Review: most selective serotonin reuptake inhibitors lead to adverse events that appear to outweigh the benefits in children


Clinical impact ratings Mental health ★★★★★ Psychiatry ★★★★★★ Paediatrics ★★★★★

Are selective serotonin reuptake inhibitors (SSRIs) safe and effective for treating depression in children?

**MAIN RESULTS**

6 published and 6 unpublished RCTs were reviewed. Fluoxetine showed a benefit for remission and response, and the adverse event data were not statistically significant (table). Paroxetine increased remission but not response and increased serious adverse events (table). Sertraline did not show a benefit for remission and led to more dropouts because of adverse events (table); a treatment effect for response had borderline significance. Citalopram led to a small reduction in depressive symptoms, and venlafaxine had no effect; adverse events were increased for both drugs (table).

**CONCLUSIONS**

In children with depression, fluoxetine improves symptoms without increasing adverse events. For paroxetine, sertraline, venlafaxine, and citalopram, the risks appear to outweigh the benefits.

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**Selective serotonin reuptake inhibitors (SSRIs) v placebo for depression in children***

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Outcomes at &lt;12 weeks (number of studies)</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>Serious AE (1)</td>
<td>0.9% v 3.6%</td>
<td>75% (−122 to 97)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Suicide attempt (1)†</td>
<td>2.4% v 1.9%</td>
<td>26% (−64 to 340)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Discontinuation (2)‡</td>
<td>5.7% v 6.3%</td>
<td>19% (−82 to 685)</td>
<td>NS</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Serious AE (2)</td>
<td>12% v 4.4%</td>
<td>155% (23 to 430)</td>
<td>15 (8 to 50)</td>
</tr>
<tr>
<td></td>
<td>Suicide attempt/ideation (2)</td>
<td>3.7% v 2.5%</td>
<td>51% (−38 to 269)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Discontinuation (1)</td>
<td>9.7% v 6.9%</td>
<td>40% (−48 to 278)</td>
<td>NS</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Serious AE (2)</td>
<td>3.7% v 3.3%</td>
<td>14% (−61 to 232)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Suicide attempt/ideation (2)</td>
<td>2.6% v 1.1%</td>
<td>143% (−52 to 1139)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Discontinuation (2)</td>
<td>9.0% v 2.7%</td>
<td>236% (27 to 793)</td>
<td>17 (9 to 50)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Suicide attempt (2)</td>
<td>7.1% v 3.6%</td>
<td>99% (−17 to 377)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Treatment emergent AE (2)</td>
<td>79% v 70%</td>
<td>13% (1 to 27)</td>
<td>12 (6 to 100)</td>
</tr>
<tr>
<td></td>
<td>Discontinuation (2)</td>
<td>8.6% v 7.1%</td>
<td>20% (−38 to 135)</td>
<td>NS</td>
</tr>
<tr>
<td>Venlafaxine*</td>
<td>Suicide related events (2)</td>
<td>7.7% v 0.6%</td>
<td>1277% (83 to 10261)</td>
<td>15 (10 to 34)</td>
</tr>
<tr>
<td></td>
<td>Discontinuation (2)</td>
<td>10% v 3.0%</td>
<td>246% (30 to 821)</td>
<td>15 (9 to 50)</td>
</tr>
</tbody>
</table>

*AE = adverse events; NS = not significant. Other abbreviations defined in glossary. †Includes unpublished data. ‡Studies combined using random effects model; fixed effects model used for all others. *Data supplied by author. **Serotonin and noradrenaline reuptake inhibitor.
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