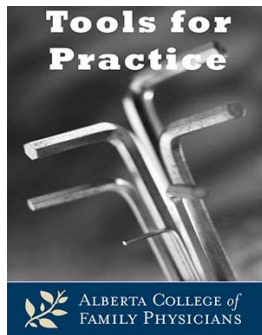


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Antipsychotics for depression: An acceptable risk/benefit profile

Clinical Question: Are antipsychotics, either added to standard antidepressants or as monotherapy, effective for the treatment of depression without psychotic features?

Evidence:

2010 Cochrane review¹ (28 trials, 8487 patients)

- Antipsychotic versus antidepressant: Equivalence is uncertain
 - Olanzapine (5 trials, 779 patients): 2 of 5 olanzapine studies found antidepressants superior (3 found no difference)
 - Quetiapine (1 trial, 309): equivalent but only one trial.
- Antipsychotic versus placebo: Only quetiapine (4 trials, 2069 patients) was studied in depression without psychosis.
 - Response Number Needed to Treat (NNT) 8 and remission NNT 17.
- Antipsychotic added to (augmenting) antidepressants: 12 trials using aripiprazole, olanzapine, quetiapine, or risperidone
 - Response NNT 7-12, and remission NNT 7-12.
- Adverse events were common, and typical of the antipsychotic studied (example 4kg weight gain with olanzapine).
 - More patients stopped due to adverse events in the antipsychotic group: Number Needed to Harm (NNH) 6-13 when used alone and NNH 12-50 when used as augmentation.
- Insufficient evidence to determine if one antipsychotic is superior to others.

Context:

- Trials in the systematic review have a high risk of bias including unclear allocation concealment, selective reporting and short trial duration (22 of 28 studies <12 weeks)
 - Although not assessed, selective publication (not publishing negative studies)² and sponsorship bias³, are common concerns in the literature.

- Canadian⁴ and American⁵ depression guidelines include the option of second-generation antipsychotics alone or as augmentation therapy in patients who have failed first-line antidepressants.
- Second-generation antipsychotics may also help in some anxiety conditions like Generalized Anxiety Disorder.⁶

Bottom-line: Second-generation antipsychotics appear effective in treating depression when given to augment antidepressants. One antipsychotic (quetiapine) appears effective in treating depression alone but equivalence to antidepressants is uncertain. The evidence has a high risk of bias and adverse events are common.

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