Pharmacological Treatments for Borderline Personality Disorder: A Systematic Review and Meta-analysis Supplementary Material

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Journal: CNS Drugs

Supplementary Material

Supplementary Material Table 1: Search Strategy

APA Original Search Strategy

Search Date: June 7, 2018

PubMed:

Search	Query	Results
#1	("Borderline Personality Disorder"[Mesh]) OR (borderline [tiab] AND personality [tiab])	8962
#2	("animals"[MeSH Terms] OR animal [tiab] OR animals [tiab] OR rat [tiab] OR rats [tiab] OR mouse [tiab] OR mice [tiab] OR rodent [tiab] OR rodents [tiab]) NOT ("humans"[MeSH Terms] OR humans [tiab] OR human [tiab])	4419530
#3	#1 NOT #2	8957
	Limit to English	7983

EMBASE:

Search	Query	Results
#1	exp *borderline state/ or (borderline and personality).ti. or (borderline and personality).ab.	11073
#2	limit #1 to (article or article in press or conference paper)	7571
#3	#2 not ((exp animal/ or nonhuman/) not exp human/)	7564
#4	#2 not ((animal or animals or rat or rats or mouse or mice or rodent or rodents) not (humans or human)).ti,ab.	7548
#5	#3 or #4	7569
#6	limit #5 to yr="1883 - 2002"	2765
#7	limit #5 to yr="2002 - Current"	4929
#8	remove duplicates from #6	2740
#9	remove duplicates from #7	4739
#10	#8 or #9	7337
#11	limit #10 to english language	6356

Cochrane Library:

Search	Query	Results
#1	MeSH descriptor: [Borderline Personality Disorder] explode all trees	390
#2	borderline and personality:ti,ab,kw (Word variations have been searched)	684
#3	#1 or #2	684
#4	#3 not (pubmed or embase):an	145 in trials 6 in Cochrane reviews 9 in Other reviews

PsycINFO:

Search	Query	Limiters/Expanders	Results
S1	MM "Borderline Personality Disorder"		5,220
S2	DE "Borderline Personality Disorder"		7,857
S3	MA "borderline personality disorder"		4,192
S4	TI "borderline personality" OR AB "borderline personality" OR SU "borderline personality" OR KW "borderline personality"		11,400
S5	S1 OR S2 OR S3 OR S4		11,400
S6	(MM "Animals" OR DE "Animals" OR DE "Vertebrates" OR DE "Amphibia" OR DE "Birds" OR DE "Fishes" OR DE "Mammals" OR DE "Pigs" OR DE "Reptiles" OR DE "Rats" OR DE "Rodents" OR DE "Mice")		329,022
S7	TI "animals" OR TI "animal" OR TI "mouse" OR TI "mice" OR TI "rodent" OR TI "rodents" OR TI "rat" OR TI "rats" OR SU "animals" OR SU "animal" OR SU "mouse" OR SU "mice" OR SU "rodent" OR SU "rodents" OR SU "rat" OR SU "rats" OR KW "animals" OR KW "animal" OR KW "mouse" OR KW "mice" OR KW "rodent" OR KW "rodents" OR KW "rat" OR KW "rats" OR AB "animals" OR AB "animal" OR AB "mouse" OR AB "mice" OR AB "rodent" OR AB "rodents" OR AB "rat" OR AB "rats"		426,155
S8		Limiters - Population Group: Animal	385,743
S9	S6 OR S7 OR S8		459,805
S10		Limiters - Population Group: Human	3,780,890
S11	TI "humans" OR TI "human" OR AB "humans" OR AB "human" OR SU "humans" OR SU "human" OR KW "humans" OR KW "human"		1,585,426
S12	S10 OR S11		3,888,530
S13	S9 NOT S12		310,376
S14	S5 NOT S13		11,398
S15		Limiters - Publication Type: All Journals	3,518,961
S16	S14 AND S15		9,386
S17	LA English		4,207,720
S18	S16 AND S17		8,116

RTI Search Strategy

Search Date: June 15, 2020

PubMed:

Search	Query	Results
#1	"Borderline Personality Disorder"[Mesh] OR "Borderline Disorder"[ti] OR "Borderline Personality Disorder"[tiab] OR "borderline-patient"[ti] OR "borderline patient"[ti] OR "borderline-patients"[ti] OR "borderline patients"[ti]	8,693
#2	#1 AND ("2018/01/01"[Date - Publication] : "3000"[Date - Publication])	1,202
#3	#2 AND English[lang]	1,161

EMBASE

Search	Query	Results
#1	('borderline state'/de OR 'borderline disorder':ti OR 'borderline-patient':ti OR 'borderline patient':ti OR 'borderline-patients':ti OR 'borderline patients':ti OR 'borderline personality disorder':ti,ab,kw) AND [2018-2020]/py AND [english]/lim	1,777
#2	'borderline personality disorder':ti,kw AND [english]/lim AND [1-1-2018]/sd	990
#3	#1 OR #2	1,924

Cochrane Library

Search	Query	Results
#1	("Borderline Disorder" OR "Borderline Personality Disorder" OR "borderline-patient" OR "borderline patient" OR "borderline-patients" OR "borderline patients"):ti,ab,kw OR [mh "Borderline Personality Disorder"]	851
#2	#1 with Cochrane Library publication date from Jan 2018 to present, in Cochrane Reviews, Cochrane Protocols, Trials, Clinical Answers, Editorials and Special collections	412

APA PsycInfo (via ProQuest)

Search	Query	Results
#1	if("Borderline Personality Disorder") OR mjsub("Borderline Personality Disorder") OR mainsubject("Borderline Personality Disorder") OR ti("Borderline Personality Disorder" OR "Borderline Disorder" OR "borderline-patient" OR "borderline patient" OR "borderline-patients" OR "borderline patients") OR ab("Borderline Personality Disorder") *Additional limits - Date: After January 01 2018; Language: English*	986

RTI Update Search Strategy

Search Date: April 6, 2021

The update search was limited to databases that yielded studies during the original searches that met our inclusion criteria.

PubMed:

Search number	Query	Results
1	"Borderline Personality Disorder"[Mesh] OR "Borderline Disorder*"[ti] OR "Borderline Personality Disorder*"[tiab] OR "borderline patient"[ti] OR "borderline patients"[ti]	9,260
2	#1 NOT ("Animals"[Mesh] NOT "Humans"[Mesh])	9,258
3	(#2) AND (("2020"[Date - Publication] : "3000"[Date - Publication]))	744

APA PsychInfo:

#	Query	Limiters/Expanders	Results
S1	DE "Borderline Personality Disorder"	Search modes - Boolean/Phrase	8,991
S2	borderline W1 (disorder# OR patient#)	Search modes - Boolean/Phrase	13,511
S3	S1 OR S2	Search modes - Boolean/Phrase	13,511
S4	S3	Limiters - Publication Year: 2020-2021; Language: English	510

Supplementary Material Table 2: Inclusion and Exclusion Criteria

Criteria	Include		Exclude

Participants / population	• Age ≥13
	• Diagnosed with BPD as defined by DSM-IV, DSM-IV-TR, DSM-5 (Section II or Section III), or ICD-10
	• For mixed population studies, BPD must account for >=75% of the total population
	• Subgroups of interest
	  ○ Co-occurring mental disorder
	  ○ Age
	  ○ Gender
	  ○ Race/ Ethnicity
	  ○ Genotypes (related to treatment selection, treatment response or adverse effects)
			• Age <13
			• Individuals with borderline traits without a specific diagnosis
			• Diagnosed with BPD as defined by DSM-III-R
			• Studies in which the primary research focus is a different diagnosis with co-occurring BPD in a subset (<75% of the total population)

Intervention(s) / exposure(s)	○ **Anticonvulsant "mood stabilizers":**
	  – Carbamazepine
	  – Divalproex Sodium
	  – Gabapentin
	  – Lamotrigine
	  – Levetiracetam
	  – Oxcarbazepine
	  – Phenytoin
	  – Pregabalin
	  – Tiagabine
	  – Topiramate
	  – Valproate
	  – Valproic Acid
	  – Vigabatrin
	  – Zonisamide
	○ **Antipsychotics:**
	  – Aripiprazole
	  – Asenapine
	  – Chlorpromazine
	  – Clozapine
	  – Fluphenazine
	  – Haloperidol
	  – Iloperidone
	  – Loxapine
	  – Lurasidone
	  – Olanzapine
	  – Paliperidone
	  – Perphenazine
	  – Pimozide
	  – Prochlorperazine
	  – Quetiapine
	  – Risperidone
	  – Thioridazine
	  – Thiothixene
	  – Trifluoperazine
	  – Ziprasidone
		○ **Antidepressants:**
		  – Amitriptyline
		  – Amoxapine
		  – Bupropion
		  – Citalopram
		  – Clomipramine
		  – Desipramine
		  – Desvenlafaxine
		  – Doxepin
		  – Duloxetine
		  – Escitalopram
		  – Fluoxetine
		  – Fluvoxamine
		  – Impiramine
		  – Isocarboxazid
		  – Maprotiline
		  – Mirtazapine
		  – Milnacipran
		  – Nefazodone
		  – Nortriptyline
		  – Paroxetine
		  – Phenelzine
		  – Protriptyline
		  – Sertraline
		  – Selegiline
		  – Tranylcypromine
		  – Trazodone
		  – Trimipramine
		  – Venlafaxine
		  – Vilazodone
		  – Vortioxetine
		  –
			• Complementary/alternative treatments
			• Somatic therapies
			• Psychotherapies
			• Other Pharmacotherapies

	○ **Benzodiazepines:**
	  – Alprazolam
	  – Clobazam
	  – Clonazepam
	  – Clorazepate
		○ **Opioid agonists and antagonists:**
		  – Buprenorphine
		  – Naloxone
		  – Naltrexone	

