Efficacy of antidepressants for late-life depression: a meta-analysis and meta-regression of placebo-controlled randomized trials

Tedeschini E, Levkovitz Y, Iovieno N, Ameral VE, Nelson JC, Papakostas GI

CRD summary
The review found that antidepressant treatment for major depression was effective, but that such treatment may have been less effective in later life than in a general adult population. Limitations in the conduct and reporting of the review, particularly lack of quality assessment, mean that the reliability and generalisability of the conclusions are uncertain.

Authors' objectives
To examine the efficacy of antidepressants for the treatment of major depressive disorder in elderly patients.

Searching
MEDLINE was searched for articles published between 1st January 1980 and 3rd March 2010. Search terms were reported. Reference lists of all identified studies were searched manually for additional studies.

Study selection
Randomised, double-blind, placebo-controlled trials of oral antidepressants for monotherapy treatment of adult major depressive disorder were eligible. Studies were restricted to those of agents licensed for use in USA, Canada, Australia, Japan or the European Union; the agents were listed in the review. Participants were required to have major depressive disorder diagnosed by established criteria, and not have other major mental health or comorbid conditions. Trials had to be parallel group studies, of at least four weeks' duration, not have been previously published. Trials had to have reported outcomes on at least one of the following scales: the Hamilton Depression Rating Scale (HDRS); the Montgomery-Asberg Depression Rating Scale (MADRS); or the Clinical Global Impressions-Improvement (CGI-I) Scale.

Studies were classified as those of adult depression, defined as patients under the age of 65 years (which excluded older patients) or of later life depression, defined as patients over 55 years. The mean age in adult studies was 44.5 years, and in later life studies was 69.7 years. Later life depression mean study duration was 8.1 weeks, the frequency of appointments was 0.8 visits per week and the proportion of women was 60.3%. Brief further details of the studies in older populations only were given in the review.

The authors did not state how many reviewers selected studies for inclusion, but did state that the final inclusion of articles was determined by consensus between the authors.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Outcome data were extracted from each study to calculate risk ratios (RR) with associated 95% confidence intervals (CIs) for clinical response and treatment discontinuation. Clinical response was defined as a 50% or greater reduction in HDRS or MADRS score, or a CGI-I score of less than 3 at the final visit. Where more than one outcome was reported, preference was given to the HDRS score. If only CGI-I scores were reported, HDRS responses were obtained from the authors, or imputed. Intention-to-treat response rates were used, and authors were contacted to request these if they were not in the original paper. If they were not available, response rates based on completers were used.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
The studies were pooled using a random-effects model in studies of all adult and later life depression separately. Heterogeneity was assessed using the Q statistic. Multi-variable meta-regression was used to compare the risk ratios of
responding to anti-depressant treatment, and of discontinuing anti-depressant treatment, in all adult versus older patients. Trials of older late-life depression (patients aged 65 or over) were included in a subgroup analysis. Anti-depressant and placebo response rates were compared using analysis of variance, adjusting for relevant variables, and from this a number-needed-to-treat was determined.

**Results of the review**
Seventy-four RCTs (20,572 participants) were included in the review. Of these, 15 trials (4,756 patients) were based on patients with depression in later life.

Antidepressants were associated with better response than placebo in adult depression (RR 1.42, 95% CI 1.35 to 1.49; p=0.047) and in later life depression (RR 1.30, 95% CI 1.15 to 1.48; p<0.001). There was significant heterogeneity for both groups of studies. Response to anti-depressant treatment and the risk of discontinuation because of adverse events were similar between studies of adults and those of later life depression.

The effect of antidepressants in older later life depression was not significantly different to placebo (RR 1.13, 95% CI 0.93 to 1.37), but there was significant heterogeneity (p<0.002).

Response rates showed that the number-needed-to-treat was six for studies of adults, eight for later life depression and 21 for older later life depression.

**Authors' conclusions**
Antidepressants were effective in later life depression, but there was significant heterogeneity across trials.

**CRD commentary**
The objectives and inclusion criteria of the review were clear, but the inclusion of trials of younger patients did not address the authors' question. Only one database was searched for published trials, and it was not stated whether the search was limited by language. Publication bias may have affected the results, and no assessment of this was reported. It appeared that more than one reviewer was involved in the study selection process, which reduced the possibility of error or bias at this stage. No quality assessment of the included studies was performed, but all studies were required to be double-blinded, so the reliability of the pooled results was unclear.

Few details of the included studies, particularly for those on younger patients, were included, which meant that the generalisability of the results was unclear. However, it was noted that the authors intended the review to focus on older adults. The methods used to pool the studies were appropriate, and subgroup analysis and meta-regression were used to explore possible reasons for the significant heterogeneity.

The authors' conclusions were based on the evidence presented. Limitations in the conduct and reporting of the review, particularly lack of quality assessment, mean that the reliability and generalisability of the conclusions are uncertain.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research was needed into factors that moderate antidepressant response in older adults.

**Funding**
None.

**Bibliographic details**

**PubMedID**
22244025
DOI
10.4088/JCP.10r06531

Indexing Status
Subject indexing assigned by NLM

MeSH
Age Factors; Aged; Aging /drug effects /physiology; Antidepressive Agents /therapeutic use; Depressive Disorder, Major /drug therapy; Humans; Middle Aged; Randomized Controlled Trials as Topic /methods; Regression Analysis; Treatment Outcome

AccessionNumber
12012002625

Date bibliographic record published
29/02/2012

Date abstract record published
01/08/2012

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.