulon, 2015[239] NA	RCT - Double-Blind 3 wks N = 30	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Mogg, 2008[240] NA	RCT - Double-blind 4 wks N = 59	NR	Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Age Psychiatric Comorbidities	Yes	Yes	NA
Mohamed, 2017[241] NA	RCT - Single-Blind 12 wks N = 1522	N	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk of behavior	None	Yes	Yes	NA
Moller, 2006[242] NA	RCT - Double-blind 6 wks N = 10	NR	Number of prior failed treatments	None	Unclear	Yes	NA
Mota-Pereira, 2011[243] NA	RCT - Single-Blind 12 wks N = 33	NR	Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Muller, 2013[244] NA	Case Control Study NR N = 20	NR	Bipolar disorder	None		NA	NR
Murphy, 2014[245] NA	RCT - Double-Blind 6 wks N = 20	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Unclear	NA
Murrough, 2013[246] Murrough, 2015[247] NA	RCT - Double-Blind 1 wk N = 73	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	No	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Nasr, 2014[248] NA	Retrospective controlled Cohort Study NA N = 153	NR	Number of prior failed treatments Bipolar disorder	None	NA	NA	NR
Nierenberg, 2006[249] STAR*D	RCT - Single-Blind 14 wks N = 142	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Nierenberg, 2006[250] STEP-BD	RCT - Open Label 16 wks N = 66	NR	Duration of current episode Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Unclear	NA
Okamoto, 2010[251] NA	Non-Randomized Controlled Study 4 wks N = 31	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	NA	NA	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Olin, 2012[252] NA	Prospective controlled cohort study 240 wks N = 636	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Coexisting Psychiatric Comorbidities	Age Suicidal risk or behavior	NA	NA	Propensity score matching
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	RCT - Double-blind 10 wks N = 325	Y	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Depressive disease severity Number of prior failed treatments	Unclear	No	NA
Paillere Martinot, 2010[257] NA	RCT - Double-blind 2 wks N = 48	NR	Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Pallanti, 2010[258] NA	RCT - Double-blind 3 wks N = 60	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Palm, 2012[259] Palm, 2013[260] NA	RCT - Double-blind 7 wks N = 22	NR	Number of prior failed treatments Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Papakostas, 2005[261] NA	Retrospective Controlled Cohort Study NA N = 85	NR	Number of prior failed treatments Bipolar disorder Coexisting Psychiatric Comorbidities	Bipolar disorder	NA	NA	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Papakostas, 2010[262] NA	RCT - Double-blind 6 wks N = 73	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Papakostas, 2012[263] NA	RCT - Double-blind 9 wks First trial N = 148 Second trial N = 75	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Papakostas, 2015[264]	RCT - Double-blind	NR	Depressive disease severity	None	Yes	Yes	NA
Mischoulon, 2017[265]	8 wks		Number of prior failed treatments				
	N = 139		Class of previous antidepressants				
NA			Dose of previous antidepressants				
			Age				
			Bipolar disorder				
			Coexisting Medical Comorbidities				
			Coexisting Psychiatric Comorbidities				
			Suicidal risk or behavior				
Patkar, 2006[266]	RCT - Double-Blind	NR	Depressive disease severity	None	Unclear	Unclear	NA
NA	4 wks		Number of prior failed treatments				
	N = 60		Class of previous antidepressants				
			Dose of previous antidepressants				
			Age				
			Bipolar disorder				
			Coexisting Medical Comorbidities				
			Coexisting Psychiatric Comorbidities				
			Suicidal risk or behavior				

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Perahia, 2008[267] NA	RCT - Open Label 10 wks N = 368	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Philip, 2016[268] NA	RCT - Open Label 6 wks N = 49	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Pilu, 2007[269] Carta, 2008[270] NA	RCT - Open-label 32 wks N = 30	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Gender	Unclear	Yes	NA
Price, 2010[271] NA	RCT - Double-blind 4 wks N = 44	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder	None	Unclear	Yes	NA
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	RCT - Double-blind 26 wks N = 5	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Quante, 2011[274] NA	RCT - Double-blind 3 wks N = 41	NR	Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Age	No	No	Statistical adjustment during analysis
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	RCT - Double-blind 24 wks N = 243	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Ravindran, 2008[277] Rizvi, 2014[278] NA	RCT - Double-blind 5 wks N = 145	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Reynolds, 2010[279] Greenlee, 2010[280] NA	RCT - Single Blind 16 wks N = 124	NR	Depressive disease severity Number of prior failed treatments Bipolar disorder Coexisting Medical Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Rossini, 2005[281] NA	RCT - Double-blind 5 wks N = 54	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Coexisting Medical Comorbidities	Depressive disease severity Duration of current episode Age Gender Bipolar disorder	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Rosso, 2012[282] NA	RCT - Single-blind 8 wks N = 49	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	No	Yes	NA
Ruhe, 2009[283] NA	RCT - Double-blind 6 wks N = 60	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	RCT - Double-blind 10 wks 235	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Rush, 2006[287] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] Rush, 2004[294] STAR*D	RCT - Open Label 12 wks N = 727	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Rybakowski, 2016[295] NA	RCT - Double-blind NA N = 30	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	NA	NA	NR
Sackeim, 2009[296] NA	RCT - Double-blind 208 wks N = 319	NR	Depressive disease severity Class of previous antidepressants Dose of previous antidepressants Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Schindler, 2007[297] NA	RCT - Open Label 8 wks N = 34	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Bipolar disorder	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Schoeyen, 2015[298] Kessler, 2014[299] NA	RCT - Single-blind 6 wks N = 73	NR	Depressive disease severity Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Schulze, 2017[300] NA	Retrospective controlled cohort study NA N = 105	NA	Number of prior failed treatments Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar Disorder	NA	NA	Statistical adjustment during analysis
Schulze-Rauschenbach, 2005[301] NA	Non-randomized Controlled Study NA N = 30	NR	Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Psychiatric Comorbidities	None	NA	NA	NA
Sharma, 2017[302] NA	RCT - Single-blind 8 wks N = 25	N	Depressive disease severity Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Shelton, 2005[303] NA	RCT - Double-Blind 8 wks N = 500	Y	Depressive disease severity Number of prior failed treatments Age	None	Unclear	Yes	NA
Sienaert, 2009[304] Sienaert, 2010[305] NA	RCT - Single-blind NR N = 81	NR	Depressive disease severity Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA
Singh, 2015[306] NA	RCT - Double-blind 1 wk N = 30	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA
Singh, 2016[307] NA	RCT - Double-Blind 4 wks N = 68	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Souery, 2011[308] NA	RCT - Opel Label NR N = 189	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	Depressive disease severity Duration of current episode Age Gender Race/Ethnicity	Unclear	No	NA
Souery, 2011[309] NA	Retrospective Controlled Cohort Study 4 wks N = 340	NR	Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder	Number of previous hospitalizations Number of prior failed treatments Dose of previous antidepressants Medical Comorbidities Melancholic features Suicidal risk or behavior	NA	NA	Statistical adjustment during analysis
Speer, 2009[310] NA	RCT - Double-blind 4 wks N = 22	NR	Number of prior failed treatments	Bipolar disorder	Unclear	Unclear	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Speer, 2014[311] NA	RCT - Double-blind 3 wks N = 24	NR	Number of prior failed treatments Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	No	NA
Sperling, 2009[312] NA	Case-control study 52 wks N = 18	NR	Bipolar disorder	None		NA	NR
Stalsett, 2012[313] NA	Prospective Controlled Cohort Study 64 wks N = 100	NR	Number of prior failed treatments Bipolar disorder Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	NA	NA	NA
Straaso, 2014[314] NA	RCT - Double-Blind 8 wks N = 65	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Thase, 2006[315] NA	RCT - Open Label 12 wks N = 232	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Thase, 2007[316] NA	RCT - Double-blind 8 wks N = 605	Y	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Class of previous antidepressants	Yes	Yes	NA
Theleritis, 2017[317] NA	RCT - Double-blind 3 wks N = 98	N	Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Town, 2017[318] NA	RCT - Single-blind 27 wks N = 60	N	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Triggs, 2010[319] NA	RCT - Double-blind 2 wks N = 48	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Unclear	Yes	NA
Trivedi, 2006[320] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] Rush, 2004[294] STAR*D	RCT - Open Label 12 wks N = 565	NR	Depressive disease severity Number of prior failed treatments Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities Suicidal risk or behavior	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	RCT - Single-blind 12 wks N = 126	NR	Depressive disease severity Number of prior failed treatments Class of previous antidepressants Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Gender Family history of MDD	Yes	Yes	NA
Trojak, 2014[325] NA	RCT - Double-blind 4 wks N = 15	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Unclear	NA
Turnier-Shea, 2006[326] NA	RCT - Single-blind 2 wks N = 16	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Unclear	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
van den Broek, 2006[327] NA	RCT - Double-Blind 24 wks N = 27	NR	Number of prior failed treatments Age Bipolar disorder Coexisting Psychiatric Comorbidities	Depressive disease severity Class of previous antidepressants	Yes	Yes	NA
Watkins, 2011[328] NA	RCT - Open Label 12 wks N = 42	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA
Wiles, 2008[329] NA	RCT - Open Label 16 wks N = 25	NR	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities MDD onset before age 20	Race/Ethnicity Psychiatric Comorbidities MDD onset before age 20	Yes	No	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	RCT - Open Label 52 wks N = 469	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Psychiatric Comorbidities	Duration of current episode	Yes	Yes	NA
Xu, 2015[334] NA	Prospective controlled cohort study 2 wks N = 36	NA	Number of prior failed treatments Dose of previous antidepressants Coexisting Psychiatric Comorbidities	None	NA	NA	Statistical adjustment during analysis
Zarate, 2006[335] NA	RCT - Double-blind 2 wks N = 18	NR	Depressive disease severity Number of prior failed treatments Dose of previous antidepressants Age Bipolar disorder Coexisting Psychiatric Comorbidities	None	Yes	Yes	NA

Table C5. Risk factors of systematic review studies from key question 9 (continued)

Author, Year Study Name	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Placebo Run-In (Yes/No)	Risk Factors Restricted	Stratification and Subgroup Analyses	Was method of randomization adequate?	RCTS ONLY Risk Factors Equally distributed after Randomization (Yes/No/NA)	Non-RCTs How did study deal with These Risk/Prognostic Factors, Other Than Restriction or Stratification/Subgroup Analyses
Zarate, 2012[336] NA	RCT - Double-Blind 4 wks N = 15	Y	Depressive disease severity Duration of current episode Number of prior failed treatments Dose of previous antidepressants Age Coexisting Medical Comorbidities Coexisting Psychiatric Comorbidities	Class of previous antidepressants	NA	NA	NA

MDD = Major Depressive Disorder; N = Number; NA = Not Applicable; NR = Not Reported; PATH-D = Practicing Alternative Techniques to Heal From Depression; REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; RCT = Randomized Controlled Trial; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; TADS = Tavistock Adult Depression Study; Wks = Weeks

Table C6. Details of key question 10 studies eligible for regression analysis

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Altamura, 2008[143] NA	RCT - Single-blind 1 wk N = 36	Pharmacotherapy	G1: Citalopram 10 mg i.v. augmentation + prior oral SSRIs N = 18 G2: Placebo i.v. augmentation + prior oral SSRIs N = 18	Response, first measure: G1: 9 G2: 0 Remission, first measure: G1: 3 G2: 0	Serious G1: 0 G2: 0 Overall G1: 9 G2: 7 Attrition Due to G1: 0 G2: 0	NR Unclear	NR	Medium	Female: 0.67 Bipolar: 0.39	Moderate NR
Avery, 2006[145] NA	RCT - Double-blind 26 wks N = 68	CNS	G1: HF rTMS to left DLPFC N = 35 G2: Sham rTMS N = 33	Response, first measure: G1: 11 G2: 2 Remission, first measure: G1: 7 G2: 1	NR	44.25 N	Public	Low	Female: 0.56	Moderate 108.8

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Barbee, 2011[150] NA	RCT - Double-blind 10 wks N = 96	Pharmacotherapy	G1: Lamotrigine 400 mg/d N = 48 G2: Placebo N = 48	Response, first measure: G1: 16 G2: 16	Serious G1: 1 G2: 2 Overall G1: 42 G2: 42 Attrition Due to G1: 7 G2: 10 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 1	NR N	Industry	Medium	Age 75 or older: 0 Female: 0.6875 Bipolar: 0 Coexisting psychiatric comorbidities: 0.198	Moderate 116.8

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Berman, 2007[159] NA	RCT - Double-blind 6 wks N = 362	Pharmacotherapy	G1: Aripiprazole augmentation N = 182 G2: Placebo augmentation N = 176	Response, first measure: G1: 61 G2: 41 Remission, first measure: G1: 47 G2: 27	Serious G1: 2 G2: 3 Overall G1: 149 G2: 110 Attrition Due to G1: 6 G2: 4 Suicidal Ideation or Behavior of Overall Events G1: 2 G2: 0	45.4 N	Industry	Low	Age 75 or older: 0 Female: 0.62 Non-white: 0.1 Bipolar: 0	Moderate 164.2

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Berman, 2009[160] NA	RCT - Double-blind 14 wks N = 349	Pharmacotherapy	G1: Adjunctive aripiprazole N = 177 G2: Adjunctive placebo N = 172	Response, first measure: G1: 81 G2: 45 Remission, first measure: G1: 64 G2: 32	Serious G1: 1 G2: 1 Attrition Due to G1: 11 G2: 3 Suicidal Ideation or Behavior of Overall Events G1: 1 G2: 0	45.3 N	Industry	Low	Age 75 or older: 0 Female: 0.731 Non-white: 0.129	Moderate 72
Blumberger, 2012[161] NA	RCT - Double-blind 6 wks N = 74	CNS	G1: Bilateral rTMS N = 28 G2: Unilateral rTMS N = 24 G3: Sham control N = 22	Response, first measure: G1: 10 G2: 1 G3: 2 Remission, first measure: G1: 9 G2: 1 G3: 1	Serious G1: 1 G2: 1 G3: 1 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 1 G3: 1	51.47 Y	Public	High	Female: 0.59 Coexisting medical comorbidities: 0.4	Severe NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Blumberger, 2016[162] NA	RCT - Double-blind 6 wks N = 121	CNS	G1: Bilateral rTMS N = 40 G2: Unilateral rTMS N = 40 G3: Sham control N = 41	Response, first measure: G1: 9 G2: 6 G3: 2 Response, second measure: G1: 11 G2: 6 G3: 5 Remission, first measure: G1: 8 G2: 3 G3: 1 Remission, second measure: G1: 7 G2: 1 G3: 1	Serious G1: 0 G2: 0 G3: 1 Attrition Due to G1: 2 G2: 2 G3: 0 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0 G3: 1	NR Y	Public, private, and industry	Low	Female: 0.64 Bipolar: 0 Coexisting psychiatric comorbidities: 0.12	Severe NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Concerto, 2015[170] NA	RCT - Opel Label 26 wks N = 30	CNS	G1: rTMS N = 15 G2: Sham rTMS N = 15	NR	Serious G1: 0 G2: 0 Overall G1: 0 G2: 0 Attrition Due to G1: 0 G2: 0 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0	NR N	NR	High	Aged 75 or older: 0 Female: 0.43 Bipolar: 0	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Cusin, 2013[172] NA	RCT - Double-blind 14 wks N = 60	Pharmacotherapy	G1: Pramipexole 0.25-1.5 mg BID + Prior antidepressant N = 30 G2: Placebo + Prior antidepressant N = 30	Response, first measure: G1: 12 G2: 8 Remission, first measure: G1: 10 G2: 7	Serious G1: 0 G2: 0 Attrition Due to G1: 4 G2: 4 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0	NR Y	Public	Medium	Female: 0.567 Bipolar: 0	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Durgam, 2016[180] NA	RCT - Double-blind 8 wks N = 819	Pharmacotherapy	G1: Cariprazine 2-4.5 mg/d + Prior antidepressant N = 276 G2: Cariprazine 1-2 mg/d + Prior antidepressant N = 274 G3: Placebo N = 269	Response, first measure: G1: 134 G2: 131 G3: 101 Response, second measure: G1: 159 G2: 158 G3: 129 Remission, first measure: G1: 87 G2: 87 G3: 79	Serious G1: 2 G2: 0 G3: 1 Overall G1: 214 G2: 189 G3: 157 Attrition Due to G1: 36 G2: 18 G3: 8 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0 G3: 0	NR N	Industry	Low	Age 75 or older: 0 Female: 0.712 Non-white: 0.13 Bipolar: 0	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
El-Khalili, 2010[183] NA	RCT - Double-blind 8 wks N = 446	Pharmacotherapy	G1: Adjunctive quetiapine XR 150 mg/d N = 148 G2: Adjunctive quetiapine XR 300 mg/d N = 150 G3: Adjunctive placebo N = 148	Response, first measure: G1: 39 G2: 39 G3: 21 Remission, first measure: G1: 50 G2: 62 G3: 35	Serious G1: 1 G2: 0 G3: 1 Overall G1: 118 G2: 127 G3: 96 Attrition Due to G1: 17 G2: 29 G3: 1	G1: 45.42 G2: 46.42 N	Industry	Medium	Age 75 or older: 0 Onset before age 20: 0 Female: 0.725 Non-white: 0.1	Severe NR
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	RCT - Double-blind 9 wks N = 225	Pharmacotherapy	G1: Aripiprazole augmentation N = 54 G2: Placebo augmentation N = 167	Response, first measure: G1: 10 G2: 29 Remission, first measure: G1: 4 G2: 16	Overall G1: 39 G2: 104 Attrition Due to G1: 0 G2: 0	45 N	Industry	Low	Age 75 or older: 0 Female: 0.68 Non-white: 0.19 Low socioeconomic status: 0.27 Bipolar: 0	Severe NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Fitzgerald, 2006[191] NA	RCT - Double-blind 6 wks N = 50	CNS	G1: Active rTMS N = 25 G2: Sham rTMS N = 25	Response, first measure: G1: 11 G2: 2 Remission, first measure: G1: 9 G2: 0	NR	45.3 Unclear	Public	Low	Female: 0.62 Bipolar: 0.16 Mean number prior failed treatments: 5.9	Moderate 26.6
Fitzgerald, 2008[193] NA	RCT - Double-blind 6 wks N = 50	CNS	G1: rTMS N = 25 G2: Sham rTMS N = 25	Response, first measure: G1: 11 G2: 2 Response, second measure: G1: 13 G2: 2 Remission, first measure: G1: 9 G2: 0	Serious G1: 0 G2: 0 Overall G1: 8 G2: 2 Attrition Due to G1: 0 G2: 0 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0	NR Unclear	Public and foundation	Low	Female: 0.62 Bipolar: 0.16 Coexisting psychiatric comorbidities: 0 Coexisting medical comorbidities: 0 Mean number prior failed treatments: 5.9	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Fitzgerald, 2016[200] NA	RCT - Double-blind 4 wks N = 46	CNS	G1: Bilateral rTMS N = 23 G2: Sham rTMS N = 23	Response, first measure: G1: 3 G2: 1 Remission, first measure: G1: 2 G2: 0	NR	NR Y	Public	Low	Female: 0.565 Bipolar: 1 Coexisting psychiatric comorbidities: 0.52	Severe NR
Garcia-Toro, 2006[204] NA	RCT - Double-blind NA N = 30	CNS	G1: Active rTMS N = 10 G2: rTMS + SPECT N = 10 G3: Sham rTMS N = 10	Response, first measure: G1: 2 G2: 2 G3: 0	NR	48.9 Unclear	Foundation	Medium	Female: 0.5	NR 130.4
George, 2010[205] McDonald, 2011[206] NA	RCT - Double-blind 6 wks N = 199	CNS	G1: Active rTMS N = 92 G2: Sham rTMS N = 98	Response, first measure: G1: 14 G2: 25 Remission, first measure: G1: 13 G2: 5	Serious G1: 1 G2: 1 Attrition Due to G1: 5 G2: 0	47.1 Y	Public	Low	Female: 0.57 Mean number prior failed treatments: 3.31	Moderate 78.3

