Reviewer's report

Title: The impact of medication side effects on adherence among patients with schizophrenia: results of a cross-sectional nationwide survey

Version: 1 Date: 21 November 2011

Reviewer: Qun Mai

Reviewer's report:

Thank you for inviting me to review this cross-sectional study of an important topic. It examined the impact of side effects of antipsychotic medications on adherence and the impact of adherence on health services utilisation in community-dwelling patients with schizophrenia based on analysing a US nationwide survey data. The objectives were well defined. However, the data source section was weak. It is not clear how this nationwide survey was conducted. Statistical analyses were appropriate. The discussion was a little disappointing. Although authors identified key limitations of the study, more explanations are required.

The authors may wish to make revisions or to comment on the following.

MAJOR COMPULSORY REVISIONS:

1. Page 4. In Methods. “Patients were recruited...”

   It has been mentioned in the abstract that the study was based on analysing a 2007-2008 nationwide survey. However, I do not think that enough is specified about the way the nation-wide data were collected. We are told that patients were recruited in one of two ways, but a little more should be specified. In particular, what reference population (or sampling frame) was used from which community-dwelling patients with schizophrenia were identified. In addition, what measures were used to control for selection and information biases.

2. Page 5. In Methods. “Patients currently taking a prescription medication to treat their schizophrenia were asked...”

   In addition to the total number of medications used, is there any information on what they are?

   Because comorbidities (physical or mental) are common in people with schizophrenia, it is highly likely that some people use multiple medications and experience more medication side effects. For them, it is necessary to distinguish what proportion of side effects is due to antipsychotic medication and what proportion is due to other medications.

Authors identified that the cross-sectional design is a limitation of this study. However, more discussion is necessary to explain why. For example:

- Many side effects assessed are not specific to antipsychotic drugs and these side effects may not be necessarily due to antipsychotic medications.
- Apart from side effects of antipsychotics, many other factors may also affect non-adherence, eg, severity of schizophrenia, comorbidities (physical or mental), polypharmacy, complicated drug regimen, unpalatable formulation or cost of medications.
- Better adherence might improve treatment benefits, but also might increase side effects.

4. Page 10. In Discussion. “It is possible that unobserved confounding variables may have influenced the observed results.”

More discussion on whether the findings (which are consistent with the rest of the literature) could be explained by bias or confounding. For example, sicker people are more likely to use more health resources. Without an adequate control of case mix, it is too simplistic to conclude that more use of hospital and ER services are due to non-adherence.

5. Page 10. In Discussion. “…the use of both online and offline respondents may have resulted in a sample that does not generalize to the community-dwelling population of patients with schizophrenia.”

Authors may want to discuss this sampling method associated selection bias.

MINOR ESSENTIAL REVISIONS:


7. Page 3. In Background. “…estimated at almost $63 billion per year in the US in 2002 [6].”

If possible, update this amount to a more recent year.

8. Page 3. “due to side effects. [8].” Remove full stop before [8].

“…side effects such medication-related obesity,” should be “such as” instead of “such"

9. Page 6. “…which consists of : …” Delete the space after “of”.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.