Author’s response to reviews

Title: Prevalence and Management Practice of First Generation Antipsychotics Induced Side Effects among Schizophrenic Patients at Amanuel Mental Specialized Hospital, Central Ethiopia: Cross-sectional Study

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Title: Prevalence of First Generation Antipsychotics Induced Side Effects and their Management Practice among Schizophrenic Patients at Amanuel Mental Specialized Hospital, Central Ethiopia: A Prospective Cross-sectional Study

Response to Editor’s and Reviewers’ Comments

First, we the authors would like to acknowledge the editor and all the reviewers for your constructive comments and suggestions on our manuscript. As per your comments, we have addressed each of them as follows.

Response to reviewer Number 1

1. Abstract

A. In the methods section of the abstract no need to mention the statistical methodology o in BMC Psychiatry authors guideline section states to include how the study was performed and statistical tests used in the methods section of the abstract and it is for this reason I included.

2. Methods:

B. In the methods section authors stated they did a cross sectional study from March to June, but in the abstract they included a statement as from April to May. Please clarify.
Apologies for the editorial error and thank you for identifying this discrepancy. The study was conducted March to June, 2017 and corrected accordingly (Abstract, methods section, line 2)

C. Sample size detection method is described in too much detail, as the study has a good sample size, I recommend authors to take this paragraph out or summarize it in 1-2 sentences. I also recommend authors to move it to statistical analysis section, if they want to.

Comment accepted and accommodated accordingly (page 5, line 63-66). Noting to BMC psychiatry journal instruction for authors guide, I have put the sample size calculation and sampling techniques as it is.

3. Authors used very good scales to assess side effects such as GASS and NADRPS.

I would recommend to perform further statistical analysis to increase the interest on this manuscript.

As the sample size is good, is this possible for authors to do sub group analysis for each FGA. I recommend authors to compare GASS and NADRPS scores for each antipsychotic, (ANOVA or Kruskal-Wallis).

- What the reviewers raised is a very good idea, but the objective of this study was just to just assess prevalence of FGAs induced side effects and their management practice. So, unfortunately, further statistical analyses such as ANOVA and Kruskal-Wallis tests are beyond the scope of this manuscript and also was not our aim to do so. We are planning to do further researches with a wider coverage of all antipsychotics and, perhaps will submit the outputs in BMC psychiatry in the future.

4. They could also investigate some correlations between GASS, NADRPS scores and duration of illness, age, number of previous episodes, number of hospitalizations etc.

- My response to this comment is similar to the above one. That is, these statistical tests are beyond the scope and objective of this study.

5. I would recommend authors to compare GASS and NADRPS scores of patients according to Table 1 and 2. I think with further statistical analysis they may find more significant findings to increase the quality of study.
We have noted that GASS score is the measure of the severity of self reported FGAS side effects whereas NADRPS is a scale to estimate the probability of adverse drug reaction caused by the FGAs or in other terms NADRPS is used to assess probability or causal association of the ADRs and FGAs implying that comparing GASS scores VS. NADRPS (which are two different things) may not have any clinical implication. It was not also our aim to go this way.

6. Could authors group patients on the antipsychotic dose. For instance, could the stratify patients according to chlorpromazine equivalent dose, as they stated in the beginning of discussion.

D. Comment accepted and corrections made accordingly (page 7, line 137 to 140).

7. Statistical analysis: This section is very short, I recommend authors to move sample size detection method to this section. I also recommend them to do further statistics with GASS scores and NADRPS scores.

• We acknowledge the reviewer’s comment on statistical analysis issue, but as it is a prevalence and assessment of management practice study, we found the stated statistical tests adequate to answer our objectives in this study.

Response to reviewer Number 2

1. Material and Methods

• Some details are missing. The diagnostic codes for schizophrenia must be reported. Now the authors only note they have studied patients with schizophrenia. In addition, the distribution of the sub-types of schizophrenia had to be reported in the text. Further, list the names of FGAs already in the text of the methods, for example, in the line 98.

o Comment accepted and the criteria to consider patients schizophrenic is stated on page 5, line numbers 75 & 76. Apart from this criteria, diagnostic codes were not recorded in the patients’ medical records.
Similarly, sub-types of schizophrenia were not fully documented in the medical records of patients that we did not abstract it. We also did not see the relevance of the subtypes with regard to side effects and ADRs development as our objective was just assessing side effects and ADRs along with management practices.

Types of FGAs are also mentioned in Table 3.

2. Results

Since the prevalence of schizophrenia and its sub-types as well as factors relating to schizophrenia are known to be gender specific, some of results are worth of reporting by gender and also test the statistical significance of difference of characteristics between genders. This also would give deeper understanding to the basic nature of the patients with schizophrenia in Ethiopia. The comment relates to all Tables 1-5.

• We appreciate the reviewer’s comments. However, our objective was not to make gender based comparisons and make advanced statistical tests. Such comparisons are beyond the scope of this study. Hopefully, such issues will be addressed in future researches.

3. Discussion

The first chapter of the discussion now repeats the results already seen in the result text. The text needs to be re-written so that the main findings are described in broader context than reporting exactly the same percentages and numbers of the analyses than in the result text. Otherwise the discussion is well-written and compared to the findings of earlier literature.

• We thank the reviewer for the suggestion. We noted that different discussion writing guidelines recommend to summarise the main findings of the study in the first paragraph. We followed similar principles in writing the discussion

4. What are the strengths of the study?

Patients with schizophrenia in Ethiopia - assumable they may differ in some characteristics compared to patients with schizophrenia in European countries, or is it so?

• Yes, it is true. In addition, the management practice may also, probably, be different due to limitation of resources in Ethiopia. The study is also the first of its kind.
Response to reviewer Number 3

Major:

a) Correlational or association analysis of occurrence of FGA side effects with socio-demographic / clinical factors should be described in the methods section. All the variables that were tested can be listed here. Whether statistical correction for multiple comparison was applied (Eg: FWE or Bonferroni) If this is not done, please explain why.

• We performed descriptive statistics and chi-square tests as stated in the methods section. We did not perform advanced tests such as FWE or Bonferroni as it is beyond the scope of the study objective.

b) This study is not a RCT, and hence validity of observations is questionable to a certain extent. This should be discussed as limitation of the study.

• Yes, we accept the reviewer’s concern. The limitations of the study are stated on page 12, line number 266-268.

Minor

a) Lack of correlation between total daily dose of antipsychotics and occurrence of side effects is intriguing. Can authors discuss the implications of such finding on formulating prescription guidelines?

• As stated, most of our patients were on sub-therapeutic dose and only 17 patients were taking supra therapeutic dose. So, this may be one of the reasons for the absence of statistical association. In addition, we did not do adjusted statistical tests to truly establish causal association. We did a chi-square test. The findings of this study should be carefully interpreted.

b) The cohort comes from localized geographic. Can authors comment on generalizability of findings to larger part of the world, specifically given the lack of concordance of certain observations with earlier studies?

• We did a chi-square test. I do not tempt to say this single centered observational study can be generalized to the wider context However, it can show us the magnitude of FGAs induced side effects and the management practice in a resource limited setting

• The findings of this study should also be carefully interpreted.