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Kamijima, 2013[213] Ozaki, 2015[214] NA	RCT - Double-blind 6 wks N = 586	Pharmacotherapy	G1: Flexible dose aripiprazole augmentation N = 194 G2: Fixed dose aripiprazole augmentation N = 197 G3: Placebo augmentation N = 195	Response, first measure: G1: 76 G2: 83 G3: 55 Remission, first measure: G1: 59 G2: 64 G3: 40	Serious G1: 3 G2: 2 G3: 3 Overall G1: 151 G2: 141 G3: 117 Attrition Due to G1: 5 G2: 5 G3: 2	38.7 N	Industry	Low	Age 75 or older: 0 Female: 0.42 Bipolar: 0	Moderate 65.2

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Keitner, 2009[216] NA	RCT - Double-blind 4 wks N = 97	Pharmacotherapy	G1: Antidepressant monotherapy + risperidone N = 62 G2: Antidepressant monotherapy + placebo N = 33	Response, first measure: G1: 35 G2: 10 Response, second measure: G1: 29 G2: 9 Remission, first measure: G1: 22 G2: 6 Remission, second measure: G1: 32 G2: 8	Attrition Due to G1: 8 G2: 7	45.21 N	Industry	Medium	Age 75 or older: 0 Female: 0.585 Non-white: 0.096	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Lenze, 2015[226] Kaneriya, 2016[227] NA	RCT - Double-blind 12 wks N = 181	Pharmacotherapy	G1: Aripiprazole augmentation N = 91 G2: Placebo augmentation N = 90	Remission, first measure: G1: 40 G2: 26	Serious G1: 4 G2: 2 Attrition Due to G1: 3 G2: 3 Suicidal Ideation or Behavior of Overall Events G1: 13 G2: 19	66 Unclear	Public and foundation	Medium	Female: 0.57 Non-white: 0.12	Mild 104

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Levkovitz, 2015[230] NA	RCT - Double-blind 16 wks N = 181	CNS	G1: dTMS N = 101 G2: Sham dTMS N = 111	Response, first measure: G1: 41 G2: 29 Remission, first measure: G1: 30 G2: 25	Serious G1: 3 G2: 4 Overall G1: 41 G2: 32 Attrition Due to G1: 3 G2: 5 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 2	46.4 Unclear	Industry	Medium	Aged 75 or older: 0 Onset before age 20: 0 Female: 0.48 Non-white: 0.094 Bipolar: 0	Moderate 82.4
Mahmoud, 2007[232] NA	RCT - Double-blind 6 wks N = 274	Pharmacotherapy	G1: Risperidone N = 141 G2: Placebo N = 133	Response, first measure: G1: 49 G2: 33 Remission, first measure: G1: 26 G2: 12	Overall G1: 63 G2: 72 Attrition Due to G1: 8 G2: 3	46.14 N	Industry	Low	Age 75 or older: 0 Female: 0.72 Non-white: 0.25	NA 16.7

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Martinot, 2010[233] NA	RCT - Double-blind 2 wks N = 50	CNS	G1: PET-Guided active TMS N = 17 G2: Standard active TMS N = 19 G3: Sham TMS N = 14	Response, first measure: G1: 8 G2: 10 G3: 3	Serious G1: 1 G2: 1 G3: 0 Attrition Due to G1: 1 G2: 1 G3: 0 Suicidal Ideation or Behavior of Overall Events G1: 0 G2: 0 G3: 0	47.14 N	Foundation and public	Low	Aged 75 or older: 0 Female: 0.65 Bipolar: 0.33 Coexisting psychiatric comorbidities: 0.58	Moderate NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
McDonald, 2006[236] NA	RCT - Double-blind 2 wks N = 62	CNS	G1: Fast Left (10 Hz) then Slow Right (1 Hz) DLPFC rTMS @ 10 Hz N = 25 G2: Slow Right (1 Hz) then Fast Left (10 Hz) DLPFC rTMS @ 10 Hz N = 25 G3: Sham TMS N = 12	Response, first measure: G1: 7 G2: 3 G3: 1 Remission, first measure: G1: 3 G2: 0 G3: 0 Relapse: G1: 3 G2: 3 G3: 1	NR	NR Y	Foundation	High	Aged 75 or older: 0 Female: 0.52 Non-white: 0.02 Bipolar: 0.13 Mean number prior failed treatments: 8	Moderate NR
Mogg, 2008[240] NA	RCT - Double-blind 4 wks N = 59	CNS	G1: rTMS DLPFC N = 29 G2: Sham rTMS N = 30	Response, first measure: G1: 9 G2: 3 Remission, first measure: G1: 7 G2: 3	Serious G1: 0 G2: 1 Attrition Due to G1: 0 G2: 2	NR Unclear	Public, industry, and foundation	Medium	Female: 0.627 Bipolar: 0.017 Mean number of prior failed treatments: 3.1	NR NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	RCT - Double-blind 10 wks N = 325	CNS	G1: Active TMS N = 155 G2: Sham TMS N = 146	NR	Serious G1: 9 G2: 7 Attrition Due to G1: 7 G2: 5 Suicidal Ideation or Behavior of Overall Events G1: 1 G2: 10	NR Y	Industry	Medium	Age 75 or older: 0 Female: 0.53 Non-white: 0.08 Bipolar: 0 Mean number prior failed treatments: 1.6	Severe NR
Paillere Martinot, 2010[257] NA	RCT - Double-blind 2 wks N = 48	CNS	G1: Standard rTMS N = 18 G2: PET-guided rTMS N = 16 G3: Sham rTMS N = 14	Response, first measure: G1: 10 G2: 8 G3: 3	Serious G1: 1 G2: 1 G3: 0 Attrition Due to G1: 1 G2: 1 G3: 0	NR N	Public	Low	Age 75 or older: 0 Female: 0.61 Biploar: 0.31	NR NR