Criteria	Include		Exclude
	– Chlordiazepoxide Diazepam – Estazolam – Flurazepam – Lorazepam – Midazolam – Oxazepam – Quazepam – Temazepam – Triazolam	○ **Sedative-hypnotic medications:** – Eszopiclone – Ramelteon – Suvorexant – Tasimelteon – Zaleplon – Zolpidem ○ **Melatonin**	
Comparator(s) / control	• Interventions listed above for inclusion • Placebo		Interventions listed as excluded above for interventions/exposures
Outcomes	**Pre-specified outcomes** A. BPD symptoms/diagnostic criteria 1. Frantic efforts to avoid real or imaginary abandonment 2. Pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation 3. Identity disturbances: markedly and persistent unstable self-image or sense of self 4. Impulsivity a. Impulsivity b. Impulsive/behavioral c. Risk taking behaviors d. Lack of restraint 5. Recurrent suicidal behavior, gestures or threats; or self-mutilating behavior a. Nonsuicidal self-injury b. Suicide attempts c. Suicide d. Suicidal ideation e. Self-destructive behavior 6. Affective instability, due to a marked reactivity of mood a. Irritability b. Mood swings c. Affective dysregulation 7. Chronic feelings of emptiness 8. Inappropriate intense anger or difficulty controlling anger a. Aggression b. Anger c. Hostility d. Aggressive behavior e. Antisocial behavior 9. Transient, stress-related paranoid ideation, or severe dissociative symptoms a. Dissociation B. Other symptoms commonly found in individuals with BPD, but not part of the diagnostic criteria. 1. Depression and Anxiety C. Clinical Global Impression D. Functioning E. Adverse Events (AEs) a. Rate of any AEs b. Overall serious treatment-related adverse event rate c. Specific serious treatment-related adverse events d. Study withdrawal due to AE • Study withdrawal for any reason		Outcomes not listed, imaging markers, and physiological markers, biomarkers Outcomes that were not pre-specified, e.g., during post-hoc, exploratory analyses

Criteria	Include	Exclude
Timing	• Treatment duration >=8 weeks	Treatment duration <8 weeks
Setting/context	• Very high Human Development Index (HDI) Countries*	All other countries

Study design	• RCTs phase 2 | 3 | 4
	• Nonrandomized clinical trials (N>=50):
	  ○ Phase 1 | 2 | 3 | 4
	• Observational studies, comparative (N>=50)
	  ○ Cross-sectional
	  ○ Prospective cohort
	  ○ Retrospective cohort
	  ○ Nonconcurrent cohort
	  ○ Case-control
	• Pooled analyses of controlled studies
		• Single-arm dose-finding trials
		• Observational, noncomparative
		• Case reports/series
		• Prognostic course/factor studies
		• Modeling studies
		• Pre-clinical
		• Narrative reviews
		• Systematic reviews/meta-analyses (will be used for hand searches)

***Very High HDI Countries:** Andorra, Argentina, Australia, Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Brunei Darussalam, Bulgaria, Canada, Chile, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hong Kong, China (SAR), Hungary, Iceland, Ireland, Israel, Italy, Japan, Kazakhstan, Korea (Republic of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Montenegro, Netherlands, New Zealand, Norway, Oman, Poland, Portugal, Qatar, Romania, Russian Federation, Saudi Arabia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Taiwan**, United Arab Emirates, United Kingdom, United States, Uruguay.

** The United Nations does not recognize Taiwan (i.e., Republic of China) as a sovereign state and does not include it in the HDI report. However, Taiwan's government calculated its HDI to be 0.885, based on 2014 data and using the same methodology as the United Nations. This HDI value would place Taiwan among countries in the "very high" human development category and will be included in this report.

Abbreviations: BPD, borderline personality disorder; KQ, key question; N, sample size; NA, not applicable; RCT, randomized controlled trial.

Supplementary Material Table 3: Excluded Studies at Full Text Level

List of Exclusion Codes:
X1: Ineligible population
X2: Ineligible intervention
X3: Ineligible comparator
X4: Ineligible outcome
X5: Ineligible timing
X6: Ineligible study design
X7: Duplicate or superseded by paper publication
X8: Non-English full text
X9: Ineligible country
X10: Not primary research

1. Amianto F, Ferrero A, Pierò A, et al. Supervised team management, with or without structured psychotherapy, in heavy users of a mental health service with borderline personality disorder: a two-year follow-up preliminary randomized study. BMC Psychiatry. 2011 Nov 21;11:181. doi: 10.1186/1471-244x-11-181. PMID: 22103890. Exclusion Code: X2.
2. Andión Ó, Ferrer M, Matali J, et al. Effectiveness of combined individual and group dialectical behavior therapy compared to only individual dialectical behavior therapy: a preliminary study. Psychotherapy (Chic). 2012 Jun;49(2):241-50. doi: 10.1037/a0027401. PMID: 22642527. Exclusion Code: X2.
3. Andreoli A, Burnand Y, Cochennec MF, et al. Disappointed Love and Suicide: A Randomized Controlled Trial of "Abandonment Psychotherapy" Among Borderline Patients. J Pers Disord. 2016 Apr;30(2):271-87. doi: 10.1521/pedi_2015_29_196. PMID: 26111250. Exclusion Code: X2.
4. Antonsen BT, Kvarstein EH, Urnes Ø, et al. Favourable outcome of long-term combined psychotherapy for patients with borderline personality disorder: Six-year follow-up of a randomized study. Psychother Res. 2017 Jan;27(1):51-63. doi: 10.1080/10503307.2015.1072283. PMID: 26261865. Exclusion Code: X1.
5. Arnevik E, Wilberg T, Urnes O, et al. Psychotherapy for personality disorders: short-term day hospital psychotherapy versus outpatient individual therapy - a randomized controlled study. Eur Psychiatry. 2009 Mar;24(2):71-8. doi: 10.1016/j.eurpsy.2008.09.004. PMID: 19097870. Exclusion Code: X1.
6. Bales DL, Timman R, Andrea H, et al. Effectiveness of Day Hospital Mentalization-Based Treatment for Patients with Severe Borderline Personality Disorder: A Matched Control Study. Clin Psychol Psychother. 2015 Sep-Oct;22(5):409-17. doi: 10.1002/cpp.1914. PMID: 25060747. Exclusion Code: X2.
7. Bales DL, Verheul R, Hutsebaut J. Barriers and facilitators to the implementation of mentalization-based treatment (MBT) for borderline personality disorder. Personality and mental health. 2017;11(2):118-31. doi: 10.1002/pmh.1368. Exclusion Code: X4.
8. Barnicot K, Crawford M. Dialectical behaviour therapy v. mentalisation-based therapy for borderline personality disorder. Psychol Med. 2019 Sep;49(12):2060-8. doi: 10.1017/s0033291718002878. PMID: 30303061. Exclusion Code: X2.
9. Barnicot K, Crawford M. Conclusions and questions from a non-randomised comparison of routine clinical services

implementing different treatment models for borderline personality disorder. Psychol Med. 2019 Dec;49(16):2812-4. doi: 10.1017/s0033291719002447. PMID: 31551098. Exclusion Code: X6.
10. Bartak A, Andrea H, Spreeuwenberg MD, et al. Effectiveness of outpatient, day hospital, and inpatient psychotherapeutic treatment for patients with cluster B personality disorders. Psychother Psychosom. 2011;80(1):28-38. doi: 10.1159/000321999. PMID: 20975324. Exclusion Code: X2.
11. Bateman A, Fonagy P. Randomized controlled trial of outpatient mentalization-based treatment versus structured clinical management for borderline personality disorder. Am J Psychiatry. 2009 Dec;166(12):1355-64. doi: 10.1176/appi.ajp.2009.09040539. PMID: 19833787. Exclusion Code: X2.
12. Bateman A, Fonagy P. Impact of clinical severity on outcomes of mentalisation-based treatment for borderline personality disorder. Br J Psychiatry. 2013 Sep;203(3):221-7. doi: 10.1192/bjp.bp.112.121129. PMID: 23887998. Exclusion Code: X6.
13. Bateman A, O'Connell J, Lorenzini N, et al. A randomised controlled trial of mentalization-based treatment versus structured clinical management for patients with comorbid borderline personality disorder and antisocial personality disorder. BMC Psychiatry. 2016 Aug 30;16(1):304. doi: 10.1186/s12888-016-1000-9. PMID: 27577562. Exclusion Code: X6.
14. Beck E, Bo S, Jørgensen MS, et al. Mentalization-based treatment in groups for adolescents with borderline personality disorder: A randomized controlled trial. Journal of Child Psychology and Psychiatry. 2020 May 2020 2020-05-18;61(5):594-604. doi: http://dx.doi.org/10.1111/jcpp.13152. PMID: 2313759274; 2019-68407-001. Exclusion Code: X7.
15. Beck E, Bo S, Jorgensen MS, et al. Mentalization-based treatment in groups for adolescents with borderline personality disorder: a randomized controlled trial. J Child Psychol Psychiatry. 2020 May;61(5):594-604. doi: 10.1111/jcpp.13152. PMID: 31702058. Exclusion Code: X2.
16. Bellino S, Bozzatello P, Rocca G, et al. Efficacy of omega-3 fatty acids in the treatment of borderline personality disorder: a study of the association with valproic acid. J Psychopharmacol. 2014 Feb;28(2):125-32. doi: 10.1177/0269881113510072. PMID: 24196948. Exclusion Code: X2.
17. Bellino S, Rinaldi C, Bogetto F. Adaptation of interpersonal psychotherapy to borderline personality disorder: a comparison of combined therapy and single pharmacotherapy. Can J Psychiatry. 2010 Feb;55(2):74-81. doi: 10.1177/070674371005500203. PMID: 20181302. Exclusion Code: X2.
18. Bellino S, Zizza M, Rinaldi C, et al. Combined treatment of major depression in patients with borderline personality disorder: a comparison with pharmacotherapy. Can J Psychiatry. 2006 Jun;51(7):453-60. doi: 10.1177/070674370605100707. PMID: 16838827. Exclusion Code: X2.
19. Bellino S, Zizza M, Rinaldi C, et al. Combined therapy of major depression with concomitant borderline personality disorder: comparison of interpersonal and cognitive psychotherapy. Can J Psychiatry. 2007 Nov;52(11):718-25. doi: 10.1177/070674370705201106. PMID: 18399039. Exclusion Code: X2.
20. Berthoud L, Pascual-Leone A, Caspar F, et al. Leaving Distress Behind: A Randomized Controlled Study on Change in Emotional Processing in Borderline Personality Disorder. Psychiatry. 2017 Summer;80(2):139-54. doi: 10.1080/00332747.2016.1220230.

