Reviewer’s report

Title: One-year risk of psychiatric hospitalization and associated treatment costs in bipolar disorder treated with atypical antipsychotics: a retrospective claims database analysis

Version: 2 Date: 30 May 2010

Reviewer: Carolyn Dewa

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Major Compulsory Revisions

There remain a number of outstanding issues with this manuscript itself. There are still a few questions that, in the spirit of scholarly transparency, should be answered. In addition, a few assertions about their methods need correction.

Page 6: The authors assert, “As the dataset in this study was derived from an insurance claim database, ethical approval and informed patient consent were not required.” Could the authors clarify whether this statement is based on the authors’ opinion or that of an ethics review board? Although the use of administrative data may not seem to require consent, it does not automatically mean that the research project does not need ethical approval from a review board.

Page 7: Why were those who had a hospitalization 7 days following an index prescription excluded from the analyses?

Page 7: The exclusion of people who discontinued antipsychotics introduces a potential bias in the analyses. It is a limitation that should be discussed. The results only hold for those who do not discontinue use. There seems to be a large proportion of people who discontinue use of the drug that the analyses find less costly. Perhaps, the authors could test whether there is a significant discontinuation among the drugs.

Page 8: The authors have misunderstood reference 15. Propensity scores do not control for unobserved confounding variables. Only instrumental variables do this, and that is why they were asked it about in the previous review. The statement that references source #15 is incorrect, and source #15 did not state this contention either.

In addition, in their response, the authors indicate that they include the variables that they did in the logistic regression because they were limited by the dataset. This is a potential limitation that should be noted and discussed.

Page 8: The authors include more information about the Charlson index in their letter. To inform readers, they should include the additional information in the manuscript.
Page 9: The authors indicate that they use a gamma regressions. To inform readers, they should also describe how they: (1) converted the coefficients to dollars, (2) calculated standard errors for the dollars, (3) tested for heteroskedasticity, and (4) what the results of their test for heteroskedasticity were. As requested in the previous review, it is important to describe the fit of the model especially since they have already indicated that they were limited with regard to the types of variables available to them.

Page 13: They should indicate that their use of propensity score matching could have resulted in treatment selection bias based on unobserved variables. One of the drawbacks of propensity score matching is that it only balances the data that one has. They have already indicated that their data are limited. If there are unobserved factors that affect the choice of treatment, these will bias the results.

Page 14: The authors assert, “However, the analysis of such complex treatment patterns within claims data may be subject to high levels of unobservable confounding and difficult to interpret with respect to contribution of individual medications across complex regimens.” The authors should discuss the implications of this on the interpretation of their results.

Page 14: Is it possible that the patients in this dataset received treatment from other health or mental health programs that are not covered in this administrative dataset? If this is a possibility, that should also be noted as a limitation and discussed how this could affect the “total healthcare” costs that the authors report.

Table 1. The previous review asked about how the p-values were calculated. Was the matching accounted for or do the p-values ignore the fact that the patients have been matched?

Table 3. It would be helpful if the title indicated what the outcome is. In addition, it is “proportional” rather than “proportionate”.

The authors might also consider including a graph of the curves from the results of the analysis presented in Table 3.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.