Author's response to reviews

Title: A retrospective study of antipsychotic drug switching in a pediatric population.

Authors:

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Version: 2 Date: 5 September 2013

Author's response to reviews: see over
Dear Prof. Teicher,

Re: MS: 1877935576848243 – revised version

Title: A retrospective study of antipsychotic drug switching in a pediatric population

Authors: David Linton, B.Sc.; Ric M. Procyshyn, Pharm.D., Ph.D.; Dean Elbe, Pharm.D., Lik Hang N. Lee, Alasdair M. Barr, Ph.D.

We have enclosed the revised version of our manuscript with changes highlighted in blue font. This cover letter also includes a point-by-point response to the two Reviewers’ comments (please see below) as well as any editorial suggestions. We are pleased that the reviewers agree that the manuscript could be a valuable contribution to BMC Psychiatry.

We thank the reviewers and yourself for the constructive comments and have carefully addressed every single recommendation in preparing our revision.

Sincerely,

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EDITORS COMMENTS:

This is an interesting article that presents data currently unavailable in pediatric populations. The basic methodology is strong given the use of electronic pharmacy records. I avidly concur with the comments of reviewer 2 regarding the difficulty in interpreting the results as reported. "Total weeks prescribed" is not a meaningful metric for clinicians. It would be much more informative to know number of patients receiving treatment with a particular drug and mean duration of use with an index of variability (SD or confidence intervals) To provide a more informative view of the data I would like to see a Table with the following information (include additional drugs if sufficient data available).

It would also improve the value of the article to include a table with the following information.

These tables should be added, summarized in results and commented upon in the discussion section.

Please find attached files.

WE THANK THE EDITOR FOR HIS POSITIVE COMMENTS. WE HAVE MADE ALL OF THE ABOVE SUGGESTED CHANGES. AS WE DESCRIBE BELOW IN MORE DETAIL FOR REVIEWER #2, WE HAVE LARGELY REPLACED “TOTAL WEEKS PRESCRIBED” AS A METRIC WITH MORE STANDARD ONES, SUCH AS NUMBER OF SUBJECTS, ETC.

WE HAVE COMPLETED TWO NEW TABLES IN THE FORMAT SUGGESTED BY THE EDITOR (TABLES 1 AND 2), WITH THE FIRST TABLE PROVIDING DETAILS ABOUT TYPE OF ANTIPSYCHOTIC MEDICATION USED IN OUR POPULATION, AND THE SECOND TABLE PROVIDING KEY DATA ABOUT DIAGNOSES. WE WERE ABLE TO COMPLETE ALMOST EVERY DETAIL OF THE TABLE, APART FROM DURATION OF DRUG TREATMENT, AS OUR ELECTRONIC PHARMACY RECORDS ONLY GO BACK FOR 14 MONTHS MAXIMUM AND MOST PATIENTS HAD BEEN TREATED FOR LONGER THAN THIS. FOR THE SECOND TABLE, A ROW HAD BEEN SUGGESTED FOR % OF PATIENTS HOSPITALIZED. IN OUR STUDY, ALL PATIENTS HAD BEEN HOSPITALIZED – WE THEREFORE INCLUDED AN ALTERNATE INDEX OF ILLNESS BY INCLUDING THE NUMBER OF PREVIOUS EMERGENCY VISITS.

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EDITORS REQUEST:

1. Competing interests:

Manuscripts should include a ‘Competing interests’ section. This should be placed after the Conclusions/Abbreviations. Please consider the following questions and include a declaration of competing interests in your manuscript:

Financial competing interests

THIS HAS NOW BEEN INCLUDED ON PAGE 11.

2. Authors’ contributions

In order to give appropriate credit to each author of a paper, the individual contributions of authors to the manuscript should be specified in this section

THIS HAS ALSO NOW BEEN INCLUDED ON PAGE 11.
Reviewer's report #1

Title: A retrospective study of antipsychotic drug switching in a pediatric population.
Version: 1 Date: 7 March 2013
Reviewer: Bruce Kinon

Reviewer's report:

Major Compulsory Revisions:
1. Not only was the cohort heterogeneous in its diagnostic complexion, but the use of antipsychotic drugs was off-indication in most instances. It is challenging for the reader to interpret the major descriptive findings of this retrospective study for the above reasons. It would probably be beneficial at a minimum if the authors would re-analyze their data subgrouping those patients receiving antipsychotics on-label.

WE UNDERSTAND THAT THE SUBJECTS DESCRIBED IN THIS STUDY REPRESENT A HETEROGENEOUS POPULATION. AS A TERTIARY CARE FACILITY, THE SITE PROVIDES SPECIALIZED CARE FOR ALL MENTAL HEALTH DISORDERS IN ITS CATCHMENT AREA. THE GOAL WAS TO ELUCIDATE ANTIPSYCHOTIC SWITCHES IN THIS POPULATION, AS WE BELIEVE THAT OUR PATIENT POPULATION WILL GENERALIZE TO THOSE OF MOST OTHER TERTIARY PSYCHIATRIC HOSPITALS IN NORTH AMERICA, AND SWITCHING ANTIPSYCHOTIC DRUGS REMAIN AN ISSUE REGARDLESS OF DIAGNOSIS.