PMID: 28767333. Exclusion Code: X6.
21. Bianchini V, Cofini V, Curto M, et al. Dialectical behaviour therapy (DBT) for forensic psychiatric patients: An Italian pilot study. Crim Behav Ment Health. 2019 Apr;29(2):122-30. doi: 10.1002/cbm.2102. PMID: 30648303. Exclusion Code: X2.
22. Blum N, St John D, Pfohl B, et al. Systems Training for Emotional Predictability and Problem Solving (STEPPS) for outpatients with borderline personality disorder: a randomized controlled trial and 1-year follow-up. Am J Psychiatry. 2008 Apr;165(4):468-78. doi: 10.1176/appi.ajp.2007.07071079. PMID: 18281407. Exclusion Code: X2.
23. Bohus M, Haaf B, Simms T, et al. Effectiveness of inpatient dialectical behavioral therapy for borderline personality disorder: a controlled trial. Behav Res Ther. 2004 May;42(5):487-99. doi: 10.1016/s0005-7967(03)00174-8. PMID: 15033496. Exclusion Code: X2.
24. Boritz T, Barnhart R, McMain SF. The Influence of Posttraumatic Stress Disorder on Treatment Outcomes of Patients With Borderline Personality Disorder. J Pers Disord. 2016 Jun;30(3):395-407. doi: 10.1521/pedi_2015_29_207. PMID: 26305394. Exclusion Code: X6.
25. Bos EH, van Wel EB, Appelo MT, et al. A randomized controlled trial of a Dutch version of systems training for emotional predictability and problem solving for borderline personality disorder. J Nerv Ment Dis. 2010 Apr;198(4):299-304. doi: 10.1097/NMD.0b013e3181d619cf. PMID: 20386260. Exclusion Code: X2.
26. Bozzatello P, Rocca P, Bellino S. Combination of Omega-3 Fatty Acids and Valproic Acid in Treatment of Borderline Personality Disorder: A Follow-Up Study. Clin Drug Investig. 2018 Apr;38(4):367-72. doi: 10.1007/s40261-017-0617-x. PMID: 29302857. Exclusion Code: X2.
27. Buchheim A, Hörz-Sagstetter S, Doering S, et al. Change of Unresolved Attachment in Borderline Personality Disorder: RCT Study of Transference-Focused Psychotherapy. Psychotherapy and Psychosomatics. 2017;86(5):314-6. doi: 10.1159/000460257. Exclusion Code: X6.
28. Cailhol L, Roussignol B, Klein R, et al. Borderline personality disorder and rTMS: a pilot trial. Psychiatry Res. 2014 Apr 30;216(1):155-7. doi: 10.1016/j.psychres.2014.01.030. PMID: 24503285. Exclusion Code: X2.
29. Carmona i Farrés C, Elices M, Soler J, et al. Effects of mindfulness training on borderline personality disorder: Impulsivity versus emotional dysregulation. Mindfulness. 2018 2018 Dec 19
2018-12-27. doi: http://dx.doi.org/10.1007/s12671-018-1071-4. PMID: 2160911109; 2018-66070-001. Exclusion Code: X2.
30. Carter GL, Willcox CH, Lewin TJ, et al. Hunter DBT project: randomized controlled trial of dialectical behaviour therapy in women with borderline personality disorder. Aust N Z J Psychiatry. 2010 Feb;44(2):162-73. doi: 10.3109/00048670903393621. PMID: 20113305. Exclusion Code: X2.
31. Chanen AM, Jackson HJ, McCutcheon LK, et al. Early intervention for adolescents with borderline personality disorder using cognitive analytic therapy: randomised controlled trial. Br J Psychiatry. 2008 Dec;193(6):477-84. doi: 10.1192/bjp.bp.107.048934. PMID: 19043151. Exclusion Code: X2.
32. Chapman AL, Rosenthal MZ, Dixon-Gordon KL, et al. Borderline Personality Disorder and the Effects of Instructed Emotional Avoidance or Acceptance in Daily Life. Journal of personality disorders. 2017;31(4):483-502. doi: 10.1521/pedi_2016_30_264. Exclusion Code: X6.

33. Clarkin JF, Levy KN, Lenzenweger MF, et al. Evaluating three treatments for borderline personality disorder: a multiwave study. Am J Psychiatry. 2007 Jun;164(6):922-8. doi: 10.1176/ajp.2007.164.6.922. PMID: 17541052. Exclusion Code: X2.
34. Cottraux J, Note ID, Boutitie F, et al. Cognitive therapy versus Rogerian supportive therapy in borderline personality disorder. Two-year follow-up of a controlled pilot study. Psychother Psychosom. 2009;78(5):307-16. doi: 10.1159/000229769. PMID: 19628959. Exclusion Code: X2.
35. Coyle TN, Shaver JA, Linehan MM. On the potential for iatrogenic effects of psychiatric crisis services: The example of dialectical behavior therapy for adult women with borderline personality disorder. J Consult Clin Psychol. 2018 Feb;86(2):116-24. doi: 10.1037/ccp0000275. PMID: 29369662. Exclusion Code: X6.
36. Davidson K, Norrie J, Tyrer P, et al. The effectiveness of cognitive behavior therapy for borderline personality disorder: results from the borderline personality disorder study of cognitive therapy (BOSCOT) trial. J Pers Disord. 2006 Oct;20(5):450-65. doi: 10.1521/pedi.2006.20.5.450. PMID: 17032158. Exclusion Code: X2.
37. Davidson KM, Brown TM, James V, et al. Manual-assisted cognitive therapy for self-harm in personality disorder and substance misuse: a feasibility trial. Psychiatr Bull (2014). 2014 Jun;38(3):108-11. doi: 10.1192/pb.bp.113.043109. PMID: 25237519. Exclusion Code: X2.
38. Davidson KM, Tyrer P, Norrie J, et al. Cognitive therapy v. usual treatment for borderline personality disorder: prospective 6-year follow-up. Br J Psychiatry. 2010 Dec;197(6):456-62. doi: 10.1192/bjp.bp.109.074286. PMID: 21119151. Exclusion Code: X6.
39. Doering S, Hörz S, Rentrop M, et al. Transference-focused psychotherapy v. treatment by community psychotherapists for borderline personality disorder: randomised controlled trial. Br J Psychiatry. 2010 May;196(5):389-95. doi: 10.1192/bjp.bp.109.070177. PMID: 20435966. Exclusion Code: X2.
40. Edel MA, Raaff V, Dimaggio G, et al. Exploring the effectiveness of combined mentalization-based group therapy and dialectical behaviour therapy for inpatients with borderline personality disorder - A pilot study. Br J Clin Psychol. 2017 Mar;56(1):1-15. doi: 10.1111/bjc.12123. PMID: 27897326. Exclusion Code: X2.
41. Einy S, Narimani M, Atadokht A, et al. Effectiveness of Mentalization based Therapy and Cognitive-Analytical Therapy on Improved Object Relationship of People with Borderline Personality Disorder: a comparison. Payesh health monitor. 2018;17(3):98-110. PMID: CN-02114870. Exclusion Code: X8.
42. Elices M, Pascual JC, Portella MJ, et al. Impact of Mindfulness Training on Borderline Personality Disorder: A Randomized Trial. Mindfulness. 2016 2016/06/01;7(3):584-95. doi: 10.1007/s12671-016-0492-1. Exclusion Code: X2.
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Supplementary Material Table 4: Study Characteristics and Findings of Included Trials

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Black (2014)[1]	Design: Double-blinded RCT Setting: Outpatient, multicenter Country: United States Funding: AstraZeneca	N=95 G1 (29): Placebo G2 (33): Quetiapine ER (150 mg/day) G3 (33): Quetiapine ER (300 mg/day) 8 weeks	Inclusion: Males and females; 18 to 45 years of age; DSM-IV criteria for personality disorders; ≥ 9 on the Zanarini Rating Scale for BPD Exclusion: History of psychotic disorder, neurological condition, cognitive impairment; current substance use disorder or abuse; medically unstable; history of lack of response to a second-generation antipsychotic; pregnant or lactating; acutely suicidal	Mean (SD) age: G1: 30 (8.8) G2: 28 (8.0) G3: 30 (8.1) % Female: 30 % Race/ethnicity: European-Caucasian: 78 Other: 21	Primary outcome: ZAN-BPD at 8 weeks G2 (but not G3) significantly more effective than G1 on ZAN-BPD (data NR; p=0.03) G3 (but not G2) significantly more effective on SCL-90 than G1 (data NR; p=0.03) G2 and G3 significantly more effective on MOAS (data NR; p=0.01) No significant differences on Barratt Impulsiveness Scale, MADRS, Sheehan Disability Scale Incidence of AEs: G1: 86% (25/29) G2: 88% (29/33) G3: 91% (30/33) Withdrawals due to AEs: NR Attrition: 33% Differential attrition: G1: 21% (6/29) G2: 33% (11/33) G3: 42% (14/33)	Moderate

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Bogenschutz (2004)[2]	Design: Double-blinded RCT Setting: Outpatient, single center Country: United States Funding: Eli Lilly and Co.	N=40 G1 (20): Placebo G2 (20): Olanzapine (2.5 to 20 mg/d) 12 weeks	Inclusion: Medically stable; 18 to 60 years of age; DSM-IV criteria for BPD Exclusion: Other psychiatric disorders; substance use disorder; actively suicidal	Mean (SD) age: 32 (10.3) % Female: 63 % Race/ethnicity: White: 58 Hispanic: 25 Asian/Pacific Islander: 8 Other: 10	Primary outcome: CGI-BPD at 12 weeks Significantly greater improvement of G2 than G1 on the CGI-BPD (data NR; p=0.03) No significant differences on SCL-90, HAM-A, HAM-D, MOAS, and GAF Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/20) G2: 20% (4/20) Attrition: 43% Differential attrition: G1: 35% (7/20) G2: 50% (10/20)	High
Bozzatello (2017)[3]	Design: Double-blinded RCT Setting: Outpatient, single center Country: Italy Funding: None	N=51 G1 (26): Olanzapine (5-10 mg/day) G2 (25): Asenapine (5-10 mg/day) 12 weeks	Inclusion: 18 to 50 years of age; DSM-5 criteria for BPD Exclusion: Dementia; schizophrenia or other psychotic disorders; bipolar disorders; co-occurring major depressive episode; substance abuse; past use of psychotropic medications and/or psychotherapy	Mean (SD) age: 25 (5.3) % Female: 63 % Race/ethnicity: NR	Primary outcome: NR No significant differences between G1 and G2 on BPDSI, CGI-S, Barratt Impulsiveness Scale, MOAS, HAM-D, and Self-Harm Inventory at 12 weeks Incidence of AEs (completers): G1: 26% (5/19) G2: 19% (4/21) Withdrawal due to AEs: G1: 11% (2/19) G2: 10% (2/21) Attrition: 22% Differential attrition: ≤10 percentage points	High

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Crawford (2018)[4] LABILE	Design: Double-blinded RCT Setting: Outpatient, multicenter Country: United Kingdom Funding: NIHR	N=276 G1 (139): Placebo G2 (137): Lamotrigine (200 mg/day) 52 weeks	Inclusion: Met DSM-IV criteria for BPD Exclusion: Met diagnostic criteria for bipolar disorder (type I or II); psychotic disorder; history of liver or kidney impairment	Mean (SD) age: G1: 36 (11.0) G2: 36 (11.0) % Female: 75 % Race/ethnicity: White: 89 Black: 4 Asian: 1 Other: 6	Primary outcome: ZAN-BPD at 52 weeks No significant differences on ZAN-BPD, Self-Harm Inventory, Social Functioning Questionnaire, and EQ-5D-3l Incidence of AEs: G1: 67% (93/139) G2: 56% (77/137 Withdrawal due to AEs: G1: 1% (1/139) G2: 4% (4/137) Attrition: 29% Differential attrition: <10 percentage points	Moderate
Frankenburg (2002)[5]	Design: Double-blinded RCT Setting: Community recruitment with advertisements Country: United States Funding: Abbott Laboratories	N=30 G1 (10): Placebo G2 (20): Divalproex sodium (250 mg/day) 24 weeks	Inclusion: Females; 18 to 40 years of age; DIB-R and DSM-IV criteria for BPD and bipolar II disorder Exclusion: Formerly treated with divalproex sodium; medically ill; seizure disorder; current substance abuse; current criteria for a major depressive episode or a hypomanic episode; current or lifetime criteria for schizophrenia, schizoaffective disorder, psychotic disorder, or bipolar I disorder	Mean (SD) age: G1: 26 (7.3) G2: 27 (7.4) % Female: 100 % Race/ethnicity: White: 67 Black: 10 Hispanic: 13 Biracial: 7	Primary outcome: MOAS; SCL-90-R (subscales on anger, interpersonal hostility, depression) at 24 weeks G2 significantly more effective than G1 on MOAS (3.0 vs. 1.9; p=0.03), and SCL-90-R subscales on anger/hostility (0.8 vs. 0.6; p=0.01) and interpersonal sensitivity (0.8 vs. 0.4; p=0.04) Incidence of AEs: NR Withdrawal due to AEs: G1: 30% (3/10) G2: 5% (1/20) Attrition: 63% Differential attrition: <10 percentage points	High

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Hollander (2001)[6]	Design: Double-blinded RCT Setting: Outpatient, single center Country: United States Funding: Abbott Laboratories, NIMH	N=16 G1 (4): Placebo G2 (12): Divalproex sodium (250 mg/day) 10 weeks	Inclusion: DSM-IV criteria for BPD Exclusion: Medical or neurological illness; psychotic disorders; current substance abuse; bipolar disorder type 1 or 2; current major depression; current suicidal ideation	Mean (SD) age: 38.6 (10.37) % Female: 52 % Race/ethnicity: White: 67 Black: 14 Hispanic: 19	Primary outcome: NR No significant differences on CGI-I, Global Assessment Scale. MOAS, and Aggression Questionnaire Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/4) G2: 0% (0/12) Attrition: 63% Differential attrition: G1: 100% (4/4) G2: 50% (6/12)	High
Linehan (2008)[7]	Design: Double-blinded RCT Setting: University hospital Country: United States Funding: Eli Lilly	N=24 G1 (12): Placebo G2 (12): Olanzapine (5 mg/day) 6 months	Inclusion: Females; 18 to 60 years of age; met SCID-II and Borderline Personality Disorder Examination criteria for BPD; MOAS irritability subscale ≥6 Exclusion: Schizophrenia; bipolar I disorder; schizoaffective disorder; major depressive disorder with psychotic features or other psychotic disorder; intellectual disability or seizure disorder; substance use disorder	Mean (SD) age: 37 (9.0) % Female: 100 % Race/ethnicity: White: 79 Black: 4 Native American: 4 Latino: 4 Other: 8	Primary outcome: NR No significant differences between G1 and G2 on MOAS and HAM-D and for self-inflicted injury Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/12) G2: 8% (1/12) Attrition: 33% Differential attrition: ≤10 percentage points	High

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Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Loew (2006)[8]	Design: Double-blinded RCT Setting: Single center or multicenter Country: Germany and Austria Funding: None	N=56 G1 (28): Placebo G2 (28): Topiramate (200 mg/day) 10 weeks	Inclusion: Females; aged 18 to 35 years; DSM-IV criteria for BPD Exclusion: Schizophrenia; current use of psychotropic medication, or psychotherapy; suicidal; substance abuse; severe somatic illness	Mean (SD) age: G1: 26 (5.7) G2: 25 (5.3) % Female: 100 % Race/ethnicity: NR	Primary outcome: SCL-90-R, SF-36, and Inventory of Interpersonal Problems at 10 weeks G2 significantly more effective than G1 on SCL-90-R (7.4 vs.1.8; p<0.001), SF-36 (data NR; p<0.01), and Inventory of Interpersonal Problems (data NR; p=NR) Incidence of AEs: NR Withdrawal due to AEs: NR Attrition: 7% Differential attrition: <10 percentage points	Low
Moen (2012)[9]	Design: Double-blinded RCT Setting: Outpatient, single center Country: United States Funding: Abbott	N=15 G1 (5): Placebo G2 (10): Divalproex sodium (NR) 12 weeks	Inclusion: 21 to 55 years of age; DSM-IV criteria for BPD; ≥150 on the SCL-90; ≥5 on the SCID-II Exclusion: Current or past history of bipolar disorder, schizophrenia, or major depression with psychotic features; current psychotropic medication; acutely suicidal; substance use disorder; seizure disorder and/or anticonvulsant medications	Mean (range) G1: 37 (22-51) G2: 34 (23-45) % Female: 80 % Race/ethnicity: White: 80 Black: 7 Hispanic: 7 Mixed: 7	Primary outcome: NR No significant differences on SCL-90, Barratt Impulsiveness Scale, and Borderline Evaluation of Severity Over Time Incidence of AEs: NR Withdrawal due to AEs: NR Attrition: 40% Differential attrition: <10 percentage points	High

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Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Nickel (2006)[10], Nickel (2007)[11]	Design: Double-blinded RCT Setting: University hospitals Country: Austria, Germany Funding: None	N=52 G1 (26): Placebo G2 (26): Aripiprazole (15 mg/d) 8 weeks	Inclusion: Males and females; 16 years of age or older; BPD assessed with DSM-IV Exclusion: Schizophrenia, current use of other psychotropic medication, past termination of aripiprazole, current psychotherapy, pregnancy, suicidal ideation, severe somatic illness, or alcohol or drug abuse	Mean (SD) age: G1: 21 (4.6) G2: 22 (3.4) % Female: 83 % Race/ethnicity: NR	Primary outcome: SCL-90-R, HAM-D, HAM-A, STAXI at 8 weeks Significantly greater improvements for G2 than G1 on SCL-90-R (15.0 vs. 4.9; p<0.001), HAM-D (6.4 vs. 2.1; p=0.002), HAM-A (7.0 vs. 3.3; p=0.007), STAXI (13.6 vs. 5.7; p<0.001) 18 months follow-up for SCL-90-R: 17.9 vs. 1.4; p<0.01 Incidence of AEs: NR Withdrawals due to AEs: NR Attrition: 25% Differential attrition: ≤10 percentage points	Moderate
Nickel (2005)[12]	Design: Double-blinded RCT Setting: Outpatient recruitment and community advertisement Country: Germany Funding: None	N=44 G1 (22): Placebo G2 (22): Topiramate (250 mg/day) 8 weeks	Inclusion: Males; at least 18 years of age; DSM IV criteria for BPD Exclusion: Acute psychosis; severe major depression, or bipolar disorder; current use of psychotropic medication, or psychotherapy; somatically ill, actively suicidal, substance use disorder	Mean (SD) age: G1: 29 (NR) G2: 30 (NR) % Female: 0 % Race/ethnicity: NR	Primary outcome: STAXI at 8 weeks G2 significantly more effective than G1 on 4 out of 5 subscales on STAXI (p-values from 0.05 to 0.01); no significant improvement on subscale assessing tendency to repress anger. Overall STAXI score: NR Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/22) G2: 0% (0/22) Attrition: 5% Differential attrition: <10 percentage points	Moderate

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Nickel (2004)[13]	Design: Double-blinded RCT Setting: Community recruitment Country: Germany Funding: None	N=31 G1 (10): Placebo (50 mg/day) G2 (21): Topiramate (250 mg/day) 8 weeks	Inclusion: Females, 20 to 35 years of age; DSM-IV criteria for BPD Exclusion: Current schizophrenia, major depression, or bipolar disorder; current use of psychotropic medication, or psychotherapy; somatically ill, actively suicidal; substance abuse	Mean (SD) age: G1: 27 (NR) G2: 26 (NR) % Female: 100 % Race/ethnicity: NR	Primary outcome: STAXI at 8 weeks G2 significantly more effective than G1 on 4 out of 5 subscales on STAXI (p-values from 0.05 to 0.01); no significant improvement on subscale assessing tendency to repress anger. Overall STAXI score: NR Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/10) G2: 0% (0/21) Attrition: 6% Differential attrition: <10 percentage points	Moderate
Pascual (2008)[14]	Design: Double-blinded RCT Setting: Outpatient, single center Country: Spain Funding: Pfizer, government funding	N=60 G1 (30): Placebo G2 (30): Ziprasidone (40 to 200 mg/d) 12 weeks	Inclusion: Males and females; 18 to 45 years of age; DSM-IV criteria for BPD; current use of medically accepted contraception for females Exclusion: Schizophrenia, drug induced psychosis, organic brain syndrome, alcohol or other substance use disorder, bipolar disorder, intellectual disability, or major depressive episode in course; CGI-S ≥ 4	Mean (SD) age: G1: 29 (6.3) G2: 29 (6.0) % Female: 82 % Race/ethnicity: NR	Primary outcome: CGI-BPD at 12 weeks No significant differences on CGI-BPD, SCL-90, HAM-A, HAM-D, and clinical psychotic symptoms. Incidence of AEs: G1: 13% (4/30) G2: 37% (11/30) Withdrawal due to AEs: G1: 0% (0/30) G2: 30% (9/30) Attrition: 52% Differential attrition: ≤10 percentage points	High

