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On the basis of their meta-analytic review, Zhou and colleagues[1] conclude that "fluoxetine (alone or in combination with CBT [cognitive behavioural therapy]) seems to be the best choice for the acute treatment of moderate-to-severe depressive disorder in children and adolescents." However, the meta-analysis has 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 are unjustifiable. Almost none of the comparisons between fluoxetine or fluoxetine plus CBT and other treatments are significant. Furthermore, the confidence intervals of most interventions versus pill placebo overlap with that of fluoxetine and fluoxetine plus 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 compared with fluoxetine plus CBT (d=1·14). A total of two trials examined psychodynamic therapy.[2,3] To conclude from such a small number of studies and number of patients that psychodynamic therapy shows inferior outcomes to fluoxetine plus CBT is an example of a well-known methodological problem—ie, the reductionistic fallacy (inappropriately drawing group-level conclusions from individual-level sample data).

Finally, a third problem with the network meta-analysis presented by Zhou and colleauges[1] involves the assumption of transitivity (ie, 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 with pill placebo or fluoxetine, meaning that establishing transitivity is vital. In the example of psychodynamic therapy, the authors suggest that psychodynamic therapy is non-significantly inferior to pill placebo (d=–0·41), even though in the two included trials, psychodynamic therapy performed comparably to family therapy (d=–0·03 *vs* placebo) and CBT (d=0·05); the direct findings from the individual trials appear to contradict the results drawn from the indirect evidence of the network analyses. Although 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 not receiving other treatments that have shown 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.

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Authors' reply

Falk Leichsenring and colleagues raise issues relating to the transitivity, inconsistency, and heterogeneity of our network meta-analysis.[1] Actually, these problems are common and difficult to avoid in a network meta-analysis, especially in the presence of pharmacological and non-pharmacological treatments, and thoughtful discussion of the potential biases can maximise transparency and avoid errors in its interpretation.[2] In our network meta-analysis, stringent inclusion criteria were used in order to limit violation of the transitivity assumption, and then multiple subgroup and meta-regression analyses were pre-planned and explore the potential effect modifiers (eg, sex ratio, mean age, and sponsorship). The results of inconsistency and heterogeneity tests were all reported and certainty of evidence was assessed using Confidence In Network Meta-Analysis. We noted that "the quality of evidence is low" and stressed that