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Pallanti, 2010[258] NA	RCT - Double-blind 3 wks N = 60	CNS	G1: Unilateral rTMS N = 20 G2: Bilateral rTMS N = 20 G3: Sham rTMS N = 20	Response, first measure: G1: 6 G2: 2 G3: 1	Serious G1: 0 G2: 0 G3: 0 Attrition Due to G1: 0 G2: 0 G3: 0	48.9 Unclear	Public	Low	Female: 0.58 Bipolar: 0 Coexisting psychiatric comorbidities: 0 Coexisting medical comorbidities: 0 Mean number of prior failed treatments: G1: 6.32 G2: 5.92	Moderate 39.9

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Papakostas, 2015[264] Mischoulon, 2017[265] NA	RCT - Double-blind 8 wks N = 139	Pharmacotherapy	G1: Escitalopram + Ziprasidone N = 71 G2: Escitalopram + Placebo N = 68	Response, first measure: G1: 25 G2: 14 Response, second measure: G1: 22 G2: 9 Remission, first measure: G1: 27 G2: 21 Remission, second measure: G1: 17 G2: 7	Serious G1: 2 G2: 2 Overall NR Attrition Due to G1: 10 G2: NR Suicidal Ideation or Behavior of Overall Events G1: 1 G2: 0	44.6 N	Industry and government	Medium	Aged 75 or older: 0 Female: 0.71 Bipolar disorder: 0	Moderate NR
Ravindran, 2008[277] NA	RCT - Double-blind 5 wks N = 145	Pharmacotherapy	G1: OROS methylphenidate augmentation N = 73 G2: Placebo augmentation N = 72	NR	Serious G1: 5 G2: 3 Overall G1: 51 G2: 43 Attrition Due to G1: 6 G2: 0	43.8 N	Industry	Low	Aged 75 or older: 0 Female: 0.648 Non-white: 0.021	Moderate 87.2

Table C6. Details of key question 10 studies eligible for regression analysis (continued)

Author, Year Study	Study Design Study Duration (Wks) Overall Sample Size (N Randomized)	Intervention Category	Intervention, N (Randomized) Control, N (Randomized)	Measures of Depression Response, Remission, and Relapse (First Measure is Primary Outcome)	Adverse Events (N)	Mean age Eligibility Criteria Included Patients ≥65 Years of Age (Y/N/ Unclear)	Funding Source	Risk of Bias Rating	Patient Level Covariates: Proportion of Participants	Depression Severity Mean Duration of Current Depressive Symptoms (Wks)
Rossini, 2005[281] NA	RCT - Double-blind 5 wks N = 54	CNS	G1: 80% MT rTMS N = 19 G2: 100% MT rTMS N = 18 G3: Sham rTMS N = 17	Response, first measure: G1: 5 G2: 22 G3: 1 Remission, first measure: G1: 5 G2: 9 G3: 0	Serious G1: 0 G2: 0 G3: 0 Overall G1: 2 G2: 5 G3: 0 Attrition Due to G1: 0 G2: 0 G3: 0	55.9 Y	NR	Low	Age 75 or older: 0 Female: 0.7 Bipolar: 0.31	Severe 49.2

BID = Twice a day; CNS = Central Nervous System; DLPFC = Dorsolateral Prefrontal Cortex; HF = High Frequency; Hz = Hertz; Mg/d = Milligrams per-day; MT = Motor Threshold; NR = Not Reported; OROS = Osmotic-Release Oral System; PET = Positron Emission Tomography; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SPECT = Single Photon Emission Computed Tomography; SSRI: Selective Serotonin Reuptake Inhibitor; TMS = Transcranial Magnetic Stimulation (r = Repetitive, d = Direct); Wks = Weeks; XR = Extended Release

