Author's response to reviews

Title: Predictors of Metabolic Monitoring among Schizophrenia Patients with a New Episode of Second-Generation Antipsychotic Use in the Veterans Health Administration

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Author's response to reviews: see over
**Reviewer’s report**

**Title:** Predictors of Metabolic Monitoring among Schizophrenia Patients Initiated on Second-Generation Antipsychotics in the Veterans Health Administration  
**Reviewer:** Elaine Morrato  

**Reviewer’s report:**
The revisions have improved the quality of the manuscript. I have a few remaining comments that should be easily addressable.

**Major Compulsory Revisions**

1. The authors have improved the metabolic syndrome prevalence reporting. Because of differential surveillance and missing values, I still find it problematic to report prevalence rates in the Mon(-) group. Given the number of individuals with missing values in the Met(+), Method 1 is also problematic. Therefore, I recommend you only report the prevalence rates using Methods 2 and 3 for just the Mon(+) group with no missing data.

**Response:**
Changes were made as the reviewer suggested. Method 1 was deleted from both manuscript text and tables. Method 2 and 3 were renumbered.

Also a sentence was added to address the problem for MetMon- group in the discussion.  
Page 19: “Furthermore, it should be cautious in the interpretation of the reported rate of metabolic syndrome among the MetSyn- group, which is very low because of no lab testing for this group.”

2. The VA quality performance measure concerned testing occurring 180 days before through 30 days after the new antipsychotic was prescribed (p. 6). However, the evaluation methods only considered testing 180 days before (p. 8). Please explain the discrepancy. I believe the methods should reflect the performance measure.

**Response:** We chose to use our current approach which only allowed the monitoring events till the index date, although the VISN 16 allowed its facilities to report the monitoring metrics up to the first month after receiving a new SGA.

The co-authors (LS and HA) had discussion on the issue when we plan the study analysis plan in 2007. The evaluation method had intentionally excluded the first 30 days after the new episode of SGA was prescribed to avoid potential misattribution of pre-existing metabolic syndrome to the index drug. It was previously shown that rapid weight gain can occur early on - within the first 2-3 weeks of treatment - particularly with certain SGA such as olanzapine (Kinon et al, 2005; Lipkovich et al 2008). Such rapid and early weight gain could lead to increase the probability that some patients who did not have a pre-existing metabolic syndrome might have met the metabolic syndrome criteria within the first 30 days post-initiation of the atypical antipsychotic. Since it was a
retrospective study design, it was hard to ascertain whether lab testing belonged to baseline monitoring or follow-up care during the first month following the prescribed index SGA was filled by patients.


Minor Essential Revisions
3. The authors have done a nice job defining a new SGA treatment episode as a switch, new start, or augmentation. Based on the findings, 10-20% of patients were switchers/augmenters and many of the “new starts” were actually restarts because these patients had significant prior antipsychotic use experience. Therefore, in order to avoid confusion, I believe it is important to use your term “new treatment episode” or “index treatment episode” rather than “antipsychotic initiation” throughout the manuscript. For the title, I believe it is more accurate to say “… schizophrenia patients receiving second-generation antipsychotics....” Or “… patients with a new episode of second generation antipsychotic use …” rather than to imply the study population represents patients newly initiating medication.

Response: Changes were made as the reviewer suggested in both text and tables removing “antipsychotic initiation”.

4. The OR’s reported in the text for # of typical and atypical antipsychotics are reversed compared to the OR’s in the table. Needs to be corrected.

Response: Changes were made as the reviewer suggested. SGA and FGA in the text were reversed so that the text and table are consistent and correct.

5. Table 5. In this table, you report antipsychotic use using different nomenclature: typical, atypical, FGA, SGA. Please pick one nomenclature and use throughout the text and table. Please clarify whether BMI was included as a continuous variable or categorical. If it was a categorical variable, please specify which category definition and reference group that you used – NHLBI or the waist circumference equivalent. Please label units for length of stay and medication duration (days, presumably).

Response:
   1. Changes were made as the reviewer suggested. Only keep FGA and SGA in both text and tables.
2. Clarify in the footnote using the waist circumference equivalent: “Baseline BMI=1 if BMI ≥28.8, which is equivalent to waist circumference of more than 102 cm (>40 inches) for men and >88cm (>35 inches) for women.”

3. Add “(days)” for length of stay and medication duration.

Discretionary Revisions
6. Another unique aspect and strength of this study that the authors may wish to recognize is the inclusion of BMI as an indicator of who got testing and who didn’t. This measure has not been available for study in the previous studies examining Medicaid and commercially-insured patients and the VA results indicate that BMI is a strong risk determinant of who got testing.

Response: This is a very good point. We added it in the decision. Also, the two peer-reviewers’ contributions have been recognized in the Acknowledgement Section.

7. Table 5. To help with the clinical translation of the findings, I suggest that the authors present the OR’s for the continuous variables with very small, but significant ORs (number of non-psychiatric outpatient visits, length of stay, and medication duration) in more clinically relevant terms than just changes in the likelihood per unit change in the measure. For example, you might use tertiles or quartiles for the number of non-psychiatric outpatient visits to show a “dose effect” relationship rather than each visit increases the likelihood of testing by 0.7%. Instead of reporting the OR for each incremental day of antipsychotic duration, you might present it as the OR for each 60 day increase in drug duration (OR= 1.06 instead of 1.001). Similarly, instead of the OR for each day of increased hospital stay, you might instead report the increased likelihood per week of hospital stay (OR=1.08 instead of 1.01).

Response: Since it is discretionary, no changes were made to expedite the revision process.