

05 - Effectiveness

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Depression and anxiety disorders CHAPTER 3 Antidepressants – general overview Effectiveness All antidepressants are more efficacious than placebo in adults with MDD¹ and there is broadly equal benefit from antidepressant treatments for mild, moderate or severe major depression.² Antidepressants are normally recommended as first-line treatment in patients whose depression is of at least moderate severity, with psychological treatments being used for milder forms. Of the moderate to severe patient group, approximately 20% will recover with no treatment at all, 30% will respond to placebo and 50% will respond to antidepressant drug treatment.³ This gives a number needed to treat (NNT) of 3 for antidepressant over true no-treatment control and an NNT of 5 for antidepressant over placebo. Response in clinical trials is generally defined by a particular percentage reduction in depression rating scale scores (e.g. 50%), a somewhat arbitrary dichotomy. Change measured using individual scale score tends to show a relatively small mean difference between active treatment and placebo (which itself is an effective treatment for depression). Drug-placebo differences may have diminished over time because of methodological changes.⁴ However, it is possible that rating scales obscure the beneficial effects of antidepressants to some extent. Hieronymus and colleagues⁵ undertook patient-level post-hoc analyses of 18 industry-sponsored placebo-controlled trials of paroxetine, citalopram, sertraline or fluoxetine, including in total 6,669 adults with major depression. The aim was to assess what the outcome would have been if the single item 'depressed mood' (rated 0–4) had been used as the sole measure of efficacy. While 18 of 32 comparisons (56%) failed to separate active drug from placebo with respect to reduction in total Hamilton Depression Rating Scale (HAM-D) score, only 3 of 32 comparisons (9%) were negative when depressed mood was used as the sole effect parameter (i.e. 91% of trials favoured the antidepressant). It is also noteworthy that even using total scale scores, placebo never performs better than an active treatment – antidepressants are always shown to be better than or the same as placebo, never worse than. This is arguably the most compelling evidence for the efficacy of antidepressants. As might be expected, network meta-analyses show robust superiority for antidepressants over placebo, with amitriptyline being the most efficacious.¹ In the same study, mirtazapine was ranked as the second most efficacious antidepressant. However, in a post-hoc analysis, the observed superiority of mirtazapine was found to be attributable to its effects on sleep and appetite, and the absence of gastrointestinal (GI) symptoms. In contrast, when it came to improving depressed mood, suicidality and psychic anxiety, SSRIs and venlafaxine demonstrated relatively greater efficacy.⁶ In a 2023 network meta-analysis of people with depression and a wide range of chronic medical conditions, antidepressants more effectively reduced depressive symptoms than placebo.⁷ The 2019 PANDA trial results support the prescription of SSRI antidepressants in a wider group of participants than previously thought, including those with mild to moderate symptoms who do not meet diagnostic criteria for

depression or generalised anxiety disorder.⁸ Antidepressant treatment seems to only modestly improve quality of life and social functioning in individuals with major depression.^{9,10}

Revision #1

Created 2026-01-04 20:14:57 UTC by Omar Ayman

Updated 2026-01-04 20:14:57 UTC by Omar Ayman