Table C7. Endpoint data from key question 11

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Aaronson, 2013[140] NA	QIDS-SR IDS-SR IDS-CR	N	Active surveillance of adverse events using Adverse Events Record; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition	N	N	N
Aaronson, 2017[50] NA	MADRS QIDS-SR	N	Passive surveillance of adverse events reported; serious adverse events	Not reported	N	N	N
Aguirre, 2011[141] NA	HAMD-17	N	Passive surveillance of adverse events reported; overall adverse event rates	Not reported	N	N	N
Allen, 2015[142] NA	HAMD-17	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Altamura, 2008[143] NA	HAMD-21 MADRS	N	Adverse events (cannot determine surveillance); overall adverse event rates	Not reported	N	N	N
Amsterdam, 2009[144] NA	HAMD-17	N	Not reported	Overall attrition	N	N	N
Avery, 2006[145] NA	HAMD-17 BDI	N	Active surveillance of adverse events reported using SAFTEE; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Baeken, 2013[146] NA	HAMD-17	N	Passive surveillance of adverse events reported; overall adverse event rates	Not reported	N	N	N
Baeken, 2014[147] NA	HAMD-17	N	Passive surveillance of adverse events reported	Not reported	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Baldomero, 2005[148] ARGOS Study	HAMD-17 CGI-S CGI-I	N	Adverse events reported (cannot determine surveillance); overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Barak, 2011[149] NA	CGI-S	N	Passive surveillance of adverse events; overall adverse event rates	None Reported	N	N	N
Barbee, 2011[150] NA	HAMD-17 MADRS SF-36 SDS CES-D	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	Y SF-36	Y	N
Bares, 2009[151] NA	BDI-SF CGI-S MADRS	N	Passive surveillance of adverse events	Overall attrition, attrition due to adverse events	N	N	N
Bares, 2009[152] NA	HAMD-17	N	Not reported	Not reported	N	N	N
Bares, 2013[153] NA	BDI-SF CGI-S CGI-I MADRS	N	Active surveillance of adverse events using FIBSER	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Bauer, 2013[154] RUBY	CGI-S CGI-I MADRS	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	Y VAS, SF-36, EQ-5D	Y	N
Bauer, 2016[155] NA	HAMD-17	N	Passive surveillance of adverse events; serious adverse events	Attrition due to adverse events	N	N	N
Bennabi, 2015[156] NA	HAMD-21 BDI MADRS	N	Adverse events reported (cannot determine surveillance)	Overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Bergfeld, 2016[157] NA	HAMD-17 MADRS	N	Active surveillance of adverse events (not described); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Bergfeld, 2017[158] NA	MADRS	N	Not reported	Adherence to treatment, overall attrition, attrition due to lack of efficacy	N	N	N
Berman, 2007[159] NA	HAMD-17 MADRS	N	Active surveillance of adverse events reported using DIEPSS, AIMS, and BARS; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y SFI	Y	N
Berman, 2009[160] NA	HAMD-17 CGI-S CGI-I MADRS SDS Q-LES-Q	N	Active surveillance of adverse events using body weight, vital signs, and 12-lead ECG, as well as SFI, SAS, AIMS, and BARS; serious adverse events; overall adverse event rates	Overall attrition	Y SDS, Q-LES-Q-SF	Y	N
Blumberger, 2012[161] NA	HAMD-17	N	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Blumberger, 2016[162] NA	HAMD-17 BDI-II	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y Increased anxiety	N	N
Bortolomasi, 2007[163] NA	HAMD-24 BDI	N	Overall adverse event rates	Not reported	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Bretlau, 2008[164] NA	HAMD-6 HAMD-17	N	Active surveillance of adverse events using UKU; overall adverse event rates	Overall attrition	N	N	N
Brunelin, 2014[165] NA	HAMD-17 BDI MADRS	N	Active surveillance of adverse events using unspecified structured interview at each session by a blinded rater; serious adverse events (systematically recorded)	Overall attrition, attrition due to lack of efficacy	N	N	N
Butler, 2011[166] Holt, 2011[167] NA	HAMD-17	N	Not reported	Not reported	N	N	Y
Chaput, 2008[168] NA	HAMD-21 CGI-S CGI-I MADRS	N	Active surveillance of adverse events using vital signs, weight, EKG, hematology, and urine-analysis; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N
Chiesa, 2015[169] NA	HAMD-21 BDI	N	None reported	Overall attrition	N	N	N
Concerto, 2015[170] NA	HAMD-21 MADRS	Y	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Corya, 2006[171] NA	CGI-S MADRS BPRS	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Cusin, 2013[172] NA	CGI-S CGI-I MADRS IDS-SR	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Dell'Osso, 2015[173] NA	HAMD-21 CGI-S MADRS YMRS SDS	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	Y
[174] NA	MADRS BPRS YMRS SDS	Y	Adverse events reported (cannot determine surveillance)	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Doree, 2007[175] NA	HAMD-17 CGI-S CGI-I MADRS BPRS	N	Active surveillance of adverse events using UKU; serious adverse events	Overall attrition, attrition due to adverse events	N	N	N
Dougherty, 2015[176] Kubu, 2017[177] NA	MADRS	N	Adverse events reported (cannot determine surveillance); serious adverse events	Overall attrition, attrition due to adverse events	N The larger study with a planned N of 208 (once completed and published) will report patient-reported outcomes from multiple scales specifically intended to capture those data.	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Dunner, 2007[178] NA	HAMD-17 CGI-S CGI-I QIDS-SR	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Duprat, 2016[179] NA	HAMD-17 BDI	N	Passive surveillance of adverse events; serious adverse events	Overall attrition, attrition due to adverse events	N	N	N
Durgam, 2016[180] NA	CGI-S MADRS SDS	N	Active surveillance of adverse events using non-leading question about overall well-being, specific queries about adverse events during clinic visits, BARS, AIMS, SAS, CSSRS; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	Y	N
Eche, 2012[181] NA	MADRS	N	Adverse events reported (cannot determine surveillance); overall adverse event rates	Attrition due to adverse events	N	N	N
Eisendrath, 2016[182] Practicing Alternative Techniques to Heal Depression	HAMD-17 CGI-I	N	None reported	Overall attrition	N	N	N
El-Khalili, 2010[183] NA	HAMD-17 CGI-S CGI-I MADRS	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	Y Satisfaction with medication	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Eschweiler, 2007[184] NA	HAMD-21 BDI CGI-S CGI-I	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events	N	N	N
Fava, 2006[185] STAR*D	HAMD-17 QIDS-SR SF-12	N	Active surveillance of adverse events using FIBSER; serious adverse events	Attrition due to adverse events	N	N	N
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	CGI-S CGI-I MADRS PHQ-9	N	Adverse events reported (cannot determine surveillance); serious adverse events, overall adverse event rates	Overall attrition, attrition due to adverse events	Y SFI	N	N
Fitzgerald, 2003[189] NA	BDI MADRS BPRS	N	Adverse events reported (cannot determine surveillance); overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Fitzgerald, 2006[190] NA	HAMD-17	N	Passive surveillance of adverse events; serious adverse events	Overall attrition, attrition due to lack of efficacy	N	N	N
Fitzgerald, 2006[191] NA	HAMD-17 BDI CGI-I MADRS GAF BPRS	N	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition	N	N	N
Fitzgerald, 2007[192] NA	MADRS	N	Not reported	Not reported	N	N	N
Fitzgerald, 2008[193] NA	HAMD-17 BDI CGI-S CGI-I MADRS GAF BPRS	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Fitzgerald, 2008[194] NA	BDI-II CGI-S MADRS GAF BPRS	N	Passive surveillance of adverse events; serious adverse events	Overall attrition, attrition due to lack of efficacy	Y GAF	N	N
Fitzgerald, 2009[195] NA	BDI-II CGI-S MADRS GAF BPRS	N	Passive surveillance of adverse events; overall adverse event rates	Overall attrition, attrition due to lack of efficacy	Y GAF	N	N
Fitzgerald, 2009[196] NA	BDI-II CGI-S MADRS GAF BPRS	N	Not reported	Overall attrition	Y GAF	N	N
Fitzgerald, 2011[197] NA	HAMD-17 HAMD-28	N	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Not reported	N	N	N
Fitzgerald, 2012[198] NA	HAMD-17 BDI-II CGI-I	N	Passive surveillance of adverse events reported; overall adverse event rates	Adherence to treatment, overall attrition	N	N	N
Fitzgerald, 2013[199] NA	HAMD-17 BDI	N	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Not reported	N	N	N
Fitzgerald, 2016[200] NA	HAMD-17 IDS-SR IDS-CR YMRS	N	Not reported	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y Changes in life circumstance, desire to seek alternative treatment	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Fonagy, 2015[201] The Tavistock Adult Depression Study (TADS)	HAMD-17 BDI-II	N	None reported	Adherence to treatment, overall attrition	Y Social functioning as evaluated by the GAF; subjective wellbeing as rated by the CORE-OM tool; and satisfaction with general activities as assessed by the Q-LES-Q questionnaire	N	Y
Fornaro, 2014[202] NA	HAMD-21 MADRS GAF	N	Active surveillance of adverse events using non-leading question ("how do you feel?"), FIBSER, GRSEB, PRISE, ASEX, YMRS; serious adverse events	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Fujita, 2006[203] NA	HAMD-17	N	Active surveillance of adverse events (cognitive function only) using MMSE, Wechsler Memory Scale-Revised, Trail making test, Digit Symbol Coding test (Wechsler Adult Intelligence Scale-Revised), Verbal and letter fluency test, Stroop test	Not reported	N	N	N
Garcia-Toro, 2006[204] NA	HAMD-21 CGI-S	N	Passive surveillance of adverse events reported	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
George, 2010[205] McDonald, 2011[206] NA	HAMD-24 CGI-S MADRS IDS-SR	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N
George, 2017[207] NA	HAMD-17	N	Active surveillance of adverse events using SAFTEE; serious adverse events; overall adverse events rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Girlanda, 2014[208] NA	QIDS-SR	N	Passive surveillance of adverse events	Overall attrition	N	N	N
Harley, 2008[209] Feldman, 2009[210] NA	HAMD-17 BDI	N	None reported	Overall attrition	Y Psychosocial functioning and life satisfaction (using LIFE-RIFT tool); functioning using SOS-10 and SAS-SR	N	N
Holtzheimer, 2012[129] NA	HAMD-17 BDI-II GAF	N	Active surveillance of adverse events (not described); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition	N	N	N
Jarventausta, 2013[211] NA	BDI CGI-I	N	Adverse events reported (cannot determine surveillance); serious adverse events	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Joffe, 2006[212] NA	HAMD-17	N	None reported	None Reported	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Kamijima, 2013[213] Ozaki, 2015[214] NA	CGI-S CGI-I MADRS IDS-SR SDS	N	Active surveillance of adverse events reported using DIEPSS, AIMS, and BARS; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	Y	N
Kayser, 2011[215] NA	HAMD-28 BDI SCL-90R MADRS	N	Active surveillance of adverse events (short term cognitive effects) using Autobiographical memory interview, verbal learning and memory ("WORDS"), visual spatial learning and memory ("SHAPES"), Wechsler Memory Scale, Abstract questions, Picture test, Verbal fluency, Neglect	Not reported	N	N	N
Keitner, 2009[216] NA	HAMD-17 CGI-S MADRS Q-LES-Q	N	Adverse events reported (cannot determine surveillance)	Adherence to treatment, overall attrition	Y Patient reports of life satisfaction	N	N
Kocsis, 2009[217] Klein, 2011[218] Shankman, 2013[219] REVAMP Trial	HAMD-24	N	Active surveillance of adverse events using frequency, intensity, and burden of side effects rating form Overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	Y	N
Kok, 2007[220] NA	HAMD-17 CGI-I MADRS Geriatric Depression Scale	N	Active surveillance of adverse events reported using SES and "clinical assessment of tolerability scores"; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Kopecek, 2007[221] NA	BDI-SF	N	Not reported	Not reported	N	N	N
Kranaster, 2011[222] NA	HAMD-21 MMSE	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Lally, 2014[223] NA	HAMD-17 MADRS	N	Not reported	Not reported	N	N	N
Lapidus, 2014[224] NA	MADRS QIDS-SR	NR	Active surveillance of adverse events using BPRS, CADSS, SAFTEE, BP and HR measures; serious adverse events; overall adverse event rates	Overall attrition	N	N	N
Lenox-Smith, 2008[225] NA	HAMD-21 CGI-S CGI-I MADRS	N	Active reporting of adverse events (details not reported); overall adverse events	Overall attrition, attrition due to lack of efficacy	N	N	N
