PEARLS Practical Evidence About Real Life Situations

Do atypical antipsychotics help treat irritability in people with autism spectrum disorder?

Clinical Question	What are the comparative benefits and harms of treating irritability in people with autism spectrum disorder (ASD) with atypical antipsychotics?
Bottom Line	A network meta-analysis of 17 studies involving 1,027 children with ASD found that risperidone and aripiprazole may reduce irritability in the short term compared to placebo. In contrast, lurasidone likely has little to no effect on irritability. The evidence on other outcomes—such as aggression, weight gain, and extrapyramidal side effects—is very uncertain. Atypical antipsychotics may also help reduce obsessive-compulsive symptoms and inappropriate speech, though the certainty of these findings ranges from moderate to very low. Overall, while some benefits are observed, the limited and low-certainty evidence highlights the need for further high-quality research.
Caveat	The certainty of the evidence was limited due to several factors. The network meta-analysis had few studies and weak connections, with many studies showing high risk of bias and imprecision. Data were scarce for children in low- and middle-income countries, adults, and long-term outcomes. Additionally, most studies focused only on risperidone and aripiprazole, offering limited insight into other atypical antipsychotics.
Context	ASD is a neurodevelopmental condition marked by challenges in social interaction, communication, and behaviour. Treatment includes both pharmacological and non-pharmacological approaches. Only risperidone and aripiprazole are FDA-approved for managing irritability in children with ASD. These atypical antipsychotics act on dopamine and serotonin receptors, with aripiprazole's partial dopamine agonism potentially reducing movement-related side effects. It also has moderate histamine receptor affinity, which may lower sedation and weight gain risks. While short-term trials show some efficacy, side effects and limited adult-focused research highlight the need for more age-specific studies to guide safe and effective treatment.
Cochrane Systematic Review	Meza N, Franco JVA, Sguassero Y, Núñez V, Escobar Liquitay CM, Rees R, Williams K, Rojas V, Rojas F, Pringsheim T, Madrid E. Atypical antipsychotics for autism spectrum disorder: a network meta-analysis. Cochrane Database of Systematic Reviews 2025, Issue 5. Art. No.: CD014965. DOI: 10.1002/14651858.CD014965.pub2. This review contains 17 trials which included 1,027 participants.

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Systematic review link:
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD014965.pub2/full