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 underestimate. 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


