Review: antidepressants plus benzodiazepines lead to fewer drop outs and less depression severity in major depression


QUESTION: In adults with major depression, does combination treatment with antidepressants and benzodiazepines lead to short term (<8 wk) or long term (>2 mo) symptomatic recovery or side effects?

Data sources
Studies were identified by searching Medline, EMBASE/Excerpta Medica, International Pharmaceutical Abstracts, Biological Abstracts, LILACS, PsycLIT, the Cochrane Library, and the trial register of the Cochrane Depression, Anxiety, and Neurosis Group (January 1972 to December 1998); hand searching major mental health and general medicine journals; scanning the reference lists of identified articles; checking SciSearch; and making personal contacts.

Study selection
Studies were selected if they were randomised controlled trials comparing combined antidepressant-benzodiazepine treatment with antidepressants alone in adults with major depression. Studies were excluded if the antidepressant dose was <100 mg of imipramine, or its equivalent daily, or the duration of the trial was <4 weeks.

Data extraction
Data were extracted on patient characteristics, treatment type and dose, duration of follow up, and main outcomes.

Main results
9 studies (679 patients) met the selection criteria. The antidepressants studied were imipramine, desipramine, amitriptyline, maprotiline, nortriptyline, clomipramine, fluoxetine, and mianserin; benzodiazepines studied included triazolam, alprazolam, diazepam, chlordiazepoxide, flunitrazepam, lorazepam, benzepame, clonazepam, and mexazolam. Patients allocated to the combined treatment group were less likely to drop out of the study than were those in the antidepressant alone group (table). Patients in the combined treatment group were also less likely to drop out because of side effects (table). More patients in the combined treatment group showed a >50% reduction from their baseline depression severity at 4 weeks than did those in the antidepressant alone group (worst case scenario for drop outs; table). This difference was no longer statistically significant at 8 weeks.

Conclusion
In adults with major depression, a combination of antidepressant and benzodiazepine treatment leads to fewer drop outs and less depression severity at 4 weeks than do antidepressants alone.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Weighted event rates</th>
<th>Combined</th>
<th>Antidepressant alone</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dropped out</td>
<td>22%</td>
<td>33%</td>
<td>37% (19 to 51)</td>
<td>10 (6 to 22)</td>
<td></td>
</tr>
<tr>
<td>Dropped out because of side effects</td>
<td>7%</td>
<td>14%</td>
<td>48% (14 to 68)</td>
<td>15 (10 to 40)</td>
<td></td>
</tr>
<tr>
<td>&gt;50% reduction in depression at 4 weeks</td>
<td>52%</td>
<td>37%</td>
<td>38% (15 to 66)</td>
<td>7 (5 to 15)</td>
<td></td>
</tr>
</tbody>
</table>