Reviewer’s report

Title: Metabolic risk factors profile associated with use of second generation antipsychotics: a cross-sectional study in a community mental health centre

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Reviewer: Christoph Correll

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Metabolic risk factors profile associated with use of second generation antipsychotics: a cross-sectional study in a community mental health centre

General:

This is a study examining point prevalence rates of abnormal glucose and lipid levels in 76 mentally ill outpatients treated with second generation antipsychotics (SGAs) compared to a reference group of 36 patients with hyperhydrosis followed at a neurological clinic. The authors examine mean levels, cases with abnormal values and odds ratios between SGA and reference group as well as the individual SGA groups.

The topic is of relevance, as SGAs are prescribed in great quantities, but are associated with potentially dangerous effects on weight and metabolic status. The study is generally sound, reconfirming a concerning association that has been described many times by now. While the presented data reinforce the need for monitoring and risk management, the study has multiple limitations in addition to the cross-sectional design and small sample size, mentioned by the authors that should be added to the discussion (see specific comments below).

Discretionary Revisions:

Page 1: Add degrees of authors.

Minor Essential Revisions:

Methods:

Page 4: The claim that “all patients treated with SGA(s) were included in the study” cannot be true. They may have been eligible. Clarify how many patients were eligible for the study and how many were consented and included in this paper.

Page 4: Clarify whether patients in the reference group were a convenience sample in whom a chart review was conducted, or whether neurological patients also signed informed consent.

Page 4: Describe methodology for obtaining and assuring fasting blood values (e.g., time of blood draw, hours of fasting, was AM medication held, etc.). Describe, how height and weight were determined. Describe the difference of methodology, why height and weight were not obtained in the reference group.
Page 5: The authors should reanalyze their data using appropriate BMI as a covariate in order to
determine whether the increased odds with some agents for certain primary endpoints are explained
by differences in this crude measure of body composition, or whether the differences in risk still
remain significant. Also, in a post-hoc analysis, the effect of diagnosis should be explored in patients receiving SGAs.

Page 5: The authors should reanalyze their data using appropriate thresholds for prediabetes (i.e.,
fasting blood glucose 100-125 mg/dL) and for diabetes (i.e., fasting blood glucose >/=126
mg/dL), as the threshold of 110 mg/dL is based on a recommendation for the definition of the
metabolic syndrome (NCEP III).

Also, I would recommend reporting point prevalence rates for obesity (i.e., BMI >/= 30, as well as for overweigh (i.e., BMI 25-29.9), as being overweight is also associated with increased risk for metabolic complications and cardiovascular disease.

Results:

Add to the results section based on the suggested methodological changes and refer also to the
suggestions regarding the tables below.

Tables:

Table 1: Report as nay patient characteristics as are available in the data base (i.e., ethnicity, social
class, duration of illness, family history of psychiatric and metabolic disorders, etc).

Table 2: Previous treatment data are displayed as row percents, rather than column percent values
as done everywhere else, which should be consistent.
Add to the table the data whether patients received more than year of treatment or not, and compare
differences across SGA groups. (If this is significant, add to covariates in ANCOVA model)

Table 3: Add to the table the continuous BMI data.

Table 4:
Add to the table the number (%) of patients who are (i.e., BMI >/= 30) and overweight (i.e., BMI
25-29.9).
Add to the table hyperglycemia data (i.e., >/= 100 mg/dL, as well as separate rows for prediabetes
(i.e., fasting blood glucose 100-125 mg/dL) and for diabetes (i.e., (i.e., fasting blood glucose >/=126
mg/dL).

Consider combining tables 3 and 4 into one table.

Discussion:

Page 8: Although this study has a control group, discuss how the limited information and lack of
matching for body composition limits the information that can be gleaned from such a comparison.

Page 10:
Discuss that based on this data, it is impossible to determine whether the differences in outcomes
are due to SGAs, differences in body composition, diet, exercise, genetics, etc. Add paper by
Henderson et al. (Arch Gen Psychiatry 2005) and data from animal studies (e.g., last author H. Romella, 2004), which suggest that certain SGAs may have additional weight-independent effects or glucose metabolism.

Page 10:
The following limitations should be added and discussed lack of detailed data on patient
characteristics (social class, ethnicity, family history of components of the metabolic syndrome, etc), lack of assessment of fat distribution, which is a major factor for abnormalities in glucose and lipid metabolism), lack of assessment of all components of the metabolic syndrome, missing information about relevant contributing / confounding factors (e.g., diet, exercise...), and lack of information about BMI in the reference group that was not well matched or representative of the general population. Another problem with the current data analysis is that the cut off for hyperglycemia was chosen based on a definition used for the metabolic syndrome.

Conclusion:
Page 10, last sentence:
Replace “the general population” with “control group chosen in this study”, as the reference group was neither matched nor “representative”.

Page 11:
Add section on how patients should be monitored and mention something about prevention and management of SGA-induced weight gain that goes beyond the choice of agents (e.g., self monitoring, healthy lifestyle counseling and behavior, non-pharmacological and pharmacological interventions, etc).

Language: Style, syntax, and grammar require revision by a native speaker.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
Consulting and/or Speaker fees by Astra Zeneca, Bristol Meyer-Squibb, Janssen Pharmaceutical and Eli Lilly