Author's response to reviews

Title: Health-related quality of life among patients treated with lurasidone: results from a switch trial in patients with schizophrenia.

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RE: Manuscript submission – revisions to Awad et al., 2013

Dear Dr. Kantrowitz,

Thank you for your review and comments on the manuscript entitled “Health-related quality of life among patients treated with lurasidone: results from a switch trial in patients with schizophrenia (version 2)”. We appreciate the thorough review and helpful comments on the study provided by the reviewers. The reviewer suggestions have been carefully considered and revisions have been implemented into the manuscript. Descriptions of these changes are presented below.

A) Reviewer: Lakshmi N.P. Voruganti

1. **Comment 1:** The distinction between race and ethnicity tabulated in Table 1 may not enhance the value of results. This reviewer appreciates the predominance of “Hispanic” populations in some US cities and its potential service implications. However, the international readers may not be able to understand the relevance unless a clear explanation, if any, is provided.

   **Revision:** In Table 1, the categorization and data for “ethnicity” has been removed.

2. **Comment 2:** The word “antecedent non-sedating antipsychotic” (page 9, para 1.) sounds very foreign to clinicians. The authors use the term “pre-switch” medication in another instance. It is important to be consistent and avoid jargon.

   **Revision:** Both instances of the word “antecedent” have been changed to “preswitch” for consistency with the rest of the manuscript.

3. **Comment 3:** The authors have failed to mention the critical variable “subjective tolerability” which is known to mediate the adherence and quality of life outcomes. This would be relevant in the discussion on switching from non-sedating versus sedating antipsychotics (page 14).

   **Revision:** The variable “subjective tolerability” has been mentioned within the Discussion (pg. 14) regarding switching from non-sedating versus sedating antipsychotics.
Comment 1: I have reviewed previous versions of this study focusing on other outcomes, and again I am concerned over the artificial distinction of sedating vs non-sedating. I am aware that this was an a priori distinction, but it is particularly misleading in this article when it allows the two most efficacious pre-switch agents (olanzapine and risperidone) to be split up for the analysis. For the present study, numerically less improvement was noted in subjects who were on olanzapine, and to a lesser extent, risperidone. The non-sedating/sedating dichotomy dilutes this finding, and is misleading. If this dichotomy is kept, then the outcomes for the individual agents needs to be further highlighted, including in the abstract. Nevertheless, I think the finding of presumably significant improvement in Qol in the combined non-olanzapine/risperidone group is of interest. In particular, a direct comparison with aripiprazole and ziprasidone would be enlightening, as they are the most similar agents in terms of side effects. The finding of superiority over these agents on Qol is interesting. I would strongly suggest focusing on the differences in outcomes among the individual agents.

Revisions: The authors appreciate reviewer’s concerns regarding the categorization of individual agents under the headings of “sedating” and “non-sedating” antipsychotics.

To address this issue, the authors have revised the manuscript in following manner:

1) The data for the individual agents are presented in Tables 3 and 6 for the PETiT scores and SF-12 results, respectively. As recommended by the reviewer, the authors have highlighted these outcomes in the abstract, the results (page 10 for the PETiT scale and page 12 for the SF-12) and the discussion section of the manuscript.

2) The sedating/non-sedating-categorized results were removed from the abstract and replaced with results focused on differences between the individual agents as suggested by the reviewer. The results still remain within the full-text and tables as this distinction was set a priori, was based on what is known about these agents and their relative propensity to be associated with sedation and/or somnolence, and are a part of core clinical study by McEvoy and colleagues.1,2,3 The clinical and now quality of life outcomes observed in the switch study suggests that this distinction may be clinically relevant to patients with schizophrenia.

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3) Discussion has been added to the limitations section on page 16 regarding the lack of available information in terms of preswitch sedation and its impact on categorization of the agents. Text has been added to explain that this categorization may not account for all of the differences within and between these two broad groups. As suggested by McEvoy’s group, stratification on the basis of agent or properties other than sedation could result in different outcomes than reported here.

Measures have also been undertaken to ensure appropriate formatting as per the journal’s style recommendations; however, there is some confusion regarding the permitted orientation of tables in the back of the manuscript. That is, the BMC checklist mandates portrait style while BMC Psychiatry’s instructions to authors indicate that either portrait or landscape orientation is suitable. We followed the journal-specific recommendations but please direct if the tables need to be reformatted.

Thank you for your time and consideration,

Mariam Hassan