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Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Reich (2009)[15]	Design: Double-blinded RCT Setting: Outpatient, single center Country: United States Funding: GlaxoSmithKline	N=28 G1 (13): Placebo G2 (15): Lamotrigine (50-275 mg/day) 12 weeks	Inclusion: DSM-IV criteria for BPD; >=8 on DIB-R; "serious" score on the affective instability item of the Zanarini Rating Scale for BPD; ≥14 on ALS Exclusion: Dementia; psychiatric disorder; bipolar disorder; psychotic disorder; substance use disorder; currently hospitalized; previous treatment with lamotrigine or psychotherapy; active suicidal or homicidal ideation	Mean (SD) age: G1: 35 (9.7) G2: 28 (9.5) % Female: 89 % Race/ethnicity: White: 89	Primary outcome: Affective Lability Scale; Affective Instability Item of the ZAN-BPD at 12 weeks Significantly greater improvements on G2 than G1 on Affective Lability Scale (vs. 0.71 vs. 0.40; p=0.012) subscale for affective lability of the Zanarini Rating Scale for BPD (1.5 vs. 1.1; p=0.043) No significant difference on ZAN-BPD Incidence of AEs: G1: 31% (4/13) G2: 40% (6/15) Withdrawal due to AEs: G1: 0% (0/13) G2: 0% (3/15) Attrition: Overall: 39% Differential attrition: <10 percentage points	High
Schulz (2008)[16]	Design: Double-blinded RCT Setting: Outpatient, multicenter Country: Multicountry Funding: Eli Lilly	N=314 G1 (159): Placebo G2 (155): Olanzapine (2.5 to 20 mg/d) 12 weeks	Inclusion: Males and females; 18 to 65 years of age; DSM-IV criteria for BPD; ZAN-BPD total score of 9 Exclusion: Schizophrenia, bipolar I disorder, delusional disorder, MDD, bipolar II disorder, substance use disorder, PTSD, panic disorder, OCD; BMI < 17; use of antidepressants, mood stabilizer, antipsychotic medication within 1 week of randomization; new psychotherapy treatment	Mean (SD) age: G1: 32 (9.6) G2: 32 (9.5) % Female: 71 % Race/ethnicity: White: 87	Primary outcome: ZAN BPD at 12 weeks No significant differences on ZAN-BPD, SCL-90-R, and MADRS, Sheehan Disability Scale, GAF, MOAS: data NR Incidence of AEs: G1: 57% (90/159) G2: 66% (102/155) Withdrawal due to AEs: G1: 11% (18/159) G2: 11% (17/155 Attrition: 43% Differential attrition: ≤10 percentage points	High

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Simpson (2004)[17]	Design: Double-blinded RCT Setting: Outpatient, single center Country: United States Funding: Eli Lilly	N=25 G1 (13): Placebo G2 (12): Fluoxetine (40 mg/day) 12 weeks	Inclusion: Admissions to the Women's Partial Program; DSM-IV criteria for BPD Exclusion: Substance use disorder; seizure disorder; unstable medical conditions; history of schizophrenia or bipolar disorder; previous adequate trial of fluoxetine	Mean (SD) age: 35 (10.1) % Female: 100 % Race/ethnicity: White: 72 Black: 20 Native American: 8	Primary outcome: NR When corrected for multiple testing, no significant differences between G1 and G2 on STAXI, MOAS, or GAF at mean of 10 weeks Incidence of AEs: NR Withdrawal due to AEs: NR Attrition: 20% Differential attrition: ≤10 percentage points	High
Soler (2005)[18]	Design: Double-blinded RCT Setting: Outpatient, single center Country: Spain Funding: Eli Lilly	N=60 G1 (30): DBT+placebo G2 (30): DBT+olanzapine (5 to 20 mg/day) 12 weeks	Inclusion: Females; 18 to 45 years of age; DSM-IV criteria for BPD; without comorbid, unstable axis I disorder; CGI severity of illness score ≥4; not receiving psychotherapy Exclusion: NR	Mean (SD) age: G1: 26 (5.4) G2: 28 (6.3) % Female: 87 % Race/ethnicity: NR	Primary outcome: NR Significantly greater improvements for G2 than G1 on HRSD (8.79 vs. 4.87; p=0.004) and the frequency of aggressive behavior (data NR; p=0.03) No significant differences on HAM-A, CGI-S, and episodes of suicide attempts and self-injury Incidence of AEs: NR Withdrawals due to AEs: NR Attrition: 30% Differential attrition: ≤10 percentage points	High

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Tritt (2005)[19]	Design: Double-blinded RCT Setting: single center or multicenter Country: Germany and Austria Funding: None	N=27 G1 (9): Placebo G2 (18): Lamotrigine (200 mg/day) 8 weeks	Inclusion: Female; 20 to 40 years of age; DSM-IV criteria for BPD Exclusion: Schizophrenia; major depression or bipolar disorder; current use of psychotropic medication, or psychotherapy; somatically ill; actively suicidal; substance abuse	Mean (SD) age: G1: 29 (NR) G2: 29 (NR) % Female: 100 % Race/ethnicity: NR	Primary outcome: STAXI at 8 weeks G2 significantly more effective than G1 on all 5 subscales of STAXI (p-values from <0.05 to <0.01; overall STAXI score: NR Assessments after 8 weeks of treatment indicated that G2 improved more than G1 with respect to all STAXI scales Incidence of AEs: NR Withdrawal due to AEs: G1: 11% (1/9) G2: 6% (1/18) Attrition: 11% Differential attrition: ≤10 percentage points	Low
Zanarini (2011)[20]	Design: Double-blinded RCT Setting: Outpatient, multicenter Country: Multicountry Funding: Eli Lilly	N=451 G1 (153): Placebo G2 (150): Olanzapine (2.5 mg/d) G3 (148): Olanzapine (5 to 10 mg/d) 12 weeks	Inclusion: Males and females; 18 to 65 years of age; DSM-IV criteria for BPD, ZAN-BPD total score ≥ 9 Exclusion: Schizophrenia, schizoaffective disorder, schizophreniform disorder, bipolar I disorder, delusional disorder, MDD, bipolar II disorder, substance use disorder within the previous 3 months; PTSD, panic disorder, OCD; actively suicidal; BMI < 17; cluster A personality disorder; new psychotherapy within the 3 months prior to visit 1; use of anticholinergic medication as prophylaxis for extrapyramidal symptoms	Mean (SD) age: G1: 34 (11.3) G2: 33 (11.2) G3: 33 (10.0) % Female: 74 % Race/ethnicity: White: 65 African descent: 7 East/Southeast Asian: 2 Western Asian: 0.2 Hispanic: 24.6 Other origin: 11.1	Primary outcome: ZAN-BPD at 12 weeks G3 significantly more effective than G1 on ZAN-BPD (-8.5 vs. -6.8; p=0.01; response: 74% vs. 60%; p=0.018) and SCL-90-R (-0.7 vs. -0.6; p<0.05) No significant differences between G1 and G3 on MADRS, GAF, MOAS No significant differences between G1 and G2 on most outcome measures Incidence of AEs: G1: 61% (93/153) G2: 65% (98/150) G3: 67% (99/148) Withdrawal due to AE: G1: 3% (5/153) G2: 3% (5/150) G3: 6% (9/148) Attrition: 35% Differential attrition: ≤10 percentage points	Moderate

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Zanarini (2004)[21]	Design: double-blinded RCT Setting: Outpatient, single center Country: United States Funding: Eli Lilly	N=45 G1 (14): Fluoxetine (10-30 mg/day) G2 (16): Olanzapine (2.5-7.5 mg/day) G3 (15): Fluoxetine (10-30 mg/day) and olanzapine (2.5-7.5 mg/day) 8 weeks	Inclusions: Female; 18 to 40 years of age; DSM-IV criteria for BPD; does not meet criteria for current major depressive disorder Exclusion: Current major depressive disorder, lifetime schizophrenia, schizoaffective disorder, or bipolar disorder; current use of psychotropic medications; medical illness; seizure disorder; substance abuse; acutely suicidal	Mean (SD) age: 23 (5.7) % Female: 100 % Race/ethnicity: White: 80	Primary outcome: NR G2 and G3 signficantly more effective than G1 on MOAS (19.7 vs. 20.2 vs. 15.4; p=0.003 for G2 vs. G1; p<0.001 for G3 vs. G1) at 8 weeks G2 and G3 signficantly more effective than G1 on MADRS (13.6 vs. 11.9 vs. 8.2; p<0.001 for G2 vs. G1; p=0.02 for G3 vs. G1) at 8 weeks Incidence of AEs: NR Withdrawal due to AEs: G1: 7% (1/14) G2: 0% (0/16) G3: 7% (1/15) Attrition: Total: 7% Differential attrition: ≤10 percentage points	Moderate

(continued)

Supplementary Material Table 4: Study Characteristics and Findings of Included Trials (continued)

Author (year) Trial name	Study characteristics	N of participants Interventions Duration	Study population including main inclusion and exclusion criteria	Sample demographics	Primary outcome; main results; attrition	Risk of bias
Zanarini (2001)[22]	Design: Double-blinded RCT Setting: Outpatients, single center Country: United States Funding: Eli Lilly	N=28 G1 (9): Placebo G2 (19): Olanzapine (2.5 mg/d) 6 months	Inclusion: Females; 18 to 40 years of age; DSM-IV criteria for BPD Exclusion: Major depression; previous treatment with olanzapine; currently on psychotropic medications; actively abusing alcohol or drugs	Mean (SD) age: G1: 26 (4.5) G2: 28 (7.7) % Female: 100 % Race/ethnicity: White: 71 Nonwhite: 29	Primary outcome: SCL-90 at 6 months Significantly greater improvements of G2 than G1 on 4 domains of the SCL-90 (interpersonal sensitivity, anxiety, anger/hostility, paranoia) Overall score of SCL-90: NR Incidence of AEs: NR Withdrawal due to AEs: G1: 0% (0/9) G2: 16% (3/19) Attrition: 68% Differential attrition: G1: 89% (8/9) G2: 58% (11/19)	High

Abbreviations: AE, adverse event; ALS, Affective Liability Scale BMI, body mass index; BPD, borderline personality disorder; BPDSI, Borderline Personality Disorder Severity Index; CGI, Clinical Global Impression Scale, CGI-BPD, Clinical Global Impression Scale for Borderline Personality Disorder; CGI-S, Clinical Global Impression–Severity Scale; DBT, dialectical behavior therapy; DIB-R, Revised Diagnostic Interview for Borderlines; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*; EQ-5D, European Quality of Life–5; ER, extended release; G1, Group 1; G2, Group 2; G3, Group 3; GAF, Global Assessment of Functioning; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; HRSD, Hamilton Rating Scale for Depression; LABILE, Lamotrigine and Borderline Personality Disorder: Investigating Long-Term Effects; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; MOAS, Modified Overt Aggression Scale; N, sample size; NIHR, National Institute for Health Research; NIMH, National Institute of Mental Health; NR, not reported; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder; RCT, randomized controlled trial; SCID-II, DSM-IV Axis II Disorders; SCL-90, Symptom Checklist-90; SCL-90-R, Symptom Checklist-90-Revised; SD, standard deviation; SF-36, Short Form Survey; STAXI, State-Trait Anger Expression Inventory; ZAN-BPD, Zanarini Rating Scale for Borderline Personality Disorder.

