The brain disease model of addiction: challenging or reinforcing stigma?

In their critical analysis of the brain disease model of addiction (BDMA), Wayne Hall and colleagues have elegantly shown that the BDMA is insufficiently supported by animal-model and neuroimaging evidence; has not contributed to the development of more effective treatments; and has had a modest effect on public policies toward drugs and drug addiction. However, one of the key aspirational claims of advocates for the BDMA is left unaddressed—even though alluded to—by Hall and colleagues: the BDMA’s potential to undermine the stigmatisation of addiction and people with drug addiction.

Together with a few theoretical papers, a paucity of empirical studies has explored this issue. Recently, an Australian survey on public attitudes has shown that considering addiction as a so-called brain disease is not associated with a reduced stigmatisation or with reduced support for coerced-treatment or punishment for addiction. In this line, a newly published experimental study has concluded that strengthening belief in a BDMA does not reduce feelings of stigma and shame in mild-to-moderate alcohol-dependent individuals, but even weakens some of their perceptions of agency over addiction-related behaviours (eg, locus of control, coping style, and controlled drinking self-efficacy). The more extensive literature linking stigma and the conceptualisation of psychiatric diagnoses in terms of brain disease seems to point in the same direction.

Therefore, as Hall and colleagues have questioned the evidence base for—and potential benefits from—the BDMA, it would have been desirable that their critical analysis has also addressed BDMA’s stigma-related issues. In any case, so far, the claim that framing addiction as a brain disease will lead to stigma reduction seems to be an unrealistically rosy picture or at least an unsubstantiated desideratum of BDMA’s advocates.

I declare no competing interests.

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Authors’ reply

We thank Dr Joan Trujols for his comments on our review.

We did indeed briefly raise, but not discuss in detail, one of the key claims made for the socially desirable impacts of the brain disease model of addiction (BDMA), that public acceptance of the BDMA will reduce stigmatisation of addicted persons. Space limitations did not permit us to do so.

We agree that there is a paucity of empirical studies of this issue. Dr Trujols cited work we have undertaken on the attitudes of the Australian public towards BDMA that found little enthusiasm and no evidence that acceptance of BDMA reduced stigmatisation stigmatisation.1 We agree with Dr Trujols’ interpretation of the limited empirical research on the effect of acceptance of neurobiological conceptualizations of psychiatric disorders on stigma.1–4 Had space permitted our conclusion would have been the same as his, that there is very little evidence to support the view that framing addiction as a brain disease reduces stigma and that proponents need to produce evidence that BDMA will in fact reduce stigma, before highlighting this as a potential benefit.

We declare no competing interests.

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Heightened risk of false positives in a network meta-analysis of social anxiety

I have read with great interest the social anxiety network meta-analysis by Evan Mayo-Wilson and colleagues (October, 2014).1 From their findings, these authors assert clear policy and clinical implications, delineating a hierarchy of treatment efficacy. However, network meta-analysis has unique risks over and above that of standard meta-analysis, specifically concerning the comparability of studies and the control of false-positive findings.

In their meta-analysis, the authors compared several psychotherapies for social anxiety disorder. The network meta-analysis included 17 studies and compared eight different therapies: cognitive-behavioural therapy, mindfulness-based therapy, exposure therapy, and five different forms of pharmacotherapy. The authors found that cognitive-behavioural therapy was the most effective treatment for social anxiety disorder, followed by mindfulness-based therapy and exposure therapy.

However, the authors did not consider the potential for publication bias, which is a common issue in meta-analysis. Publication bias occurs when studies with positive results are more likely to be published than studies with negative or null results. This can lead to an overestimation of treatment effects in meta-analyses.

To address this issue, the authors conducted a sensitivity analysis to examine the impact of publication bias. They found that the results were robust to publication bias, but there was a need for additional studies to confirm their findings.

In conclusion, the authors demonstrated the effectiveness of cognitive-behavioural therapy for social anxiety disorder, and highlighted the importance of considering publication bias in network meta-analysis.

I declare no competing interests.