Lenze, 2015[226] Kaneriya, 2016[227] NA	MADRS	N	Active surveillance of adverse events using UKU; serious adverse events	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y SF-36	N	N
Lenze, 2016[228] NA	CGI-I MADRS BPRS	N	Active surveillance of adverse events reported using SAFTEE-SI; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Levkovitz, 2009[229] NA	HAMD-24	N	Passive surveillance of adverse events reported; overall adverse event rates	Not reported	N	N	N
Levkovitz, 2015[230] NA	HAMD-21	Y	Active surveillance of adverse events with patients asked at each visit and coded using Medical Dictionary for Regulatory Activities; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y Suicidal ideation, subject felt no improvement	N	N
Loo, 2016[231] NA	MADRS BPRS PHQ-9	N	Active surveillance of adverse events using SAFTEE; serious adverse events	Not reported	N	N	N
Mahmoud, 2007[232] NA	HAMD-17 CGI-S CGI-I SDS Q-LES-Q	N	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y Q-LES-Q	Y	N
Marcus, 2008[95] NA	CGI-S CGI-I MADRS QIDS-SR IDS-SR	N	Active surveillance of adverse events using SAS; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events; attrition due to lack of efficacy	N	N	N
Martinot, 2010[233] NA	HAMD-21 CGI-S MADRS	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N
Martiny, 2010[234] NA	HAMD-6 HAMD-17 SCL-90R Melancholia Scale	N	Active surveillance of adverse events using UKU; overall adverse event rates	Adherence to treatment, overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Mazeh, 2007[235] NA	HAMD-21 CGI-S CGI-I Generic Depression Scale	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events	N	N	N
McDonald, 2006[236] NA	HAMD-17 BDI CGI-S CGI-I	Y	Not reported	Not reported	N	N	N
McGrath, 2006[237] STAR*D	HAMD-17 QIDS-SR SF-12	N	Active surveillance of adverse events using FIBSER; serious adverse events; overall adverse event rates	Attrition due to adverse events	N	N	N
Miniussi, 2005[238] NA	HAMD-21 BPRS	N	Not reported	Overall attrition	N	N	N
Mischoulon, 2015[239] NA	HAMD-17	N	Active surveillance of adverse events using PRISE	Overall attrition	N	N	N
Mogg, 2008[240] NA	HAMD-17 BDI-II	Y	Passive surveillance of adverse events; serious adverse events	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N
Mohamed, 2017[241] NA	CGI-S CGI-I QIDS-CR	N	Active surveillance of adverse events using SAFTEE-Specific Inquiry; adverse events; overall adverse events rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Moller, 2006[242] NA	HAMD-17	N	Passive surveillance of adverse events reported; overall adverse event rates	Not reported	N	N	N
Mota-Pereira, 2011[243] NA	HAMD-17 BDI-II CGI-S GAF	N	Not reported	Adherence to treatment, overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Muller, 2013[244] NA	HAMD-17	N	None reported	None Reported	N	N	N
Murphy, 2014[245] NA	HAMD-17 MADRS	N	None reported	None Reported	N	N	N
Murrough, 2013[246] Murrough, 2015[247] NA	CGI-S CGI-I MADRS QIDS-SR	Y	Active surveillance of adverse events using PRISE, CADSS, and BPRS; serious adverse events; overall adverse event rates	Overall attrition	Y Blood pressure	N	N
Nasr, 2014[248] NA	QIDS-SR	N	Passive surveillance of adverse events	Attrition due to adverse events	N	N	N
Nierenberg, 2006[249] STAR*D	HAMD-17 QIDS-SR SF-12	N	Active surveillance of adverse events using FIBSER; serious adverse events	Attrition due to adverse events	N		
Nierenberg, 2006[250] STEP-BD	NR	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Attrition due to adverse events	N	N	N
Okamoto, 2010[251] NA	HAMD-17	N	Passive surveillance of adverse events reported; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Olin, 2012[252] NA	MADRS	N	Active surveillance of adverse events using FIBSER; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	HAMD-17 CGI-S CGI-I MADRS IDS-SR	N	Passive surveillance of adverse events reported; serious adverse events	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y Self-reported depression symptoms	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Paillere Martinot, 2010[257] NA	HAMD-21 CGI-S	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Pallanti, 2010[258] NA	HAMD-17	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events	N	N	N
Palm, 2012[259] Palm, 2013[260] NA	HAMD-24 BDI	N	Active surveillance of adverse events reported by systematically asking patients for adverse events	Overall attrition	N	N	N
Papakostas, 2005[261] NA	CGI-S CGI-I	N	Not reported	Not reported	N	N	N
Papakostas, 2010[262] NA	HAMD-17	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Papakostas, 2012[263] NA	HAMD-17 CGI-S CGI-I QIDS-SR	N	Adverse events reported (cannot determine surveillance); overall adverse event rates	Overall attrition	N	N	N
Papakostas, 2015[264] Mischoulon, 2017[265] NA	HAMD-17 CGI-S CGI-I MADRS	N	Active surveillance of adverse events (not described); serious adverse events	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Patkar, 2006[266] NA	HAMD-21 CGI-S SF-12	N	Active surveillance of adverse events using SAFTEE-GI; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Perahia, 2008[267] NA	HAMD-17 CGI-S CGI-I	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events	Y EQ-5D, SQ-SS, SF-36, and VAS	N	N
Philip, 2016[268] NA	HAMD-24 CGI-S MADRS IDS-SR PHQ-9	Y	Passive surveillance of adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Pilu, 2007[269] Carta, 2008[270] NA	HAMD-17 CGI-S GAF	N	Not reported	Not reported	Y WHOQOL-BREF	N	N
Price, 2010[271] NA	HAMD-17 BDI	N	Passive surveillance of adverse events reported; overall adverse event rates	Not reported	N	N	N
Puigdemont, 2015[272] Puigdemont, 2012[273] NA	HAMD-17 CGI-I MADRS	Y	Overall adverse event rates	Overall attrition	N	N	N
Quante, 2011[274] NA	HAMD-28 BDI MADRS Young Mania Rating Scale	N	Active surveillance of adverse events (cognitive function only) using Verbal Learning Recognition Memory Test, Wechsler Memory Scale, Regensburger Wortflüssigkeits-Test (for attention and executive function)	Not reported	N	N	N
Rapaport, 2006[275] Alexopoulos, 2008[276] NA	HAMD-17 CGI-S CGI-I MADRS	Y	Adverse events reported (cannot determine surveillance); overall adverse event rates	Overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Ravindran, 2008[277] Rizvi, 2014[278] NA	CGI-I MADRS	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y SEX-FX sex effects scale	N	N
Reynolds, 2010[279] Greenlee, 2010[280] NA	HAMD-17	N	Not reported	Overall attrition, attrition due to lack of efficacy	N	N	N
Rossini, 2005[281] NA	HAMD-21 CGI-S CGI-I	N	Adverse events reported (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Rosso, 2012[282] NA	HAMD-17 CGI-S CGI-I GAF	N	Not reported	Overall attrition, attrition due to adverse events	N	N	N
Ruhe, 2009[283] NA	HAMD-17 IDS-SR Multidimensional Assessment of Fatigue	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Rush, 2005[284] Burke, 2006[285] George, 2005[286] NA	HAMD-24 CGI-S CGI-I MADRS IDS-CR SF-36 YMRS	N	Adverse events reported (cannot determine surveillance); serious adverse events	Overall attrition, attrition due to adverse events	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Rush, 2006[287] Rush, 2004[294] Rush, 2008[288] Gaynes, 2012[289] Hansen, 2012[290] Gaynes, 2011[291] Perlis, 2012[292] Warden, 2009[293] STAR*D	HAMD-17 QIDS-SR	N	Active surveillance of adverse events using FIBSER; serious adverse events; overall adverse event rates	Adherence to treatment, attrition due to adverse events	N	N	N
Rybakowski, 2016;[295] NA	HAMD-17	N	Active surveillance of adverse events (cognitive function only) using Benton visual retention test, Trail making test, Rey-Osterrieth complex figure test, Digit span (from Wechsler Adult Intelligence Scale), AVLT, Verbal fluency test, Stroop test	Not reported	N	N	N
Sackeim, 2009[296] NA	HAMD-24 BDI-SF CGI-S CGI-I	Y	Passive surveillance of adverse events reported; serious adverse events; overall adverse event rates	Not reported	N	N	N
Schindler, 2007[297] NA	HAMD-17 CGI-S CGI-I	N	Adverse events reported (cannot determine surveillance); serious adverse events	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Schoeyen, 2015[298] Kessler, 2014[299] NA	CGI-S CGI-I MADRS IDS-SR IDS-CR YMRS	N	Active surveillance of adverse effects using UKU; serious adverse events; overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Schulze, 2017[300] NA	HAMD-17 BDI	N	Not reported	Not reported	N	N	N
Schulze-Rauschenbach, 2005[301] NA	HAMD-17 BDI	N	Active surveillance of adverse events (cognitive function only) using AVLT, Memory for Persons Test, Autobiographical Memory Interview, Retrograde AVLT, Four-card task (recall and recognition of depicted objects), Squire Subjective Memory Questionnaire, MMSE, Trail Making Test, Digit span (Wechsler Adult Intelligence Scale), Letter-number span, Word fluency: Leistungs-Pruf-System	Attrition due to adverse events	N	N	N
Sharma, 2017[302] NA	HAMD-6 BDI-II	N	Not reported	Not reported	N	N	N
Shelton, 2005[303] NA	CGI-S MADRS	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Sienaert, 2009[304] Sienaert, 2010[305] NA	HAMD-17 BDI-II CGI-S CGI-I	N	Not reported	Overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Singh, 2015[306] NA	CGI-S CGI-I MADRS QIDS-SR	N	Active surveillance of adverse events reported using safety assessments that included TEAEs, clinical laboratory tests, 12-lead electrocardiogram, vital signs, physical examinations, C-SSRS, CADSS, BPRS, and MGH-CPFQ; serious adverse events; overall adverse events	Overall attrition, attrition due to adverse events	N	N	N
Singh, 2016[307] NA	CGI-S CGI-I MADRS	N	Active surveillance of adverse events (not described); serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Souery, 2011[308] NA	CGI-S CGI-I MADRS	N	Not reported	Overall attrition, attrition due to adverse events	N	N	N
Souery, 2011[309] NA	HAMD-17	N	Not reported	Not reported	N	N	N
Speer, 2009[310] NA	HAMD-28	N	Not reported	Overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Speer, 2014[311] NA	HAMD-28	N	Not reported	Not reported	N	N	N
Sperling, 2009[312] NA	HAMD-28	N	Not reported	Adherence to treatment	N	Y	Y
Stalsett, 2012[313] NA	BDI SCL-90R	N	None reported	Overall attrition	N	N	N
Straaso, 2014[314] NA	HAMD-6 HAMD-17	N	Active surveillance of adverse events using UKU side effect rating scale and PRISE	Adherence to treatment, overall attrition, attrition due to lack of efficacy	Y WHO-5 well-being scale	N	N
Thase, 2006[315] NA	HAMD-21 CGI-S CGI-I	N	Adverse events reported (cannot determine surveillance)	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	N	N	N
Thase, 2007[316] NA	CGI-S MADRS BPRS SF-36 SDS	N	Adverse events reported (cannot determine surveillance); overall adverse event rates	Overall attrition, attrition due to adverse events, attrition due to lack of efficacy	Y SF-36	Y	N
Theleritis, 2017[317] NA	HAMD-17 CGI-S	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Adherence to treatment, overall attrition, attrition due to adverse events	N	N	N
Town, 2017[318] NA	HAMD-17 PHQ-9	N	Passive surveillance of adverse events; serious adverse events; overall adverse event rates	Overall attrition	N	N	N
Triggs, 2010[319] NA	HAMD-24	N	Passive surveillance of adverse events; serious adverse events	Overall attrition	N	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Trivedi, 2006[320] Rush, 2004[294] Thase, 2007[321] Rush, 2008[288] Gaynes, 2012[289] STAR*D	HAMD-17 QIDS-SR	N	Active surveillance of adverse events using FIBSER; serious adverse events; overall adverse event rates	Adherence to treatment	N	N	N
Trivedi, 2011[322] Greer, 2016[323] Suterwala, 2016[324] NA	HAMD-17 QIDS-SR IDS-CR SF-36 Q-LES-Q	N	Not reported	Overall attrition, attrition due to adverse events	Y SF-36, SAS-SR, and the Q-LES-Q	N	N
Trojak, 2014[325] NA	HAMD-21 MADRS	N	Active surveillance of adverse events using UKU; overall adverse event rates	Overall attrition	N	N	N
Turnier-Shea, 2006[326] NA	HAMD-17	N	Not reported	Not reported	N	N	N
van den Broek, 2006[327] NA	HAMD-17 CGI-I	N	Not reported	Not reported	N	N	N
Watkins, 2011[328] NA	HAMD-17 BDI-II SCID	N	None reported	Adherence to treatment, overall attrition	N	N	N
Wiles, 2008[329] NA	BDI	N	None reported	Adherence to treatment, overall attrition	Y Patient out-of-pocket expenses	N	Y
Wiles, 2013[330] Wiles, 2014[331] Hollinghurst, 2014[332] Wiles, 2016[333] NA	BDI-II SF-12 PHQ-9 GAD-7	N	None reported	Adherence to treatment, overall attrition	Y SF-12	N	N

