Based on their meta-analytic review, Zhou and colleagues[1] conclude that "fluoxetine (alone or in combination with CBT) seems to be the best choice for the acute treatment of moderate-to-severe depressive disorder in children and adolescents" (p. 581). The meta-analysis, however, suffers from several statistical and methodological flaws that belie this and other conclusions.

First, *the authors' own data* indicate that the conclusions about the superiority of fluoxetine (FLU) are unjustifiable. Almost none of the comparisons between FLU/FLU+CBT and other treatments are significant (Figure 3). Furthermore, Figure 4 demonstrates that the confidence intervals of most interventions vs. pill placebo overlap with that of FLU and FLU+CBT, indicating that none should be considered superior to any other.

Second, the meta-analysis gives false impressions of the precision of individual effects. Take, for example, the conclusion regarding the relative inefficacy of psychodynamic therapy (PDT) compared to fluoxetine (FLU) plus CBT (d = 1.14). The total number of trials that examined PDT was two.[2,3] In one of these studies,[3] 74% of patients treated with PDT achieved remission post-therapy and 100% in the 6-month follow-up; in the other,[2] short-term PDT demonstrated comparable outcomes to both CBT and a manualized Brief Psychosocial Intervention (BPI), which was incorrectly categorized by the authors as a "psychological placebo." These data are hardly compatible with the conclusion of PDT being inferior to FLU + CBT or that PDT is non-significantly inferior to *pill placebo* (p. 596).

Part of the problem with the network meta-analysis presented by Zhou et al.[1] involves the assumption of transitivity, i.e., that studies share similar characteristics relevant to estimating an effect size, permitting the comparison of treatments that have never been directly contrasted.[4] Most psychological treatments in the meta-analysis have never been compared to pill placebo or FLU, meaning that establishing transitivity is vital. In the example of PDT, the authors suggest that psychodynamic therapy is non-significantly inferior to pill placebo (d = -0.41), even though in the two included trials, PDT performed *very* comparably to family therapy (d = -0.03 vs. placebo) and CBT (d = 0.05); the *direct* findings from the individual trials, then, appear to contradict the results drawn from the *indirect* evidence of the network analyses. While the authors argue that inconsistency was within tolerated bounds, consistency tests are very underpowered under conditions like the present analysis;[5] the assessed inconsistency is likely an *und*erestimate. Consistency is also impossible to estimate if there are ***no*** direct comparisons.

The authors' conclusions could have the unfortunate consequence of patients failing to receive other treatments that have demonstrated efficacy, and not just fluoxetine. Access to effective evidence-based mental health care is challenging enough, and recommending that clinicians provide one treatment over others—when those other treatments are *just as useful*—only exacerbates the situation.

References

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