

# Review: Newer and older antidepressants have similar efficacy and total discontinuation rates but different side effects

Mulrow CD, Williams JW Jr, Trivedi M, et al. *Treatment of depression: newer pharmacotherapies*. Rockville, MD: Agency for Health Care Policy and Research; February 1999. AHCPR publication no. 99-E014. <http://www.ahcpr.gov/clinic/deprsumm.htm>.

## QUESTION

In patients with depressive disorders, do newer and older pharmacotherapies have similar efficacy and adverse effects?

## DATA SOURCES

Studies were identified by searching the Cochrane Collaboration Depression, Anxiety, and Neurosis Controlled Trials Registry; scanning trial article references and 46 meta-analyses; and contacting experts.

## STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) with an active intervention of  $\geq 6$  weeks; compared a "newer" antidepressant with another antidepressant, placebo, or psychosocial intervention in patients with depressive disorders; and assessed depression symptoms, functional status, or quality of life.

## DATA EXTRACTION

2 reviewers independently extracted data on participant and diagnostic descriptors, setting, intervention, study methods, adverse effects, and outcomes (response rate, dropouts, and dropouts because of adverse events).

## MAIN RESULTS

315 studies met the selection criteria. Similar response and total discontinuation rates existed for newer and older antidepressants. Newer antidepressants led to greater response rates in patients with major depression (51% vs 32%, weighted relative benefit increase [RBI] 60%, 95% CI 50% to 70%); dysthymia (59% vs 37%, weighted RBI 70%, CI 30% to 130%); and recurrent depression (47% vs 28%, weighted RBI 50%, CI 20% to 90%) than did placebo. SSRIs and tricyclic antidepressants led to similar response rates (RBI 0%, CI -10 to 10), but specific side effects differed. SSRIs led to more patients with diarrhea {absolute risk difference (RD) 9%, CI 5% to 13%}\* , headache (RD 3%, CI 0.2% to 4%), insomnia {RD 6%, CI 3% to 8%}\* , and nausea (RD 10%, CI 6% to 11%), whereas tricyclics resulted in more patients with blurred vision (RD 4%, CI 1% to 5%), constipation (RD 12%, CI 7% to 14%), dizziness (RD 11%, CI 6% to 13%), dry mouth (RD 30%, CI 23% to 33%), tremors (RD 4%, CI 1% to 5%), and urinary disturbance (RD 5%, CI 1% to 8%). Insufficient evidence exists to establish whether newer antidepressants are effective

for other depressive syndromes or to compare them with psychosocial therapy. Methodologic weakness compromised evidence for the effectiveness of St. John's wort. First-generation tricyclic agents led to a greater adverse effect-related dropout rate.

## CONCLUSIONS

Newer antidepressants are efficacious in the treatment of major depression and dysthymia. Response and discontinuation rates are similar among newer and older antidepressants, but specific side effects and related dropout rates differ. It is unknown whether antidepressants are more effective than herbal treatment or psychosocial interventions.

*Source of funding:* U.S. Agency for Health Care Policy and Research.

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## COMMENTARY

The introduction of SSRIs and other new antidepressants in the past decade increased the options available for tackling depressive illnesses. But has a major advance occurred in the treatment of this group of disorders so commonly encountered by family practitioners and hospital physicians? Mulrow and colleagues' comprehensive report lends support to the findings of previous high-quality systematic reviews that compared newer with older antidepressants (1). It also examines herbal remedies and psychosocial therapies.

All the meta-analyses have concluded that newer and older antidepressants have equivalent efficacy. Therefore, initial prescribing decisions have to be based on consideration of patient acceptability and cost. Dropout rates in RCTs have been used as the best available proxy measure for tolerability, and Mulrow and colleagues found that tricyclic antidepressants and SSRIs are almost identical in this respect. However, side-effect profiles differ, and patients should be informed of these differences so that their wishes can be considered when choosing medicine.

For complementary practitioners and their patients, some evidence exists that St. John's wort has antidepressant properties, but more research is required.

Purchasers of health care should reevaluate their spending on depression. The introduction of SSRIs has prompted a vast increase in spending, which is simply not justified by the available scientific data on efficacy and side effects.

This meticulously done meta-analysis highlights that the evidence does not address all common clinical problems. Insufficient research exists to guide prescribing in mild, severe, treatment-resistant, or comorbid depressive illnesses. We cannot depend on the pharmaceutical industry to guide the use of important and widely used medicines; 94% of the antidepressant studies for which a funding source could be identified were industry financed. Health maintenance organizations, insurance companies, and especially governments should take note.

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## Reference

- Geddes JR, Freemantle N, Mason J, Eccles MP, Boynton J. SSRIs versus other antidepressants for depressive disorder. Cochrane Review, latest version 22 Oct 1999. In: The Cochrane Library. Oxford: Update Software.