

Combining mirtazapine with SSRIs or SNRIs for treatment-resistant depression: the MIR RCT

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Plain English summary

The MIR Trial

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Plain English summary

Antidepressants are very often prescribed for people with depression, but many patients who take antidepressants in an adequate dose for an adequate length of time remain depressed. We have called this treatment-resistant depression (TRD). One possible way of helping patients with TRD is to combine two antidepressants, adding a second when the first does not help. Some small studies have suggested that it might be beneficial to add the antidepressant mirtazapine to patients' usual antidepressant, as it works in a slightly different way from the widely used antidepressants such as fluoxetine, and that the combination is well tolerated by patients.

We tested this idea in a large study including 480 participants. All of the participants who entered the study were depressed and had been taking an antidepressant for at least 6 weeks. They were randomly assigned to take either mirtazapine or an inactive placebo in addition to their usual antidepressant. The medications were identical in appearance, and the participants and the study team did not know which group the participants had been assigned to.

After 12 weeks of treatment, we reassessed participants' depression to see whether or not the combination of their usual antidepressant with mirtazapine was more effective than the combination with placebo. We did not find convincing evidence of a clinically important benefit for mirtazapine in addition to another antidepressant over placebo in this treatment-resistant group of depressed patients in general practice. Mild adverse events were more common in the mirtazapine group and more participants in this group stopped the treatment before the end of the study.

Based on this study, we cannot recommend this combination of antidepressants with confidence as a routine treatment for patients who have not responded to a single antidepressant.

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