Supplementary Material Table 5: Certainty of Evidence Ratings

Table 5.1 Certainty-of-evidence ratings for second-generation antipsychotics versus placebo

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Effect with placebo	Difference in effect with second-generation antipsychotics
Severity of BPD assessed with Zanarini Rating Scale for BPD follow-up: range 8 weeks to 12 weeks	860 (3 RCTs)[1, 16, 20]	⊕⊕◯◯ LOW[a] for no effect of SGA	-	The mean score at endpoint was **10.3** points*	mean **1.2 points lower**
Anger assessed with: STAXI follow-up: mean 8 weeks	52 (1 RCT)[10]	⊕⊕◯◯ LOW[b] for effect of SGA	-	The mean score at endpoint was **26.2** points	mean **7.7 points lower** (p<0.001)
Aggression assessed with: Modified Overt Aggression Scale follow-up: range 8 weeks to 12 weeks	515 (3 RCTs) [2, 7] [20]	⊕⊕◯◯ LOW[a,c] for no effect of olanzapine	-	The mean score at endpoint was **18.6** points*	mean **14.7 points lower** (ns)
Aggression assessed with: Modified Overt Aggression Scale follow-up: range 8 weeks to 12 weeks	95 (1 RCT)[1].	⊕⊕◯◯ LOW[b] for effect of quetiapine ER	-	The mean score at endpoint was NR	NR
Depression assessed with: HAM-D and MADRS follow-up: range 8 weeks to 21 weeks	497 (5 RCTs)[7, 10, 14, 18, 20]	⊕⊕◯◯ LOW[d,e] for no effect of SGA	-	The mean score at endpoint was **NR**	mean **0.28 SDs (Cohen's d) greater** (-0.05 to 0.60)
Impulsiveness assessed with: Barratt Impulsiveness Scale follow-up: range 8 weeks to 12 weeks	155 (2 RCTs))[1, 14]	⊕⊕◯◯ LOW[d,f] for no effect of SGA	-	The mean score at endpoint was **69.1** points*	mean **1.4 points lower** (ns)
General Psychopathology assessed with: SCL-90 follow-up: range 8 weeks to 12 weeks	698 (5 RCTs)[1, 2, 10, 14, 20]	⊕⊕⊕◯ MODERATE[a] for effect of SGA	-	The mean score at endpoint was **10.3** points*	mean **1.2 points lower** (ns)
Functioning assessed with: GAF and Sheehan Disability Scale follow-up: mean 8 weeks to 12 weeks	586 (3 RCTs)[1, 2, 20]	⊕⊕⊕◯ MODERATE[g] for no effect of SGA	-	The mean score at endpoint was **63.2***	mean **2.9 higher** (ns)
Incidence of Adverse Events	920 (4 RCTs)[1, 14, 16, 20]	⊕⊕⊕◯ MODERATE[a] for higher risk with antipsychotics	**RR 1.10** (1.00 to 1.21)	571 per 1,000	**57 more per 1,000** (0 fewer to 120 more)
Withdrawal due to Adverse Events	917 (5 RCTs)[2, 7, 14, 16, 20, 22, 23]	⊕⊕◯◯ LOW[a,h] for similar risks	**RR 1.91** (0.83 to 4.43)	69 per 1,000	**63 more per 1,000** (12 fewer to 237 more)
Incidence of Serious Adverse Events	957 (6 RCTs)[1, 2, 10, 14, 16, 20]	⊕◯◯◯ VERY LOW[i] for higher risk with placebo	**RR 0.46** (0.23 to 0.95)**	44 per 1,000	**24 fewer per 1,000** (34 fewer to 2 fewer)

*Effect estimate from largest study or the study with the lowest risk of bias (Zanarini et al., 2011[43] or Black et al., 2014[25]).

**Effect estimate from Zanarini et.al., 2011;[43] The other studies reported that no serious adverse events occurred.
The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
[a] The majority of studies were high risk of bias; downgraded 2 steps for study limitations.
[b] Small study, does not meet optimal information size; downgraded 2 steps for imprecision.
[c] Schulz et al. assessed MOAS but did not report data; downgraded 1 step for reporting bias.
[d] At least half of studies were high risk of bias; downgraded 1 step for study limitations.
[e] Inconsistent effects, largest study shows substantially smaller treatment effect; downgraded 1 step for inconsistency.
[f] Small study, does not meet optimal information size; downgraded 1 step for imprecision.
[g] Does not meet optimal information size; downgraded 1 step for imprecision.
[h] Few events; downgraded 1 step for imprecision.
[i] Very few events; downgraded 2 steps for imprecision.
Abbreviations: BPD, borderline personality disorder; CI, confidence interval; GAF, Global Assessment of Functioning; GRADE Grading of Recommendations Assessment, Development, and Evaluation; HAM-D, Hamilton Depression Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; NR, not reported; ns, not significant; RCT, randomized controlled trial; RR, risk ratio; SCL-90, Symptom Checklist-90, SD, standard deviation; SGA, second-generation antipsychotics; STAXI: State-Trait Anger Expression Inventory.

Table 5.2 Certainty-of-evidence ratings of studies comparing anticonvulsants with placebo

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Effect with placebo	Difference in effect with anticonvulsants
Divalproex sodium					
Severity of BPD assessed with: Borderline Evaluation of Severity Over Time follow-up: mean 12 weeks	15 (1 RCT)[9]	⊕◯◯◯ VERY LOW[a,b] for no effect of divalproex sodium	-	The mean score at endpoint was **30.0** points	mean **1.3 points lower** (ns)
Aggression assessed with: MOAS; SCL-90-R subscale for anger and hostility follow-up: range 10 weeks to 24	46 (2 RCTs)[5, 6]	⊕◯◯◯ VERY LOW[a,c,d] for effect of divalproex sodium	-	The mean score on MOAS was **3.2** points*	mean **0.6 points lower** (p=0.03)
Impulsiveness assessed with: Barratt Impulsiveness Scale-Motor follow-up: mean 12 weeks	15 (1 RCT)[9]	⊕◯◯◯ VERY LOW[a,b] for no effect of divalproex sodium	-	The mean score at endpoint was **18.2** points	mean **5.7 points higher** (ns)
General Psychopathology assessed with: SCL-90-R, CGI-I follow-up: range 10 weeks to 12 weeks	31 (2 RCTs)[6, 9]	⊕◯◯◯ VERY LOW[a,d] for no effect of divalproex sodium	-	The mean score at endpoint on SCL-90 was **114.2** points*	mean **22.8** points higher (ns)
Withdrawals due to adverse events follow-up: range 10 to 24 weeks	46 (2 RCTs)[5, 6]		**RR 0.26** (0.03 to 2.35)	136 per 1,000*	**101 fewer per 1,000** (132 fewer to 184 more; ns)
Lamotrigine					
Severity of BPD assessed with: ZAN-BPD follow-up: range 12 weeks to 52 weeks	304 (2 RCTs)[4, 15]	⊕⊕⊕◯ MODERATE[e] for no effect of lamotrigine	-	The mean score at endpoint was **11.5** points*	mean **0.5** points lower (ns)
Affective lability assessed with: Affective Lability Scale follow-up: mean 12 weeks	28 (1 RCT)[15]	⊕◯◯◯ VERY LOW[b,f] for effect of lamotrigine	-	The mean at endpoint score was **1.52** points	mean **0.27** points lower (p=0.012)
Alcohol and substance use assessed with ASSIST follow-up: mean 52 weeks	160 (1 RCT)[4]	⊕⊕◯◯ LOW[b] for no effect of lamotrigine	-	The mean score at endpoint was **23** points	mean **4** points higher (ns)
Anger assessed with: STAXI follow-up: mean 8 weeks	27 (1 RCT)[19]	⊕⊕◯◯ LOW[b] for effect of lamotrigine	-	The mean score at endpoint was **NR**	**NR** (4 of 5 subscales significantly improved)
Functioning assessed with: Social Functioning Questionnaire follow-up: mean 52 weeks	276 (1 RCT)[4]	⊕⊕⊕◯ MODERATE[e,g] for no effect of lamotrigine	-	The mean score at endpoint was **12.3** points	mean **0.1** points higher (ns)

Incidence of Adverse Events follow-up: range 10 weeks to 52 weeks	304 (2 RCTs)[4, 15]	⊕⊕◯◯ LOW[g] for similar risks	**RR 0.86** (0.71 to 1.03)	630 per 1,000*	**88 fewer per 1,000** (183 fewer to 19 more; ns)
Incidence of Serious Adverse Events follow-up: mean 52 weeks	276 (1 RCT)[4]	⊕⊕◯◯ LOW[h] for similar risks	**RR 0.82** (0.52 to 1.31)	230 per 1,000	**41 fewer per 1,000** (111 fewer to 71 more; ns)
Withdrawal due to Adverse Events follow-up: range 10 weeks to 52 weeks	328 (3 RCTs) [4, 15, 19]	⊕◯◯◯ VERY LOW[i,h] for similar risks	**RR 3.79** (0.82 to 17.57)	12 per 1,000	**35 more per 1,000** (2 fewer to 206 more; ns)
Topiramate					
Anger assessed with: STAXI follow-up: mean 8 weeks	75 (2 RCTs)[12, 13]	⊕⊕◯◯ LOW[d] for effect of topiramate	-	The mean score at endpoint was NR	NR (4 of 5 subscales significantly improved)
General Psychopathology assessed with: SCL-90 follow-up: range 8 weeks to 12 weeks	56 (1 RCT)[8]	⊕⊕◯◯ LOW[b] for effect of topiramate	-	The mean score at endpoint was **70.1** points	mean **5.9** points lower (p<0.001)
Withdrawal due to Adverse Events	75 (2 RCTs)[12, 13]	⊕◯◯◯ VERY LOW[d,j] for similar risks	RR 1.95 (0.77 to 4.94)	0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)

*Effect estimate from largest study or the study with the lowest risk of bias.

