

Commentary on: Weitz ES, Hollon SD, Twisk J, et al. Baseline Depression Severity as Moderator of Depression Outcomes Between Cognitive Behavioral Therapy vs Pharmacotherapy: An Individual Patient Data Meta-analysis. *JAMA Psychiatry*. 2015;72(11):1102-9.

Author's declarative title:

No evidence that CBT is less effective than antidepressants in moderate to severe depression.

Commentary

What is already known on this topic

Some guidelines for the treatment of severe depression recommend that antidepressant medication be used instead of cognitive behavioural therapy (CBT), the most commonly used psychotherapeutic treatment for depression. This is inconsistent with some evidence collating individual patient data (IPD).¹ IPD from multiple randomized controlled trials (RCTs) is one way of increasing power and analyzing depressive symptoms of varying severity; however the previous IPD study included only four studies, so may still have lacked statistical power.

Methods of the study

Weitz and colleagues requested IPD from previous RCTs comparing psychotherapy and antidepressants. RCTs were identified via database searches (PubMed, PsycINFO, EMBASE, Cochrane Registry of Controlled Trials) in a systematic review. The authors selected studies that had compared CBT alone with antidepressants alone, in adults diagnosed with depression. Relapse prevention or maintenance treatment studies and RCTs with inpatients were excluded. 24 RCTs met inclusion criteria and raw data were obtained from 16 (67%), with 1,700 outpatients (794 who had received CBT and 906 who had received a range of antidepressants). Post-treatment scores on the Hamilton Rating Scale for Depression (HAM-D-17) or Beck Depression Inventory (BDI I and II) were used as the main outcomes (10 studies contributed both HAM-D and BDI scores, 2 contributed only the BDI and 4

contributed only the HAM-D). Models were also run using binary outcomes, response (50% reduction in HAM-D scores post-treatment) and remission (score of less than 7 on the HAM-D post-treatment). Multilevel statistical models that treated each study as a separate cluster were implemented to control for unobserved heterogeneity between studies.

What does this paper add

- By using IPD from 16 RCTs, this is the most highly powered study to compare CBT and antidepressants for depression of varying severity. The use of IPD is a major advance. Such an investigation would not be possible with study-level data which would include only the mean depressive symptom scores at baseline with no variation in severity.
- No evidence was found that CBT was less effective than antidepressants for patients with more severe depressive symptoms (regression coefficient 0.00 HAM-D points, 95% CI -0.16 to 0.16, and similar for the BDI (regression coefficient 0.00, 95% CI -0.14 to 0.14). Results were similar when response (OR 0.99, 95% CI 0.93 to 1.05) and remission (1.00, 0.94 to 1.06) were outcome variables. Similarly, when only the more severely depressed groups were examined (defined as >23 on the HAMD or >29 on the BDI), differences after treatment were small (0.10, 95% CI -0.35 to 0.15 and 0.14, -0.30 to 0.03 for HAM-D and BDI, respectively). The authors do not mention if their thresholds for severe depression were specified a priori. The results are not consistent with the recommendation that more severe depression be treated with antidepressant medication rather than psychotherapy.

Limitations

- Even for this large study, the confidence intervals for the most severe group were non-statistically significant: -0.35 to 0.15 on the HAMD and -0.30 to 0.03 on the BDI. The results are therefore compatible with a benefit for antidepressants of around 0.3 standard deviations that could be clinically important.
- The data analysed did not contain many people with very severe depressive symptoms. They defined severe depression as a HAMD score of over 23 and a BDI score of over 29. In many UK trials of depression, the mean BDI score has been over 30, for example 33.7.² In this IPDMA, the mean scores at baseline were 19.2 on the HAM-D and 30.9 on the BDI. They also excluded trials of inpatients with the most severe depressions.

What next in research

More studies of the relative effectiveness of CBT versus antidepressant medication are required to increase statistical power and investigate more severe cases of depression. This might include inpatients or patients with depression and psychotic symptoms. Alternatively, studies could specifically recruit people with high scores on depressive symptom questionnaires. Future studies could also further examine whether antidepressant medication combined with psychotherapy is more effective for severe depression than either treatment alone. This combined treatment is recommended for moderate to severe depression by the National Institute for Health and Care Excellence (NICE).³

Do these results change your practices and why?

Yes. The findings by Weitz and colleagues highlight that some guidelines for the treatment of moderate to severe depression are not supported by the most current evidence. The most important implication is that clinicians might have been deterred from using CBT for severe depression based upon current guidelines. These results from the largest study to date have provided no evidence that CBT is less effective than antidepressants in the more severe depressions. This is important given that CBT may be better at reducing relapse⁴ and some patients with severe depression may also prefer CBT to medication which could increase the likelihood they will persist with treatment.

References

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Competing interests: None

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Competing interests

None

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