Reviewer's report

Title: Predictors of Metabolic Monitoring among Schizophrenia Patients Initiated on Atypical Antipsychotics in the Veterans Health Administration

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Reviewer: Elaine Morrato

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The authors investigated patient factors associated with receiving glucose and lipid testing among patients with schizophrenia starting atypical antipsychotics and being treated in the U.S. Veterans Health Administration. The retrospective cohort study design using claims and medical records is appropriate for the research question. Several studies have reported on rates and predictors of metabolic testing in Medicaid and commercially-insured populations. This study provides important new information on metabolic testing among veterans following the implementation of a quality improvement program to ensure metabolic screening and establish performance measures.

Major Revisions

1. A description of the MetMon program should be provided. A reference is given to a conference, but I could not find the specific proceedings the authors were referencing. What specific monitoring, within what timeframe, was recommended for which type of patients? If the recommended monitoring included more than fasting serum glucose and lipid testing, why did the authors only report those results? How was the program implemented?

2. The study cohort selection is described, but remains unclear as it relates to the MetMon program definition. As I understand, the MetMon program was targeted to a new SGA treatment episode. That should include new starts, switches, and therapy augmentation. As currently described, the authors are only examining testing in patients who have switched or augmented therapy. Surely, there were some new starts that were not switches? Why were people initiating treatment with 2 or more antipsychotics excluded? Why were schizophrenia patients excluded if they also had a diagnosis of bipolar disorder or dementia?

3. Criteria for determining the index prescription should be explained. Was it the first atypical antipsychotic (Methods, p. 7, para 2) or any antipsychotic claim (Methods, p 8, para 1) in the study period to which the definitions of the treatment episodes were applied? If it was the first claim, then how did the authors determine prior antipsychotic use to classify the episode as a switch? Later the authors say that all treatment episodes were further classified, does this mean that a patient may have had multiple treatment episodes during the 3-year period and therefore the episodes are not independent of one another? Please explain. Maybe a pictoral diagram would help the reader.
4. The VHA and VISN network of care should be described because not all readers will have knowledge of this U.S. system of care. For example, the VHA population will skew older than a Medicaid or a commercially insured population. Metabolic screening is more likely to occur in older adults therefore one would expect average VHA rates of screening to be higher than average rates of screening in Medicaid or commercially insured patients. Also, be careful because different time windows for the “baseline” period have been used in different studies and this will influence the reported rates of screening, too. These points should be noted in the discussion.

5. Time variance should be included in the adjusted model or at least explained why it was not included. The study period encompasses nearly 3 years of observation which included the issuance of an FDA diabetes warning for this class of drugs and ADA/APA monitoring recommendations. I would expect that adoption of monitoring changed over time and that the types of patients being screened may also have varied over time – e.g., higher risk patients early on working toward a more broad acceptance of screening later.

6. Was there significant variation between the 22 VHA sites in terms of testing rates and determinants of testing? Was this interaction addressed in the logistic regression?

7. The authors report that monitoring results were similar between atypical antipsychotic agents. Please present the data supporting this statement since no data on the index SGA or the most recent antipsychotic agent were provided.

8. The prevalence of metabolic syndrome should only be calculated for those patients with all 5 parameters reported. For example in Table 4, none of the Mon(-) patients had 3 or more positive metabolic syndrome parameters – that is because by definition none of them had glucose and lipid assessments. Therefore, you can’t say with certainty they had <3 positive MES parameters. As a result, the observed prevalence of MES in the VHA population should not be compared directly to the CATIE rates because the parameters were not ascertained on everyone and selection biases were likely influencing which VHA patients got testing.

Moreover, the authors only considered abnormal laboratory values not whether the patient was being treated for diabetes, dyslipidemia, or hypertension. That is, a patient’s blood pressure may be in the normal range because they are being treated with an antihypertensive. The author’s definition only captured untreated or inadequately treated hypertension. It would be better to define high blood pressure as a high reading or being on medication. This same analogy should be applied to the glucose/diabetes and lipid/dyslipidemia parameters, too.

9. Testing rates are also highly dependent upon pre-existing diabetes and dyslipidemia status and patient age (see Morrato et al, J Clin Psych 2008). Rates of pre-existing diabetes and dyslipidemia should be reported and these factors should be included in the multivariate model. Did the authors examine whether
age (e.g., decade of life) was associated with MetMon in the multivariate model?

Minor Revisions

10. Depending upon how the above concerns regarding the study cohort are addressed, the title of the paper should be revised to reflect the study population, e.g., “... schizophrenia patients switching or augmenting atypical antipsychotic therapy”.

11. Please specify in the Methods section that a step-wise progression method used to select the most parsimonious multivariate model as is stated in Table 5.

12. For the patients with non-VA insurance, how was data on lab testing ordered by a non-VA provider linked with the study dataset? Are the testing records in the patient’s medical records? What is the magnitude of underreporting as a source of misclassification bias?

13. Table 1: It should be footnoted that “received metabolic monitoring” means a serum glucose or a serum lipid test in the 180 days before a new atypical antipsychotic treatment episode. Criterion #3 should state that patients without a new treatment episode were excluded.

14. Table 2: Include the units of measurement for CCI (mean (SD)?), mean? Number of office visits (SD), and mean (SD) number of hospital admissions? There is an error in the Mon(-) cell under all episodes for “other” race.

15. Table 3. Use one terminology (FGA vs. SGA or typical and atypical), not both. Why is the number of different typical and atypical antipsychotics for Mon(-), augmentation, patients missing?

16. Table 5: It appears that many of the variables (e.g., number of visits, number of antipsychotics) were included as continuous variables within the model. Did the authors test for linearity? I would recommend categorizing the data into meaningful groups based on the distribution, particularly since the data distribution for these variables are likely skewed. Please footnote #5 like you did in Table 4.

17. Please quote the adjusted OR’s in the abstract rather than the unadjusted associations.

18. Some places refer to hospitalization in the prior year. Other places refer to hospitalization in the 6 months prior. Please clarify and if there is a different time criteria, please explain why did you do that.

Discretionary

19. The authors defined MetMon as glucose or lipid testing. Based on Table 4, all Mon(+) subjects had glucose testing and 80% of those also had lipid testing. It would be interesting to know the characteristics of those patients who did not get the lipid testing.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

In the past 5 years, I received grant funding through my University from Pfizer to investigate changes in metabolic monitoring rates for Medicaid and commercially-insured users of antipsychotic medication.

I have no other competing interests.