Reviewer's report

Title: Reconsidering the prognosis of major depressive disorder across diagnostic boundaries: full recovery is the exception rather than the rule

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Reviewer: Augustus John Rush

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This is an important interesting and well written report. It provides strong epidemiologic data to indicate that the longer-term prognosis of major depression or its associated conditions is not as "rosy" as some might have expected. There are some areas for improvement.

The contention that Frank and Kupfer created by a chimera- an illusion if you will- that the course of major depression is relatively benign in my view is unfair and indeed unnecessary. The Frank-Kupfer articles and their work in general was aimed at individuals who enter randomized controlled trials and for whom the evaluation of long-term prophylaxis was essential. Thus, however, the rosy picture was limited to the less comorbidly ill.

I do not dispute the view that many believe depression to be more benign than it is in reality. This report is important as it reports evidence that addresses this misperception. I would tone down the personal accusations as I do not think these two were quite so causal as claimed. In fact, one could argue that the rosy picture might be in part be attributed to the fact that in these sorts of trials typically exclude real world patients (see Wisniewski et al AM J Psych STAR-D report 2007-2009). Furthermore, stringent treatment control and treatment delivery in RCTs likely leads to better outcomes than seen in practice.

In fact, the authors might also cite STAR*D results that showed in real world patients results that match their findings. which show the limited efficacy of available treatments in real world patients.

Secondly, I believe a stronger rationale for why anxiety disorders should be strongly considered as part of the overall picture of major depression should be made. I think there is a stronger case than has been made in the report.

With regard to limitations, further commentary on the delivery of treatment or the lack thereof, may strengthen the case for arguing that these data are representative of true course, but they also do not address whether carefully deliver treatment could change outcomes more profoundly.
In addition, as noted this is a slightly older sample, and it is known that general medical conditions affect the likelihood of achieving as well as sustaining remission. Perhaps this should be mentioned in the discussion.

I believe the manuscript could be strengthened by - made more clinically relevant by -- describing the patient characteristics perhaps in a separate table that distinguish those with different trajectories of illness at the four and/or six year time point. That is, do sample characteristics at baseline distinguish amongst the four trajectory groups that are identified at 4 or 6 year measurement occasions amongst those with major depressive disorder; affective disorder; and affective and anxiety disorders?

This would require more space.. so that is editorial decision in my view.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

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Yes

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