Table C7. Endpoint data from key question 11 (continued)

Author, Year Study Name	Scales of Treatment Success and Failure from Narrative Question 3	Time to Relapse (Durability - Y/N)	List Any of the Following Reported: Adverse Events (If *Active Surveillance* of Adverse Events, Describe), Serious AEs, Overall AE Rates	List Any of the Following Reported: Adherence to Treatment, Overall Attrition, Attrition Due to AEs, Attrition Due to Lack of Efficacy	Improvement in or Worsening of Patient-Selected Factors of Importance (Y/N) If Yes, Description	Improvement in or Worsening of Employment or Disability Status (Y/N)	Improvement in or Worsening of Use of Medical Resources (Y/N)
Xu, 2015[334] NA	MADRS	N	Not reported	Not reported	N	N	N
Zarate, 2006[335] NA	HAMD-21 BDI BPRS YMRS	N	Passive surveillance of adverse events reported; serious adverse event rates	Overall attrition, attrition due to adverse events	N	N	N
Zarate, 2012[336] NA	HAMD-17 BDI MADRS	N	Adverse events (cannot determine surveillance); serious adverse events; overall adverse event rates	Overall attrition	N	N	N

AE = Adverse Event; AIMS = Abnormal Involuntary Movement Scale; ASEX = Arizona Sexual Experience Scale; AVLT = Auditory Verbal Learning Test; BARS = Barnes Akathisia Rating Scale; BDI = Beck Depression Inventory; BP = Blood Pressure; BPRS = Brief Psychiatric Rating Scale; CADSS = Clinician Administered Dissociative States Scale; CAM = complementary and alternative medicine; CSSRS = Columbia-Suicide Severity Rating Scale; CGI = Clinical Global Impressions Scale (S= severity, I = improvement); CORE-OM = Clinical Outcomes in Routine Evaluation – Outcome Measures; DIEPSS = Drug-Induced Extrapyramidal Symptoms Scale; EQ-5D = EuroQoL Health Utility Index; FIBSER = Frequency, Intensity, and Burden of Side Effects Rating; GAF = Global Assessment of Functioning Scale; GRSEB = Global Rating of Side Effect Burden; HAM-D = Hamilton Rating Scale for Depression; HR = Heart Rate; IDS = Inventory of Depressive Symptomatology (C = clinician rated, SR = self-rated; LIFE-RIFT = Range of Impaired Function Tool; MADRS = Montgomery–Åsberg Depression Rating Scale; MGH-CPFQ = Massachusetts General Hospital-Cognitive and Physical Functioning Questionnaire; MMSE = Mini–Mental State Examination; NR = Not Reported; PATH-D = Practicing Alternative Techniques to Heal From Depression; PRISE = Patient Related Inventory of Side Effects; QIDS = Quick Inventory of Depressive Symptomatology (C = Clinician Rated, SR = Self Rated); Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire (SF = Short Form); REVAMP = Research Evaluating the Value of Augmenting Medication with Psychotherapy; SAFTEE = Systematic Assessment for Treatment Emergent Events (GI = General Inquiry, SI = Systematic Inquiry); SAS = Simpson-Angus Scale; SAS-SR = Social Adjustment Scale-Self-Report; SDS = Sheehan Disability Scale; SES = Symptoms, Sign, Side-Effect Checklist; SEX-FX = Sex Effects Scale; SF = Short-Form Health Survey (36-Item or 12-Item); SFI = Sexual Function Inventory; SOS-10 = Schwartz Outcome Scale-10; SQ-SS = Symptom Questionnaire-Somatic Subscale; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; TADS = Tavistock Adult Depression Study; TEAEs = Treatment-Emergent Adverse Events; UKU = Udvalg for Kliniske Undersøgelser Side Effect Rating Scale; VAS = Visual Analogue Scales; WHO-5 = WHO Well-Being Index; WHOQOL-BREF = World Health Organization Quality of Life Instrument; YMRS = Young Mania Rating Scale.

Appendix D. Risk of Bias Ratings

Table D1. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis

Author, Year Study	Randomization adequate?	Allocation concealment adequate?	Baseline characteristics similar? (Especially With Regard to KQ10 Patient-Level Covariates)	Outcome assessors masked?	Care providers masked?	Patients masked?	% Completed Treatment
Altamura, 2008[143] NA	Unclear	Unclear	No	Yes	No	Yes	Overall: 100 G1: 100 G2: 100
Avery, 2006[145] NA	Yes	Unclear	Yes	Yes	No	Yes	Overall: 91 G1: 91 G2: 91
Barbee, 2011[150] NA	Yes	Yes	No	Yes	Yes	Yes	Overall: 68 G1: 71 G2: 65
Berman, 2007[159] NA	Unclear	Yes	Yes	Yes	Yes	Yes	Overall: 88 G1: 90.9 G2: 87.9
Berman, 2009[160] NA	Unclear	Unclear	Yes	Yes	Unclear	Yes	Overall: 85 G1: 83 G2: 87
Blumberger, 2012[161] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 59 G1: 64 G2: 46 G3: 68
Blumberger, 2016[162] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 84 G1: 83 G2: 83 G3: 85
Concerto, 2015[170] NA	Unclear	Unclear	Yes	Unclear	No	Yes	Overall:100 G1: 100 G2: 100
Cusin, 2013[172] NA	Unclear	Yes	No	Unclear	Yes	Yes	Overall: 70 G1: 73 G2: 67