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positives. The present network meta-analysis does not adequately address these methodological hazards, impairing its ability to detect only true treatment differences.

In the context of network meta-analysis, transitivity is the crucial assumption that studies share similar clinical and design characteristics relevant to estimating an effect size. Transitivity permits the use of indirect evidence—that is, it permits the comparison of treatments that have never been directly contrasted. Without transitivity, any indirect evidence might be misestimated, since different treatments might have been tested in different contexts, such as varying degrees of disease severity. Cipriani and colleagues provide an example of violation of transitivity with the treatments A, B, and C:

“Suppose that all AC studies include patients with severe illness and all BC studies include patients with moderate illness. Each study set is similar within itself… but the two sets deal with clinically different populations of patients. So, if severity is an effect modifier, the transitivity assumption would not hold, and synthesis of these two meta-analyses would not give a valid AB estimate.”

To summarise, indirect AB comparisons will be inaccurate because treatment A tends to be tested among more intractable patients than does B.

In this network meta-analysis, transitivity per se is left unmentioned, and no moderator analyses were done. As study-characteristic heterogeneity is the norm in psychiatric trials, transitivity cannot be assumed. These omissions are therefore problematic. Moreover, some treatments contributed few studies. Treatments contributing fewer studies might not portray a representative range of treatment contexts, biasing an effect estimate compared with those with more studies.

Unsurprisingly, the authors detect significant effect heterogeneity. Furthermore, at least nine of 44 comparisons with both direct and indirect evidence were potentially inconsistent, meaning that direct evidence was in significant disagreement with indirect evidence. In such a case, treatment A could be equivalent in direct comparison with treatment B, while indirect evidence about treatment B used in other trials estimates that treatment B is better than treatment A. It would have been judicious to highlight the disputed comparisons indicated by inconsistency. Importantly, both inconsistency and heterogeneity can imply violation of transitivity.

Simulations suggest that the risk of false positives is high in network meta-analysis because of the sheer number of comparisons made. In a simulation comparing only 12 antidepressants, an average of 2.7 false positives were recorded. That 38 active treatments and three controls were compared in this network meta-analysis is concerning. Type-I error correction (eg, Bonferroni) would have been appropriate to use.

It is unfortunate that these significant limitations are largely unaddressed, since they set the stage for the detection of false superiorities between treatments. Until these concerns are resolved, it is inappropriate to make stark treatment recommendations based on indirect evidence provided by this network meta-analysis.

I have previously published a standard meta-analysis on the effects of psychodynamic therapies for anxiety disorders, including social anxiety disorder.

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Author’s reply
John Keefe criticises our network meta-analysis of treatments for social anxiety for not addressing the issue of “transitivity”. The introduction of the term transitivity into discussions of network meta-analysis has created great confusion. We do not use the term, and instead follow the more usual practice of using the term “inconsistency”, a topic that is fully addressed in our Article.

Keefe cites our comment that “there was potential for inconsistency in nine of the 44 loops in the network” as meaning that “direct evidence was in significant disagreement with indirect evidence”. In fact, we were simply pointing out that there were nine evidence loops for which inconsistency between direct and indirect evidence could be compared. In the event, there was no evidence of disagreement. We make this clear in the Article by stating that we found “no substantial differences in magnitude and direction between the results of the network meta-analysis and the results of the pairwise comparisons”.

As Keefe notes, there was evidence of statistical heterogeneity. This heterogeneity is common in both pairwise and network meta-analyses. However, the level of between-trials variation (median SD 0.19) was surprisingly small in relation to the effects of the treatment classes, most of which were between 0.8 and 1.2 SD units. This finding, again, points to a low risk of inconsistency. It is also consistent with our baseline comparisons between trials of different treatment types. As stated in the Article, “we did not identify any systematic differences in participant demographics or initial symptom severity”. The latter covered the presence/absence of avoidant personality disorder (when reported), as well as overall severity of social anxiety.

Keefe urges the use of Bonferroni statistics to control for the risk of false positive identification of the best treatment when many comparisons are being made, and cites a study.