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[a] High attrition; downgraded 1 step for risk of bias.

[b] Small study, does not meet optimal information size; downgraded 2 steps for imprecision.

[c] Conflicting results of two studies; downgraded 1 step for inconsistency.

[d] Small studies, do not meet optimal information size; downgraded 2 steps for imprecision.

[e] Sample size probably does not meet optimal information size; downgraded 1 step for imprecision.

[f] Trial with high risk of bias, downgraded 1 step for risk of bias.

[g] Few events; downgraded 2 steps for imprecision.

[h] Very few events; downgraded 2 steps for imprecision.

[i] Proportions vary substantially; downgraded 1 step for inconsistency.

[j] One study does not report data on withdrawal due to adverse events; downgraded 1 step for outcomes reporting bias.

Abbreviations: ASSIST, Alcohol, Smoking, and Substance Involvement Screening Test; BPD, borderline personality disorder; CGI-I, Clinical Global Impressions–Improvement Scale; CI, confidence interval; GRADE Grading of Recommendations Assessment, Development, and Evaluation; MOAS, Modified Overt Aggression Scale Checklist; NR, not reported; ns, not significant; RCT, randomized controlled trial; RR, risk ratio; SCL-90, Symptom Checklist-90; SCL-90-R, Symptom Checklist-90-Revised; STAXI, State-Trait Anger Expression Inventory; ZAN-BPD, Zanarini Rating Scale for Borderline Personality Disorder.

Table 5.3 Certainty-of-evidence ratings of studies comparing antidepressants with placebo

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Effect with placebo	Difference in effect second-generation antidepressants
Anger assessed with: STAXI follow-up: mean 10 weeks	25 (1 RCT)[17]	⨁◯◯◯ VERY LOW[a,b] for no effect of fluoxetine	-	The mean score at endpoint was **27.6** points	mean **7.1 lower** (ns)
Aggression assessed with: MOAS follow-up: mean 10 weeks	25 (1 RCT)[17]	⨁◯◯◯ VERY LOW[a,b] for no effect of fluoxetine	-	The mean score at endpoint was NR	NR (ns)
Functioning assessed with: GAF follow-up: mean 10 weeks	25 (1 RCT)[17]	⨁◯◯◯ VERY LOW[a,b] for no effect of fluoxetine	-	The mean score at endpoint was **59.3** points	mean **0.6 higher** (ns)

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

[a] No intention-to-treat analysis; downgraded 1 step for risk of bias.

[b] Small study, does not meet optimal information size; downgraded 2 steps for imprecision.

Abbreviations: CI, confidence interval; GAF, Global Assessment of Functioning; GRADE Grading of Recommendations Assessment, Development, and Evaluation; MOAS, Modified Overt Aggression Scale; NR, not reported; ns, not significant; RCT, randomized controlled trial; STAXI, State-Trait Anger Expression Inventory.

Table 5.4 Certainty-of-evidence ratings of studies comparing second-generation antipsychotic with second-generation antidepressants

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Effect with antidepressants	Difference in effect with second-generation antipsychotics
Olanzapine vs. Fluoxetine					
Aggression assessed with: MOAS follow-up: mean 8 weeks	30 (1 RCT)[21]	⊕◯◯◯ LOW[b] for greater effect of olanzapine	-	The mean score at endpoint was **7.83** points	mean **4.3 points lower** (p=0.003)
Depression assessed with: MADRS follow-up: mean 8 weeks	30 (1 RCT)[21]	⊕◯◯◯ LOW[b] for greater effect of olanzapine	-	The mean score at endpoint was **6.2** points	mean **1.0 points lower** (p<0.001)
Olanzapine+Fluoxetine vs. Fluoxetine					
Aggression assessed with: MOAS follow-up: mean 8 weeks	29 (1 RCT)[21]	⊕◯◯◯ LOW[b] for greater effect of olanzapine+fluoxetine	-	The mean score at endpoint was **7.83** points	mean **4.8 points lower** (p<0.001)
Depression assessed with: MADRS follow-up: mean 8 weeks	29 (1 RCT)[21]	⊕◯◯◯ LOW[b] for greater effect of olanzapine+fluoxetine	-	The mean score at endpoint was **6.2** points	mean **1.8 points lower** (p=0.02)
Withdrawals due to Adverse Events follow-up: mean 8 weeks	29 (1 RCT)[21]	⊕◯◯◯ VERY LOW[a,b] for similar risks	**RR 0.94** (0.06 to 13.68)	71 per 1,000	**4 fewer per 1,000** (67 fewer to 906 more)

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

[a] Unclear how withdrawal due to adverse events was determined; downgraded 1 step for indirectness.

[b] Small study, does not meet optimal information size; downgraded 2 steps for imprecision.

Abbreviations: CI, confidence interval; GRADE Grading of Recommendations Assessment, Development, and Evaluation; MADRS, Montgomery-Åsberg Depression Scale; MOAS, Modified Overt Aggression Scale; RCT, randomized controlled trial; RR, risk ratio.

Table 5.5 Certainty-of-evidence ratings of studies comparing second-generation antipsychotics with second-generation antipsychotics

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Effect with olanzapine	Difference in effect with asenapine
Severity of BPD assessed with: BPD Severity Index follow-up: mean 12 weeks	51 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar effects	-	The mean score at endpoint was **49.12**	mean **2.23 lower** (ns)
Aggression assessed with: MOAS follow-up: mean 12 weeks	51 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar effects	-	The mean score at endpoint was **4.8**	mean **1.4 higher** (ns)
Impulsiveness assessed with: Barratt Impulsiveness Scale follow-up: mean 12 weeks	51 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar effects	-	The mean score at endpoint was **72.9**	mean **8.2 lower** (ns)
Self-harm assessed with: Self-Harm Inventory follow-up: mean 12 weeks	51 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar effects	-	The mean score at endpoint was **10**	mean **2 lower** (ns)
Global Impression assessed with: CGI-S follow-up: mean 12 weeks	51 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar effects	-	The mean score at endpoint was **3.9**	mean **0.2 lower** (ns)
Incidence of Adverse Events follow-up: mean 12 weeks	40 (1 RCT)[3]	⊕◯◯◯ VERY LOW[a,b] for similar risks	**RR 1.38** (0.43 to 4.40)	263 per 1,000	**100 more per 1,000** (150 fewer to 895 more)

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

[a] High attrition; downgraded 1 step for risk of bias.

[b] Small study, does not meet optimal information size; downgraded 2 steps for imprecision.

Abbreviations: BPD, borderline personality disorder; CGI-S, Clinical Global Impression- Improvement Scale; CI, confidence interval; GRADE Grading of Recommendations Assessment, Development, and Evaluation; MOAS, Modified Overt Aggression Scale Checklist; ns, not significant; RCT, randomized controlled trial; RR, risk ratio.

Supplementary Material Table 6. Summary of Clinical Assessment Scales for Borderline Personality Disorder

Measure	Full name	Description	Minimally important difference
ALS	Affective Lability Scale	Items: 54 item self-report measure of lability of anger Scale: 0 to 3 (greater affective lability) Scoring: Patients rate different features of mood instability on a 4-point Likert scale from 0 (very uncharacteristic) to 3 (very characteristic); the total score is the mean of all item responses divided by the number of responses	NR
BIS-11	Barratt Impulsiveness Scale	Items: 30-item self-report questionnaire designed to measure impulsivity, items describe common impulsive or nonimpulsive behaviors and preferences Scale: 30 to 120 (greater impulsivity) Scoring: Each item is rated on a 4-point Likert scale from 1 (rarely/never) to 4 (almost always/always); overall score is calculated from the sum of the 30 items	NR
BEST	Borderline Evaluation of Severity Over Time	Items: 15-item self-report questionnaire designed to assess change in the severity of BPD during the prior month Scale: 12 (best) to 72 (worst) Scoring: Each item is rated on a 5-point Likert scale from 1 (none/never) to 5 (extreme/almost always); items are divided among 3 subscales (A, B, C); total score is calculated by adding together the scores of subscales A and B then subtracting the total from subscale C and adding a correction factor of 15	NR
BPDSI	Borderline Personality Disorder Severity Index	Items: 70-item semi-structured clinical interview measure assessing frequency and severity of BPD-related symptoms among nine symptom areas corresponding to DSM-IV criteria Scale: 0 to 90 (scores above 15 signify BPD pathology) Scoring: Each item is rated on an 11-point scale from 0 (never) to 10 (daily); for each DSM criterion an average score is derived (range=0-10) with the sum of these 9 scores providing the total score	NR
CGI-I	Clinical Global Impression scale, Improvement item	Items: 1-item clinician-rated instrument to conduct global assessment of illness improvement Scale:1 to 7 Scoring: A clinician rates patient's mental illness on a scale from 1 (very much improved) to 7 (very much worse)	NR
CGI-S	Clinical Global Impression Scale, Severity item	Items: 1 item clinician-rated instrument to conduct global assessment of illness severity Scale: 0 to 7 Scoring: A clinician rates patient's mental illness on a 7-point scale: 1 (normal, not at all ill), 2 (borderline mentally ill), 3 (mildly ill), 4 (moderately ill), 5 (markedly ill), 6 (severely ill), 7 (among the most extremely ill patients); the score should reflect the average severity level across the past 7 days	NR