Table D1. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis (continued)

Author, Year Study	Randomization adequate?	Allocation concealment adequate?	Baseline characteristics similar? (Especially With Regard to KQ10 Patient-Level Covariates)	Outcome assessors masked?	Care providers masked?	Patients masked?	% Completed Treatment
Durgam, 2016[180] NA	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 82 G1: 76 G2: 83 G3: 87
El-Khalili, 2010[183] NA	Yes	Unclear	Yes	Unclear	Unclear	Yes	Overall: 77 G1: 77 G2: 70 G3: 85
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 88 G1: 86 G2: 90
Fitzgerald, 2006[191] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 94 G1: 100 G2: 88
Fitzgerald, 2008[193] NA	Unclear	Unclear	Yes	Yes	No	Yes	Overall: 94 G1: 100 G2: 88
Fitzgerald, 2016[200] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 87 G1: 83 G2: 91
Garcia-Toro, 2006[204] NA	Unclear	Unclear	Unclear	Yes	No	Yes	Overall: 100 G1: 100 G2: 100
George, 2010[205] McDonald, 2011[206] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 81 G1: 78 G2: 83
Kamijima, 2013[213] Ozaki, 2015[214] NA	Unclear	Yes	Yes	Yes	No	Yes	Overall: 92 G1: 92 G2: 91 G3: 91

Table D1. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis (continued)

Author, Year Study	Randomization adequate?	Allocation concealment adequate?	Baseline characteristics similar? (Especially With Regard to KQ10 Patient-Level Covariates)	Outcome assessors masked?	Care providers masked?	Patients masked?	% Completed Treatment
Keitner, 2009[216] NA	Unclear	Unclear	No	Yes	No	Yes	Overall: 86 G1: NR G2: NR
Lenze, 2015[226] Kaneriya, 2016[227] NA	Yes	Yes	Unclear	Yes	No	Yes	Overall: 94 G1: 96 G2: 92
Levkovitz, 2015[230] NA	Yes	Yes	Yes	Yes	Yes	Yes	5 week (primary endpoint) Overall: 88 G1: 92 G2: 86 End of study Overall: 39 G1: 48 G2: 30
Mahmoud, 2007[232] NA	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 85 G1: 81 G2: 88
Martinot, 2010[233] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 96 G1: 94 G2: 95 G3: 100
McDonald, 2006[236] NA	Unclear	Unclear	No	Yes	Unclear	Yes	Overall: NR G1: NR G2: NR
Mogg, 2008[240] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 93 G1: 97 G2: 90

Table D1. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis (continued)

Author, Year Study	Randomization adequate?	Allocation concealment adequate?	Baseline characteristics similar? (Especially With Regard to KQ10 Patient-Level Covariates)	Outcome assessors masked?	Care providers masked?	Patients masked?	% Completed Treatment
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	Unclear	Unclear	Yes	Yes	Yes	Yes	Full Sample Overall: 86 G1: 87 G2: 84 Modified ITT sample Overall: 92 G1: 92 G2: 92
Paillere Martinot, 2010[257] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 96 G1: 94 G2: 100 G3: 95
Pallanti, 2010[258] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 100 G1: 100 G2: 100 G3: 100
Papakostas, 2015[264] Mischoulon, 2017[265] NA	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 73 G1: 69 G2: 78
Ravindran, 2008[277] NA	Unclear	Unclear	Yes	Yes	Unclear	Yes	Overall: 90 G1: 85 G2: 94
Rossini, 2005[281] NA	Yes	Yes	Yes	Yes	No	Yes	Overall: 96 G1: 95 G2: 100 G3: 94

G = Group; ITT = Intention to Treat; KQ = Key Question; NR = Not Reported; TRD = Treatment Resistant Depression

Table D2. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis, part 2

Author, Year Study	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Method of Handling Dropouts in ITT Analysis	Could selective reporting of outcomes be an issue?	Other bias?	Risk of Bias	Notes Explain High Risk of Bias Ratings
Altamura, 2008[143] NA	No	No	Yes	NA	No	Yes	Medium	NA
Avery, 2006[145] NA	No	No	Yes	LOCF	No	No	Low	NA
Barbee, 2011[150] NA	Yes	No	Yes	LOCF	No	No	Medium	NA
Berman, 2007[159] NA	No	No	Yes	LOCF	No	Unclear	Low	NA
Berman, 2009[160] NA	No	No	Yes	LOCF	No	No	Low	NA
Blumberger, 2012[161] NA	Yes	Yes	Yes	Not reported	No	No	High	Unclear
Blumberger, 2016[162] NA	No	No	Yes	Not reported	No	No	Low	NA
Concerto, 2015[170] NA	No	No	N/A	NA	No	No	High	Blinding of outcome assessor not clear
Cusin, 2013[172] NA	Yes	No	Yes	LOCF	No	No	Medium	NA
Durgam, 2016[180] NA	No	No	Yes	Not reported	No	Unclear	Low	NA
El-Khalili, 2010[183] NA	Yes	No	Yes	LOCF	No	No	Medium	NA

Table D2. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis, part 2 (continued)

Author, Year Study	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Method of Handling Dropouts in ITT Analysis	Could selective reporting of outcomes be an issue?	Other bias?	Risk of Bias	Notes Explain High Risk of Bias Ratings
Fava, 2012[186] Dording, 2013[187] Mischoulon, 2012[188] NA	No	No	Yes	LOCF	No	No	Low	NA
Fitzgerald, 2006[191] NA	No	No	Yes	LOCF	No	No	Low	NA
Fitzgerald, 2008[193] NA	No	No	Yes	LOCF	No	No	Low	NA
Fitzgerald, 2016[200] NA	No	No	Yes	LOCF	No	Unclear	Low	NA
Garcia-Toro, 2006[204] NA	No	No	No	NA	Unclear	No	Medium	NA
George, 2010[205] McDonald, 2011[206] NA	no	No	Yes	Not reported	No	No	Low	NA
Kamijima, 2013[213] Ozaki, 2015[214] NA	No	No	Yes	LOCF	No	Unclear	Low	NA
Keitner, 2009[216] NA	No	Unclear	Yes	Not reported	No	No	Medium	NA
Lenze, 2015[226] Kaneriya, 2016[227] NA	No	No	Yes	Not reported	No	No	Medium	NA
Levkovitz, 2015[230] NA	No	No	Yes	LOCF	No	Unclear	Medium	NA

Table D2. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis, part 2 (continued)

Author, Year Study	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Method of Handling Dropouts in ITT Analysis	Could selective reporting of outcomes be an issue?	Other bias?	Risk of Bias	Notes Explain High Risk of Bias Ratings
Mahmoud, 2007[232] NA	No	No	Yes	LOCF	No	No	Low	NA
Martinot, 2010[233] NA	No	No	Yes	Modified ITT	No	No	Low	NA
McDonald, 2006[236] NA	Unclear	Unclear	Unclear	Not reported	No	Yes	High	Unclear if care providers blinded to treatment assignment, in particular whether providers or technicians set up the TMS/placebo procedure. Procedure for collecting all measures was inconsistent, sometimes collected by patients and sometimes collected by research assistants. Not possible to determine direction of potential bias resulting from this. Information on treatment completion, attrition, missing data are poorly reported, making it difficult to be confident about these elements. It is possible (but unclear) all participants completed treatment, but data missing for about 18% of sample. Although authors state that they used ITT analyses, lack of clear reporting of dropouts or missing data makes it difficult to confirm that a true ITT analysis was performed.

Table D2. Risk of bias assessments for TRD studies eligible for Key Question 10 regression analysis, part 2 (continued)

Author, Year Study	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Method of Handling Dropouts in ITT Analysis	Could selective reporting of outcomes be an issue?	Other bias?	Risk of Bias	Notes Explain High Risk of Bias Ratings
Mogg, 2008[240] NA	No	No	Yes	Not reported	No	Unclear	Medium	NA
O'Reardon, 2007[253] Lisanby, 2009[254] Solvason, 2014[255] Janicak, 2008[256] NA	No	No	Yes	LOCF	Yes	No	Medium	NA
Paillere Martinot, 2010[257] NA	No	No	Yes	LOCF	No	No	Low	NA
Pallanti, 2010[258] NA	No	No	No	NA	No	No	Low	NA
Papakostas, 2015[264] Mischoulon, 2017[265] NA	Yes	No	Yes	Not reported	No	Unclear	Medium	NA
Ravindran, 2008[277] NA	No	No	Yes	Not reported	No	Unclear	Low	NA
Rossini, 2005[281] NA	No	No	No	NA	No	Unclear	Low	NA

ITT = Intention to Treat; LOCF = Last Observation Carried Forward; NA = Not Applicable; TRD = Treatment Resistant Depression; TMS = Transcranial Magnetic Stimulation.