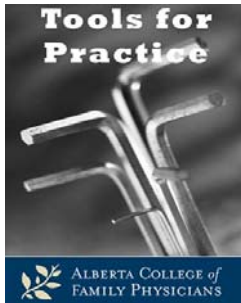


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Are some 2nd generation antidepressants more equal than others?

Clinical Question:

In adults suffering from depression, are any of the 2nd generation antidepressants better than others?

Evidence:

Two recent systematic reviews compared the benefits and harms associated with 2nd generation antidepressants.

- The 2008 systematic review¹ included 203 studies and examined change on depression scales and specific adverse events.
 - There was no important difference in effectiveness. The few statistical differences found were not clinically important,
 - e.g. escitalopram 1.13 points better than citalopram on the 60 point MADRS scale (minimal clinically important difference ≥ 2)
 - Sponsorship may have played a role in these subtle differences
 - Adverse Events similar in amount (61% of patients had ≥ 1) but types varied
 - e.g. Venlafaxine 11% more nausea & vomiting, Sertraline 3% more diarrhea,
- 2009 systematic review² included 117 studies and examined response to treatment and withdrawal.
 - Identified some small differences in efficacy and acceptability.
 - Efficacy Top 4: mirtazapine, escitalopram, venlafaxine, sertraline
 - Acceptability Top 4: escitalopram, sertraline, bupropion, citalopram

Context:

Antidepressant evidence suffers from significant bias. For example,

- $\leq 10\%$ are high quality studies¹⁻³
- Selective publication (and republication) of positive trials (publication

- bias)⁴
 - Interpretation of results in favour of the sponsor (funding bias)⁵
- Other reviews have attempted to determine if one antidepressant is superior but the results are inconsistent.^{3,6}
- The 2009 review² has important concerns regarding validity including,
 - They treated all depression scales as the same (and they are not),
 - Using odds ratios exaggerated the differences they found,
 - Importantly, when they tried to account for sponsorship bias, the differences between the drugs were reduced.
- Both reviews^{1,2} did some indirect comparison of drugs from different studies, which is less reliable than direct comparison in the same study.
- The 2008 review did not have quite as many concerns with validity.

Bottom-line: Among 2nd generation antidepressants, there is little or no reliable difference in the efficacy or frequency of adverse events, but the types of adverse events do vary. Clinician should select antidepressants based on adverse effects profile and cost, not on efficacy differences.

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1. [Ann Intern Med. 2008;149: 734-750.](#)
2. [Lancet 2009; 373: 746-58.](#)
3. [Ann Intern Med. 2005;143 :415-26.](#)
4. [BMJ. 2003; 326: 1171-73.](#) [NEJM 2008; 358: 252-60.](#)
5. [BMJ 2004; 328: 879-83](#)
6. [Cochrane 2005;\(4\): CD004185.](#) [Curr Med Res Opin. 2009; 25:161-75.](#) [Cochrane 2009;\(2\): CD006117.](#)

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. Archived articles are available on the Towards Optimized Practice website.

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