(continued)

Supplementary Material Table 6. Summary of Clinical Assessment Scales for Borderline Personality Disorder (continued)

Measure	Full name	Description	Minimally important difference
EQ-5D	European Quality of Life–5 Dimension	Items: 5-item instrument to measure health-related quality of life in Europe Scale: 0 (worst) to 100 (best) Scoring: Each item can be rated at one of 3 response levels: “slight problems,” “moderate problems,” “extreme problems”	NR
GAF	Global Assessment of Functioning	Items: 100-item clinician-rated instrument indicating overall psychosocial functioning during a specified period on a continuum from psychological sickness to health Scale: 0 to 100 (severely impaired to extremely high functioning) Scoring: GAF rating can be based on many things, including: an interview or questionnaire, medical records, information from medical providers, caregivers, or relatives, police or court records about violent or illegal behavior; the summary score reflects the level of an individual’s overall functioning	NR
HAM-A	Hamilton Anxiety Rating Scale	Items: 14-item questionnaire used to assess patients’ anxiety Scale: 0 to 56 (<17=mild severity, 18-24=mild to moderate severity, >25=severe) Scoring: Each item is rated on a 5-point Likert scale from 0 (not present) to 4 (most severe); the sum of the score indicates the severity of anxiety	NR
HAM-D	Hamilton Depression Rating Scale	Items: 17 or more item questionnaire used to assess patients’ depression Scale: 0 to 53 (0-7 considered normal and >20 considered moderate severity) Scoring: Each item is rated on a 3- or 5-point Likert scale from 0 to 2 or 0 to 4; the sum of the score indicates the severity of depression	NR
MOAS	Modified Overt Aggression Scale	Items: 20-item clinician-administered, semi-structured interview designed to assess various manifestations of aggressive behavior in outpatients Scale: 0 to 100 (no symptoms to severe) Scoring: 4 subcomponent types of aggression are scored between 0 (no aggression) and 4 with a potential cumulative score of 10 for each subcomponent with each subcomponent is weighted differently; total score is calculated by multiplying sum score of each subcomponent by the weight for that category, then summing the weighted scores	NR
MADRS	Montgomery-Åsberg Depression Rating Scale	Items: 10-item clinician-rated measure of severity of ten depressive symptoms Scale: 0 to 60 (0-6 is defined as symptom absent and >34 is defined as severe depression)	NR

Measure	Full name	Description	Minimally important difference
		Scoring: Each item is rated on a scale from 0 to 6, with 6 as the most severe description of the symptom; total score is the sum of scores for each item	

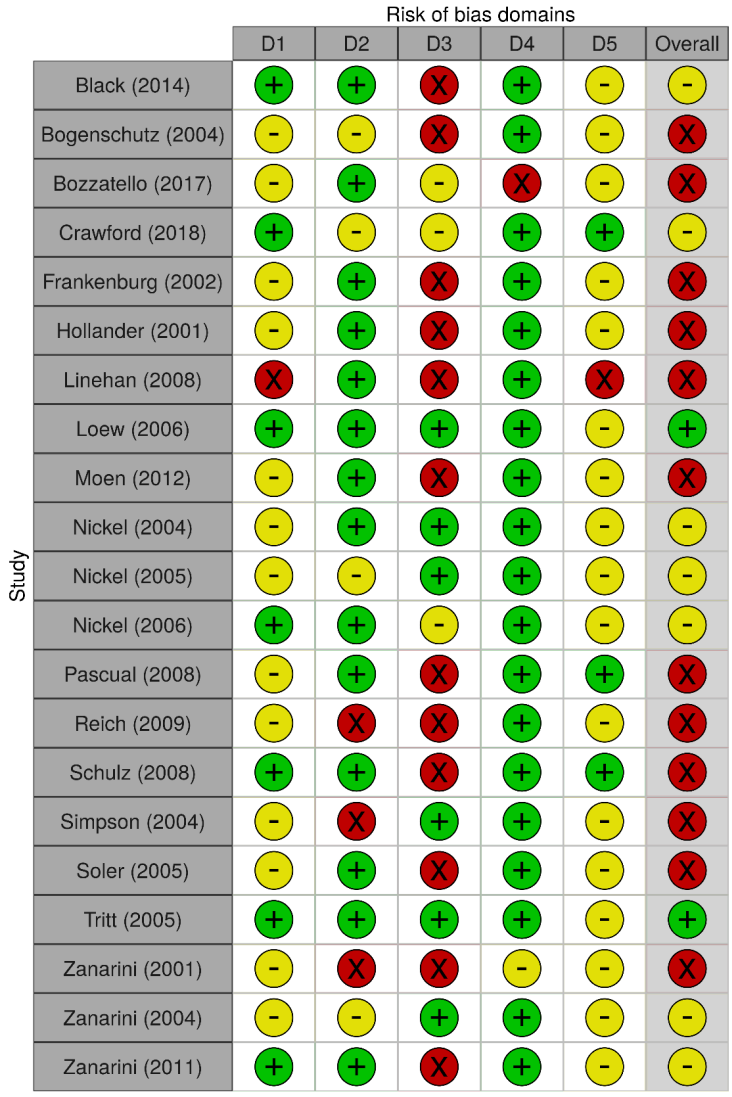
(continued)

Supplementary Material Table 6. Summary of Clinical Assessment Scales for Borderline Personality Disorder (continued)

Measure	Full name	Description	Minimally important difference
MOAS	Overt Aggression Scale—Modified	Items: 20-item clinician-administered, semi-structured interview designed to assess various manifestations of aggressive behavior in outpatients Scoring: Manifestations of aggression from the preceding week are scored between 0 (no events within that category) and 5 (most severe form of aggression within that category), frequency of events is then multiplied by a weighted severity level for that category (0 to 5) to produce a raw score for each subscale; each subscale is also weighted (1 to 3x) and total score is calculated by summing weighted scores from each subscale	NR
STAXI	State-Trait Anger Expression Inventory	Items: 69-item self-report questionnaire that focuses on anger expression Scoring: Each item is rated on a 4-point scale for frequency of exhibiting behavior (almost always, often, sometimes, almost never)	NR
SCL-90-R	Symptom Checklist-90-Revised	Items: 90-item self-report screening measure of general psychiatric symptomatology along nine symptom constructs Scale: 0 to 4 Scoring: Each item is scored on a 5-point Likert scale from 0 (not at all bothered) to 4 (extremely bothered); Global Severity Index (GSI) can be calculated as the average score of the 90 items in the questionnaire	NR
ZAN–BPD	Zanarini Rating Scale for Borderline Personality Disorder	Items: 9-item semi structured interview Scale: 0 to 36 (no symptoms to severe) Scoring: Each item is rated on a 5-point Likert scale from 0 (no symptoms) to 4 (severe symptoms) on each of nine items corresponding to the nine DSM-IV criteria for BPD, total score is the sum of all items	NR

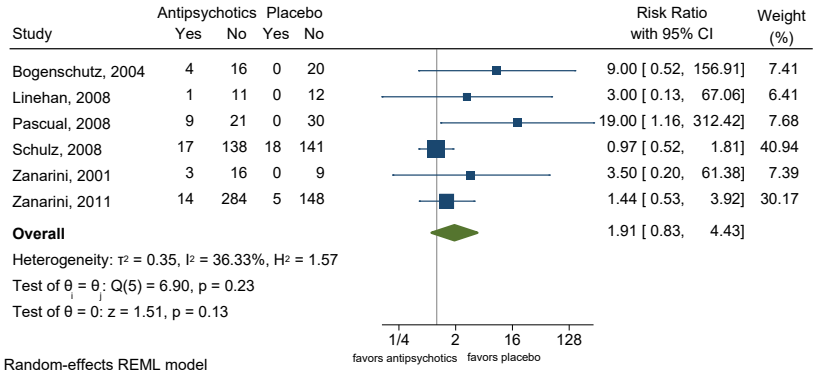
Abbreviations: BPD, BPD, borderline personality disorder; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*; GAF, Global Assessment of Functioning; GSI, Global Severity Index; MCID, minimal clinically important difference ; NR, not reported; SCL-90, Symptom Checklist-90; STAXI, State-Trait Anger Expression Inventory.

Supplementary Material Figure 1: Risk of Bias Ratings



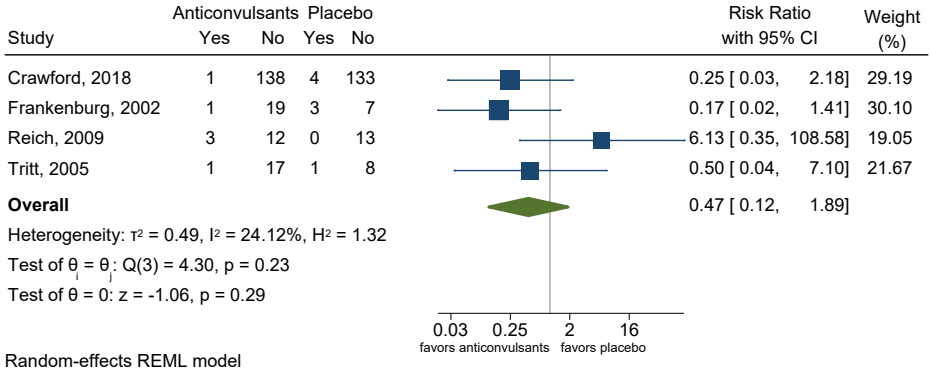
Domains:
D1: Bias arising from the randomization process
D2: Bias due to deviations from intended interventions
D3:Bias due to missing outcome data
D4: Bias in measurement of the outcome
D5: Bias in selection of reported results

Supplementary Material Figure 2: Random effects meta-analysis of withdrawal due to adverse events comparing second-generation antipsychotics with placebo



Abbreviations: CI, confidence interval; REML, restricted maximum likelihood.
References: Bogenschutz, 2004[2]; Linehan, 2008[7]; Pascual, 2008[14]; Schulz, 2008[16], Zanarini, 2001[22]; Zanarini, 2011[20]

Appendix Figure 3. Random effects meta-analysis of withdrawal due to adverse events comparing anticonvulsant medications with placebo



Abbreviations: CI, confidence interval; REML, restricted maximum likelihood.
References: Crawford, 2018[4]; Frankenburg, 2002[5]; Reich, 2009[15]; Tritt, 2005[19]

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