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Controversies in recommending treatments for depression - a debate

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Abstract

According to the author guidelines an abstract is not required for a perspective/debate article.

In a previous comment[1], we raised concerns about Malhi et al.'s recommendation that cognitive behavior therapy (CBT), antidepressant, and counseling should be preferred to short-term psychodynamic therapy (STPP) for the treatment of depression.[2]

(1) We pointed out that the treatment ranking by the NICE guidelines for depression[3] which Malhi et al. refer to is affected by several methodological flaws.[1] In addition we showed that this ranking is neither consistent with the head-to-head comparisons carried out by the NICE committee itself nor with evidence provided by recent meta-analyses of psychotherapy of depression (for references see our previous comment[1]).

(2) Furthermore, we explained that the recommendations by Malhi and colleagues misinterpret the NICE guidelines which list several treatments as first-line treatments including STPP. As emphasized by NICE, the choice of a specific treatment depends on several factors, including patient preference, availability and costs.[3]

Recently, Malhi and colleagues reopened the debate in this journal.[4] With regard to the first set of arguments noted above and labeled by Mahli et al. [4, p. 1] as "Concern 1", Malhi and colleagues do not provide any argument refuting any of the methodological concerns we raised and which we summarize again below.[1] The only argument they put forward in favor of their interpretation of treatment ranking, is that counseling is more available and less cost intensive than STPP in the UK. Yet, no studies have investigated whether counseling is more cost-effective compared to STPP, and counseling could be expected to be more available and less cost effective than CBT, too. However, Malhi and colleagues do not apply this argument to CBT, although they note that for NICE "access and cost were perhaps more important than subtle differences in efficacy per se" . [4, p. 3] Furthermore, Malhi and colleagues argue that "accessibility [is a] key clinical factors when treating depression" (p.1) and that "there is little

point in selecting treatment that is simply not available" (p. 3). [4] However, as most patients do not achieve remission through the treatments offered by the IAPT (Improving Access to Psychological Therapies) programme [5], this represents a circular argument in that guidelines continue to recommend established treatments only, rather than to encourage services to offer a *variety* of efficacious treatments. Only in this case, personalized treatment selection is possible, in which clinicians and patients make an informed decision together about the choice of treatment as recommended by NICE. Malhi and colleagues argue that the NICE and RANZCP for depression are "pragmatic" and "practical", however, for a somatic disease (e.g., cancer) it would be considered unreasonable and unethical to offer a patient a very limited range of treatments with limited efficacy if other treatments might improve symptoms for some patients. In general, as the first choice, the most efficacious, cost-effective and best tolerable treatment should be offered to a patient. If it is not available, the treatment ranked next should be considered.

Moreover, Malhi et al. assert that we criticized that NICE based their treatment rankings on effect sizes based on comparisons with placebo/TAU, instead of direct head-to-head comparisons. While this is true, we also showed that these comparisons with placebo/TAU were flawed.[1] NICE, for example, compared the placebo/TAU-controlled effect sizes between treatments without performing a test of statistical significance. In addition, NICE did not assess the clinical significance of the differences in placebo/TAU-controlled effect sizes between treatments. Thus, when a treatment A had a placebo/TAU- controlled effect size of SMD= 0.20, for instance, and treatment B an effect size of d = 0.40, treatment B was ranked above treatment A (provided that there were no differences in costs and availability) - a flawed procedure since the differences in effect sizes were not assessed for statistical or clinical significance (for references see our previous comment[1]). As a consequence, neither

NICE nor Malhi et al. take into account the fact that no clinically significant differences were found between the placebo/TAU-controlled effect sizes of individual STPP compared to individual CBT, individual behavior therapy or SSRIs in both less and more severe depression. All of these differences are below the threshold defined by NICE for clinical significance (SMD=0.50). Thus, these comparisons do not justify the rankings made by NICE. This is true for data on costs as well, since differences in costs between CBT and STPP, for instance, were not shown. Thus, in fact the NICE committee based their recommendations ultimately on "their clinical experience". [3 , B, p. 66] However, as we noted[1], it is unclear whether clinical experience can offer any solid guidance when treatment differences are modest, uncertainty is high and bias is substantial.

Furthermore, Malhi and colleagues continue to ignore or downplay the results of head-to-head comparisons carried out by the NICE committee. These comparisons did not show "subtle" differences [4, p. 3] for STPP compared with counseling in less severe depression, but a statistically and clinically significant difference in favor of STPP (SMD=0.61). NICE, however, ranked STPP below counseling[3], and Malhi et al. recommended counseling over STPP.[2] As noted above, this cannot be justified by referring to costs or availability too. Furthermore, Malhi et al. continue to ignore the fact that the NICE head-to head comparisons did not find statistically or clinically significant differences in efficacy between STPP compared to CBT or SSRIs in more severe depression, with small between-group effect sizes (SMDs: -0-06, 0.04, respectively).

With regard to the second set of issues described above and labeled by Malhi and colleagues as "Concern 2" [4, p. 2] they just state that they do not feel they have misinterpreted NICE rankings.[4] Instead, they suggest that Heim and colleagues have misinterpreted the meaning of

first line treatments.[4, p.2]: "First line simply means 'can be considered first', there is no indication that all first line treatments are necessarily 'equal'. For treatments to be equal, they would have to be exactly the same, that is identical, or indistinguishable, and this is not implied." This argument does not make sense to us. We have never claimed that the treatments are equal, but that they are likely to have, on average, similar effects (i.e., that there is no evidence for superiority of one specific treatment among the empirically supported treatments), with the choice of a specific treatment depending on patient preferences and other factors. In addition, Malhi et al claim that the NICE guidelines state that all listed treatment "can" be used as first-line treatments, but that "can" does not imply that they "should" be used as first line.[4, p. 3] This is nothing but a play with words. If all listed treatments 'can' be used as first-line treatments, this is not compatible with ranking treatments.

In summary, Malhi and colleagues did not convincingly address our concerns. They did not refute any of the methodological concerns we have raised regarding the placebo/TAU-controlled comparisons ("Concern 1") performed by NICE. In addition, they continue to ignore or downplay the results of the head-to-head comparisons and of recent meta-analyses which do not support the treatment ranking by Malhi et al. and NICE. This applies to arguments of costs and availability as well. With regard to the interpretation or misinterpretation of the NICE treatment ranking ("Concern 2"), the arguments by Malhi et al. are simply not convincing. Treatment guidelines should first and foremost consider the evidence for the efficacy and cost effectiveness of treatments and should be an incentive to ensure that evidence-based treatments are made widely available. They should not encourage the exclusive or preferred use of treatments that happen to be available because of historical reasons.

Conflicts of interest

The following authors have been trained in psychodynamic therapies: FL, AA, PL
NH is currently undergoing training in psychodynamic therapy
PL received royalties from Guilford Press, Wiley, Routledge and Cambridge University Press.
AA received royalties from Seven Leaves Press
FL received royalties from Hogrefe Publisher

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