Table 5. Relapse prevention in bipolar affective disorder

AUTOR, YEAR	***POPULATION (number and setting)***	***ASSESSMENT***	***TYPE OF STUDY***	***COMPARATOR***	***OUTCOME***	***SECOND OUTCOME***	***MAIN FINDINGS***
Bond and Anderson, 2015	Participants with bipolar disorder who are not in the acute phase 16 RCTs (average of 70 participants)	Psychoeducation (i) a discrete psychological intervention involving primarily the patient with bipolar disorder; (ii) providing information about bipolar disorder and/or its treatment; and (iii) relating this information to aiding self-management of the disorder.	Systematic review with meta-analysis	1.Usual treatment 2. placebo	Relapse prevention in bipolar affective disorder (BD) any episode (critérios do DSM IV)	N/A	Although the heterogeneity in the data warrants caution, psychoeducation appears to be effective in preventing: a) any relapse [n = 7; OR: 1.98–2.75; (NNT)***: 5–7, depending on the analysis method] b) relapse/manic/hypomanic (n = 8; OR: 1.68–2.52; NNT: 6–8), c) depressive relapse was not effective Caution: relatively few studies, with different methodologies and small number of participants
Cipriani, Reid, et al., 2013	6 RCTs (875 participants) with BAD on long-term treatment with valproate or any other mood stabilizer, antipsychotic drug or placebo	Continuation and maintenance treatment with valproate	Systematic review with meta-analysis	1. placebo 2. lithium 3. olanzapine	Relapse prevention in bipolar affective disorder (BD) any episode	Improved overall funcioning	Valproate was more effective than placebo in preventing the relapse of any mood episode (RR 0.68, 95% CI 0.49 to 0.93; NNTB 8),

https://doi.org/10.25118/2763-9037.2026.v16.1542

					(critérios do DSM IV)		No difference in efficacy was found between valproate and lithium (RR 1.02, 95% CI 0.87 to 1.20). Combination therapy with lithium plus valproate was more likely to prevent relapse than valproate monotherapy (RR 0.78, 95% CI 0.63 to 0.96).
Kishi, et. al., 2016	7 RCTs (n=1016) Adults) with bipolar disorder in remission	Use of long-acting injectable antipsychotics: flupentixol risperidone	Systematic review with meta-analysis	1. Placebo 2. Oral medication (MS, antidepressant, AP)	Relapse prevention in bipolar affective disorder (BD) (criteria of DSM IVA)		Long-acting injectable antipsychotic risperidone was superior to placebo for study-defined relapse rate (hazard ratio = 0.63, p<.0001), relapse of manic symptoms (hazard ratio = 0.42, P <.(hazard ratio=0.75, P=0.007). Pooled long-acting injectable antipsychotics did not outperform oral medications on the primary endpoint, but with significant heterogeneity (I2 = 74%). Sensitivity analysis, including only studies with rapid cycling or high frequency of patients

https://doi.org/10.25118/2763-9037.2026.v16.1542

							with relapse, revealed that long-acting injectable antipsychotics were superior to oral drugs (I2=0%, RR=0.58, P=0.0004)
Kishi, 2021	8 RCTs (1456 Stable adults with bipolar disorder using: 3 aripriprazole + mood stabilizer (EH) 1 lurasidone + EH 2 quetiapine + EH 1 Ziprasidone + EH 1 olanzapine + EH	Use of a mood stabilizer (MS) and/or second-generation antipsychotic	Systematic review with meta-analysis	Mood stabilizer + placebo and discontinuation of AP Second generation antipsychotics (SGA) Limitations – small samples in some included studies	Relapse prevention in bipolar affective disorder (BD) (criteria of DSM IV)	recurrence of manic/hypomanic/mixed and depressive episodes and all causes discontinuation within 6 months.	RR (95% CI) of recurrence at 6 months was: 0.51 (0.39–0.86) for any mood episode, 0.42 (0.30–0.59) for manic/hypomanic/mixed episodes - 0.39 (0.28–0.54) for depressive episodes. The RR for all-cause discontinuation was 0.67 (0.50–0.89). Both aripiprazole+SH and quetiapine+SH outperformed placebo+SH in recurrence of any mood, manic/hypomanic/mixed, and depressive episodes at 6 months.
Oya et. al., 2019	Stable adults with bipolar disorder 2 RCT with lithium (n=218) 4 RCTs with lamotrigine (n=706)	use of lamotrigine or lithium	Systematic review with meta-analysis	Placebo	Relapse prevention in bipolar affective disorder (BD) (criteria of DSM IV)	N/A	Both drugs were superior to placebo for reducing the rate of relapse due to any mood episode [lithium: RR = 0.52 (0.41-0.66), P < 0.00001, I 2 = 0%, NNT = 2.3 (1.6-4.2); lamotrigine: RR = 0.81

							(0.70-0.93), P = 0.004, I 2 = 0%, NNT = 8.3 (5.0-25.0)] and discontinuation for all causes. There were no significant differences in other outcomes between the lithium or lamotrigine and the placebo groups. Few studies and small samples
Severus et. al., 2014	7 RCT (n= 1580) Adults over 16 years of age with total or partial remission of a mood episode in bipolar disorder.	use of lithium	Systematic review with meta-analysis	1. Placebo 2. Anticonvulsivants	Relapse prevention in bipolar affective disorder (BD) (criteria of DSM III-R, -IV; ICD 10)	N/A	Lithium was more effective than placebo in preventing general mood episodes (random effects RR 0.66, 95% CI 0.53 to 0.82), manic episodes (random effects RR 0.52, 95% CI 0. 38 to 0.71) and, depressive episodes (random effects RR 0.78, 95% CI 0.59 to 1.03; fixed effect RR 0.73, 95% CI 0.60 to 0.88). In preventing manic episodes, lithium showed superiority over anticonvulsants (random effects RR 0.66, 95% CI 0.44 to 1.00)

Source: The authors

https://doi.org/10.25118/2763-9037.2026.v16.1542