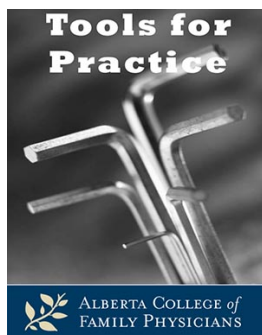


**Tools for Practice** is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,400 family physicians, family medicine residents and medical students in Alberta. Established over sixty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. [www.acfp.ca](http://www.acfp.ca)

**Reviewed: June 9, 2015**  
**Evidence Updated: 5 systematic reviews added, context updated**  
**Bottom Line: Unchanged**  
**First Published: January 23, 2012**



## **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?**

**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.**

### **Evidence:**

- 2010 Cochrane review<sup>1</sup> (28 trials, 8487 patients):
  - Antipsychotic versus antidepressant: Equivalence is uncertain.
    - Olanzapine (five trials, 779 patients): Two of five olanzapine studies found antidepressants superior (three found no difference).
    - Quetiapine (one trial, 309 patients): Equivalent but only one trial.
  - Antipsychotic versus placebo: Only quetiapine (four trials, 2,069 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 4 kg 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.
- Newer systematic reviews found similar.<sup>2-5</sup>

### **Context:**

- Trials in systematic reviews 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)<sup>6</sup> and sponsorship bias<sup>7</sup> are common concerns in the literature.
- Canadian<sup>8</sup> and American<sup>9</sup> depression guidelines include the option of second-generation antipsychotics alone or as augmentation therapy in patients who have failed first-line antidepressants.
- Efficacy of second-generation antipsychotics is minimal in some anxiety conditions (like Generalized Anxiety Disorder) but may help others (like Obsessive Compulsive Disorder).<sup>10</sup>

### **Original Authors:**

Ricky Turgeon BSc Pharm, G. Michael Allan MD CCFP

### **Reviewed:**

Adrienne J Lindblad BSP ACPR PharmD

### **Updated:**

G. Michael Allan MD CCFP

### **References:**

1. Komossa K, Depping AM, Gaudchau A, *et al.* Cochrane Database Syst Rev. 2010 Dec 8; (12):CD008121.
2. Wen XJ, Wang LM, Liu ZL, *et al.* Braz J Med Biol Res. 2014 Jul; 47(7):605-16.
3. Spielmans GI, Berman MI, Linardatos E, *et al.* PLoS Med. 2013; 10(3):e1001403.
4. Zhou X, Keitner GI, Qin B, *et al.* Int J Neuropsychopharmacol. 2015 May 25. pii: pyv060. doi: 10.1093/ijnp/pyv060. [Epub ahead of print]
5. Edwards SJ, Hamilton V, Nherera L, *et al.* Health Technol Assess. 2013 Nov; 17(54):1-190.
6. Turner EH, Matthews AM, Linardatos E, *et al.* N Engl J Med. 2008 Jan 17; 358(3):252-60.
7. Heres S, Davis J, Maino K, *et al.* Am J Psychiatry. 2006; 163:185–194.
8. Kennedy SH, Lam RW, Parikh SV, *et al.* J Affect Disord. 2009; 117 Suppl 1:S26-43.
9. Gelenberg AJ, Freeman MP, Markowitz, *et al.* Practice guideline for the treatment of major depressive disorder. Available at: [http://psychiatryonline.org/pb/assets/raw/sitewide/practice\\_guidelines/guidelines/mdd.pdf](http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf). Last accessed June 9, 2015.
10. Lindblad AJ, Freeman L. Tools for Practice. April 15, 2015. Available at: [https://www.acfp.ca/wp-content/uploads/tools-for-practice/1428937715\\_tfpotypicalantipsychoticsforanxietytftpfv2.pdf](https://www.acfp.ca/wp-content/uploads/tools-for-practice/1428937715_tfpotypicalantipsychoticsforanxietytftpfv2.pdf). Last accessed June 9, 2015.

**Tools for Practice** is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at <http://bit.ly/signupfortfp>. Archived articles are available on the ACFP website.

This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.