

# Drug treatment of mania in children and adolescents: a systematic review

DIARMAID O'SULLIVAN<sup>1</sup>, NIAMH LIDDY<sup>2</sup>, LUKE O'SULLIVAN<sup>3</sup>, HENRY O'CONNELL<sup>4</sup>

<sup>1</sup> West Clare CAMHS, Co Clare, <sup>2</sup> Psychiatry of Old Age, North Mayo Team, Co Mayo, <sup>3</sup> UCD School of Veterinary Medicine, Dublin, <sup>4</sup> Laois-Offaly Mental Health Services, Co Laois

## Introduction

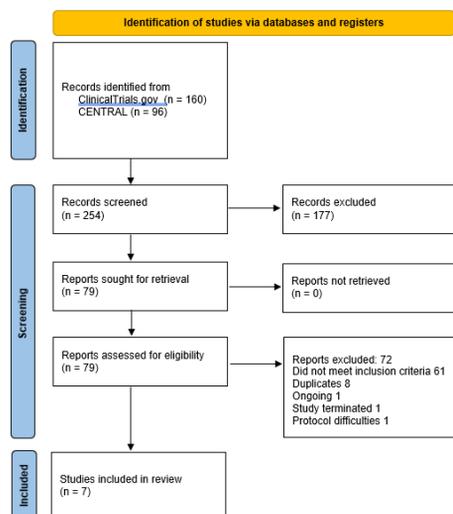
Bipolar Affective Disorder (BPAD) is a mental disorder defined by episodic periods of elated or irritable mood (manic or hypomanic episodes) and episodes of depression. In mixed affective states or episodes, there is a combination of depressive and elated features.

## Aim

To identify evidence for the efficacy of drug treatments in children and adolescents with acute manic or mixed episodes in the context of BPAD I.

## Method

We identified articles by searching the Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov. Studies were included based on predetermined criteria. These included: double-blind, placebo-controlled trials (RCTs) where the primary purpose was treatment and the primary outcome was measure of efficacy, the measure used being the Young Mania Rating Scale (YMRS). Age range was 10 - 17 years. Among our exclusion criteria were trials that included diagnoses of BPAD type 2 or other forms of bipolar or psychotic disorder.



## Results

We identified seven trials; six published trials and a recently completed trial of Ziprasidone that has yet to be peer reviewed. The medications are: Aripiprazole, Asenapine, Divalproex (sodium valproate and valproic acid) Olanzapine, Quetiapine, Risperidone, and Ziprasidone.

The trials contained 1,636 individuals in total. All the antipsychotic drugs showed efficacy, while Sodium Divalproate failed to demonstrate superiority to placebo. Numerically low dose risperidone resulted in the largest decrease in symptoms (in terms of YMRS change) but this was not statistically significant.

Territory	Sponsor	Therapeutic	Participants	Ages	Dosage	Duration	Endpoint difference from placebo in LS Means (95% CI)	Statistically Significant
United States	Otsuka	Aripiprazole	296	10 - 17 years	10mg /day	4 weeks	-5.86 (-8.46, -3.27)	Yes
					30mg /day		-8.56 (-11.17, -5.95)	Yes
Russian Federation & United States	Merck	Asenapine	404	10 - 17 years	2.5mg BID	3 weeks	-3.2 (-5.6, -0.8)	Yes
					5mg BID		-5.3 (-7.7, -2.9)	Yes
					10mg BID		-6.2 (-8.6, -3.8)	Yes
United States	Abbott	Divalproex	151	10-17 years	250 mg and/or 500 mg /day	4 weeks	-0.9	No
United States & Puerto Rico	Eli Lilly	Olanzapine	161	13 - 17 years	Flexible, 2.5 to 20 mg/day	3 weeks	-7.7	Yes
United States	AstraZeneca	Quetiapine	284	10 - 17 years	400 mg/day	3 weeks	-5.23 (-8.13, -2.32)	Yes
					600 mg/day		-6.57 (-9.49, -3.66)	Yes
United States	Johnson & Johnson	Risperidone	169	10-17 years	0.5-2.5mg / day	3 weeks	-9.2	Yes
					3-6mg / day		-8	Yes
Ukraine & United States	Pfizer	Ziprasidone	171	10 - 17 years	Flexible dose	4 weeks	-4.23 (7.14 to -1.32)	Yes

## Conclusions

Six antipsychotic drugs demonstrated efficacy in the treatment of BPAD I, manic or mixed episode, in children and adolescents between ages 10 to 17 years old, as measured by the change from baseline to week 3 or week 4 on the Young Mania Rating Scale (YMRS).

## Selected References

- Dinh, P., Zhang, J., Zornberg, G. and Kiedrow, K. (2008).** Statistical Review and Evaluation Clinical Studies *NDA/Serial Number: 21-463 / S021*. [online]. Available at: <https://www.fda.gov/media/71102/download> [Accessed 24 Jul. 2021].
- Ritter, M. (2008).** *NDA: 22-267 Clinical Review*. [online] [www.fda.gov/](https://www.fda.gov/). Available at: <https://www.fda.gov/media/71468/download> [Accessed 25 Jul. 2021].
- Alfaro, C. (2008).** *020592 Olanzapine Clinical S040-041 PREA*. [online] [www.fda.gov/](https://www.fda.gov/). Available at: <https://www.fda.gov/media/download> [Accessed 25 July 2021].
- Dinh, P., Yang, P. and Hung, H.M.J. (2009).** *Statistical Review and Evaluation Clinical Studies*. [online] [www.fda.gov](https://www.fda.gov/). Available at: <https://www.fda.gov/media/78137/download> [Accessed 25 Jul. 2021].
- Lawrence, J., Yang, P. and Hung, H., 2006.** *N20-272S046 N20-272S046 Risperidone Clinical Statistical BPCA/FDASIA*. [ebook] FDA. Available at: <https://www.fda.gov/media/85421/download> [Accessed 26 July 2021].