WE HOPE THAT TABLES 1 AND 2, AS SUGGESTED BY THE EDITOR, WILL BE VERY HELPFUL IN THIS REGARD. THEY NOW PROVIDE IMPORTANT INFORMATION ABOUT EACH OF THE MAJOR PSYCHIATRIC DIAGNOSES IN THE STUDY POPULATION, AS WELL AS THE PROPORTION OF ON- AND OFF-LABEL DRUG USE.

2. The authors provide no clear explanation for the reason they analyzed their data across a heterogeneous diagnostic cohort. They should provide a compelling reason for this strategy and provide their understanding of the value of this approach, as opposed to at least look secondarily at more homogeneous diagnostic subgroups also.

IN OUR STUDY, THE MAJORITY OF ANTIPSYCHOTIC DRUGS WERE USED FOR DIAGNOSES OTHER THAN PSYCHOSIS. THIS IS BECAUSE THE DRUGS ARE COMMONLY USED TO TREAT SYMPTOMS, RATHER THAN A DIAGNOSIS PER SE, AND THESE SYMPTOMS COMMONLY SPAN ACROSS WIDE DIAGNOSTIC BOUNDARIES. WE HAVE ADDRESSED THIS POINT IN THE MANUSCRIPT ON PAGE 4.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

Declaration of competing interests:
I am an employee of Eli Lilly and Company
Reviewer's report #2
Title: A retrospective study of antipsychotic drug switching in a pediatric population.
Version: 1 Date: 1 July 2013
Reviewer: Nancy Covell

Reviewer's report:
This report offers new information regarding switching antipsychotic medications in pediatric populations.

Discretionary Revisions

1) Throughout, when describing the results, it would be helpful to also include some summary statistics for individual-level variables. In addition to aiding with interpretation of the current findings, prescribers may find the individual-level summaries helpful as they consider prescribing decisions with children and their families. For example, the paper notes that “there were 4818 weeks of antipsychotic prescription which were given to a total of 137 patients”. It would be helpful to also know the minimum, maximum, median, and mean trial length for individual children.

WE HAVE SIGNIFICANTLY ALTERED THE RESULTS SECTION ON PAGE 7 TO MAKE THIS PART OF THE MANUSCRIPT CONSISTENT WITH THE REVIEWER’S SUGGESTION. RATHER THAN CITING NUMBER OF WEEKS OF DRUG PRESCRIPTION, WE NOW MOSTLY INCLUDE THE TOTAL NUMBER OF PATIENTS IN EACH CATEGORY. ADDITIONAL INFORMATION, SUCH AS DRUG DOSES, IS ALSO PRESENTED IN TABLES 1 AND 2.

2) Similarly, when discussing “Antipsychotic polypharmacy (i.e., concurrent administration of two or more antipsychotic drugs) was noted in 451 weeks”, it would be helpful to understand the number of children with polypharmacy along with summary statistics describing the trial lengths of the polypharmacy.

THE NUMBER OF CHILDREN TREATED WITH ANTIPSYCHOTIC POLYPHARMACY IS NOW INCLUDED IN THE RESULTS ON PAGE 7. UNFORTUNATELY, AS NOTED ABOVE, OUR PHARMACY RECORDS ONLY EXTEND FOR 14 MONTHS AND SO WE ARE NOT ABLE TO PROVIDE TRIAL LENGTHS AS MANY DRUGS ARE GIVEN FOR LONGER THAN THIS.

3) As another example, understanding trial lengths for risperidone, quetiapine and olanzapine would help the reader interpret statements like “Risperidone was the most commonly prescribed antipsychotic drug prior to hospital admission (2680 weeks, 55.6%) followed by quetiapine (1339 weeks, 27.8%), and olanzapine (444 weeks, 9.2%)”. Risperidone might be prescribed for significantly more weeks due to more children, longer trial lengths or a combination of both.

ON PAGE 7 WE NOW REPORT ANTIPSYCHOTIC DRUG USE BASED ON THE PROPORTION OF PATIENTS WHO WERE DISCHARGED FROM THE HOSPITAL ON THE DRUG, MEANING THAT THERE WILL BE NO CONFUSION AS TO WHETHER DRUG USE REFLECTS TRIAL LENGTH OR NUMBER OF PATIENTS.

4) Finally, in Figure 1, it appears that the type of switch after hospitalization was predominantly titrated (6 of the 9 switches after hospitalization). While this may or may not differ from pre-hospitalization switches, it may be worth discussing some possible reasons for this apparent difference.

WE THANK THE REVIEWER FOR MAKING THIS ASTUTE OBSERVATION. WE HAVE ADDRESSED THIS INTERESTING POINT IN THE DISCUSSION ON PAGE 10.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests