Paroxetine versus placebo and other agents for depressive disorders: a systematic review and meta-analysis


CRD summary
This review concluded that there were no consistent and valid differences to suggest that multiple modes of action improved clinical outcomes between paroxetine and other antidepressants for depressive disorders. This was a generally well-conducted review. The authors' conclusions appear to be reliable.

Authors' objectives
To examine the efficacy of paroxetine versus placebo and other antidepressants in the treatment of depressive disorders.

Searching
MEDLINE, EMBASE, CINAHL, all Evidence-Based Medicine Reviews, HealthSTAR, BIOSIS Previews and PsycINFO were searched from inception to Feb 2004. Search terms were provided. Reference lists of potentially relevant studies were checked. Full-text papers from potentially relevant conference abstracts were also obtained and experts contacted. The searches were not restricted by language, publication type or study design.

Study selection
Randomised controlled trials (RCTs) that compared paroxetine with placebo or other antidepressants for patients with depressive disorders were eligible for inclusion. Trials of patients with bipolar disorder or who were medically ill (for example, patients with human immunodeficiency virus (HIV) or cancer) were excluded. Trials that used off-label antidepressants (for example in adolescent populations) or electroconvulsive therapy were also excluded. To be eligible for inclusion, trials had to evaluate a clinically homogenous study population. The primary outcomes of interest were remission, clinical response and symptom reduction.

Treatment dosages were reported; the median duration of treatment was six weeks (range four to 52 weeks). Comparative antidepressants included amitriptyline, clomipramine, fluoxetine, imipramine, mirtazapine, sertraline, venlafaxine and others. The trials included adult patients (mean age ranged from 34 to 87 years, where reported) with major depressive disorder, depressive disorder or other diagnoses (for example, dysthymia). Patients were mainly assessed in outpatient settings, mostly located in Europe. The majority of patients were female.

Two reviewers independently selected the studies, with any disagreements resolved by discussion.

Assessment of study quality
Trial quality was assessed in terms of randomisation, double-blinding, and drop-outs using the Jadad scale to obtain a quality score out of a maximum of 5 points; allocation concealment was also assessed. Two reviewers independently assessed quality, with any disagreement resolved by discussion.

Data extraction
Data were abstracted and analysed using intention-to-treat, and observed-case analyses. Percentage differences in remission, clinical response and drop-outs were extracted. Three reviewers independently extracted data from the trials.

Methods of synthesis
Meta-analyses examining pooled rate difference with 95% confidence intervals were performed using a random-effects model. Heterogeneity was assessed using the $\chi^2$ test. Subgroup and sensitivity analyses were conducted by removing trials with differing diagnostic criteria, and by omitting smaller trials. Funnel plots were used to assess publication bias.

Results of the review
Sixty-two randomised controlled trials (n=not clear) were included in the review. The sample sizes ranged from 24 to
953. The median quality score was 3 points (range 2 to 5). Allocation concealment was adequately reported in 8% of the trials, and was unclear in 92% of the trials.

Individuals who were treated with paroxetine demonstrated significantly improved remission (rate difference 10%, 95% confidence interval (CI): 6 to 14; six trials), clinical response (rate difference 17%, 95% CI: 7 to 27; five trials) and symptom reduction (change score from baseline) (effect size 0.21, 95% CI: 0.10 to 0.30; nine trials) when compared to placebo. However, paroxetine was associated with significantly more drop-outs due to adverse events when compared to placebo (rate difference 8%, 95% CI: 4 to 13; eight trials). Results for all outcomes were inconsistent when paroxetine was compared with other antidepressants.

No publication bias was detected.

Authors' conclusions
There were no consistent and valid differences between paroxetine and other antidepressants to suggest that multiple modes of action improved clinical outcomes.

CRD commentary
This review addressed a clear question and was supported by appropriate inclusion criteria. Attempts were made to identify all published studies by searching a number of databases and other sources. Unpublished studies were not included in the review, so some relevant studies may have been missed. However, the authors did attempt to assess publication bias and reported no evidence of bias. Validity was assessed according to published criteria. A number of reviewers were involved in the systematic review process, limiting reviewer error and bias. Comprehensive details of the individual trials were reported, with the exception of quality assessment results. It appeared that the trials were appropriately summarised using meta-analyses, although results from statistical tests of heterogeneity were not reported. More detailed analyses of adverse events would have been beneficial to assess the overall clinical effectiveness of the intervention. This was a generally well-conducted review. The authors' conclusions appear to be reliable.

Implications of the review for practice and research
Practice: The authors stated that clinicians must focus on improving adherence regimens, past response rates and other practical considerations when choosing an antidepressant for a patient.

Research: The authors did not state any implications for research.

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