Author's response to reviews

Title: Can authorities appreciably enhance the prescribing of oral generic risperidone to conserve resources?: findings from across Europe and the implications

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Author's response to reviews: see over
Addressing Reviewers' Comments

Reviewer 1

a) In view of the increasing pharmaceutical expenditures on antipsychotic medications and the potential for utilization of generic agents to reduce such costs, a study of the experience of various countries following the introduction of generic risperidone is of value. The manuscript's introduction notes the range of relevant issues and gaps in the literature, but could be more succinct. The methodology is reasonable and is adequately described. The results are fairly presented and include findings of a reduction in overall risperidone utilization and variations in the use of generic risperidone use across countries. The authors conclude that the introduction of generic formulations does not result in an increase in their utilization in the absence of demand-side initiatives encouraging their use.

The study is timely and addresses an important topic. The study design is reasonable.

Author response

We thank the reviewer for these comments

b) While the results are clearly presented, some additional information would be important.

1. Only administrative databases were accessed- while this is reasonable, what proportion of total antipsychotic expenditures of the nation did they represent and were there changes in this proportion over the timeframe of the study.

Author response

We thank the reviewer for these comments and have now added in greater details regarding the situation in Europe and the goal of equitable and comprehensive healthcare for all. Consequently, the figures typically represent 100% or close to 100% for the population in each country (apart from Ireland where we only assessed the GMS population). We hope this clarifies this issue

2. While proportion of risperidone use the focus of this manuscript, numerical trends over the period in the use of other antipsychotic agents would provide useful background information. 3. What was the status of introduction of long-acting risperidone (microspheres, "Consta") in the various countries and its use over this period? 4. What was the status of introduction of oral and long-acting injectable paliperidone in the various countries and patterns of its utilization in these countries and specific systems in them?

Author response

We thank the reviewer for these helpful comments and have now added in further details of long acting risperidone and paliperidone into the revised manuscript. We hope we have addressed this issue.

5. Were absolutely no demand-side measures utilized in any of the countries? and 6. Were any educational efforts to promote generic risperidone employed in these countries (if so, what was their nature and extent) and were any incentives provided to prescribers, pharmacists, or health-care systems to promote its use?

Author response

We thank the reviewer for these 2 comments and have now clarified this to include limited demand side measures to encourage the prescribing of risperidone once generics became available. We have also added in further details in the discussion about the measures in Scotland and Sweden to achieve high dispensing rates for oral generic vs. originator risperidone. We hope this is now OK.

c) Some implications of the study are well discussed- i.e., the absence of a spill-over effect from other pharmaceutical classes and the absence of any apparent clinical issues with generic risperidone.
Some evident conclusions (e.g. significant inverse relationship between cost differential between generic versus branded risperidone and utilization of generic risperidone as proportion of total risperidone; OR regression towards mean in risperidone utilization across countries in context of overall decline in risperidone use) are not. The possibility that decline in risperidone utilization might parallel decline in olanzapine utilization (“oldest atypical antipsychotics”) should be considered.

Author response

We thank the reviewer for these helpful comments and have added more details about the policies (or lack of them) to encourage the dispensing of generic risperidone as well as obtain low prices. In addition, added more details about e.g. aripiprazole and quetiapine to give additional reasons for the general decline in the utilisation of risperidone. We hope this is now OK.

d) Finally, some conclusions are not fully substantiated- e.g., "demand-side initiatives encouraging the prescribing of generic atypicals are likely to have only limited impact")- what, if any, demand-side initiatives were employed across the different countries?

Author response

We thank the reviewer for this comment and hope we have now addressed this building on earlier comments.

f) There are grammatical and syntactical errors in the manuscript that need correction; in particular, there are several incomplete sentences- e.g., third sentence of the abstract)

Author response

We thank the reviewer for the comment and have been through the manuscript to enhance this.

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

Author response

As above

Statistical review: Yes, and I have assessed the statistics in my report.

Author response.

Thank you for this.

Reviewer 2

a) This manuscript is an interesting analysis of the utilization of generic risperidone in some European countries. Their general conclusion is that generic, and less expensive, risperidone has not increased as much as one would have expected to save money on medication purchase. The analyses appear to have been carefully carried out. The results are in general adequately discussed.

Author response

We thank the reviewer for these helpful comments.

b) Here are some issues to be addressed by the authors.

1) It is striking that the rate of utilization of generic risperidone is directly proportional to the decrease in price (table 4). Yet, no emphasis is put on this. For instance in Ireland, the difference between brand and generic is only 28% and the rate of generic is 14%. Basically, why attempt a switch if there is little financial gain.
Author response

We thank the reviewer for this comment. Generally, the gains are for the health authority with close to 100% coverage and limited patient co-payments (now added in). Hence measures to try and increase the use of low cost generics where possible. However, the differences arise due to differences in the aggressiveness of the different countries to obtain low prices for generics and enhance their use. This is down to local issues including for instance appreciable pharmaceutical manufacturing in Ireland – hence limited supply- and demand-side measures to date; although this is changing. We have upgraded the manuscript to include a number of these points – and hope this is now OK.

2) On page 6, it is mentioned that marketing activities may influence prescribing, which is obviously true. However, some of these commercial efforts are often driven by availability of new data. For instance, clinicians have recognized the general weight neutrality of aripiprazole and later the benefits of the medication in major depressive disorder in patients with incomplete response to an antidepressant. Similarly, quetiapine ER was shown to be beneficial in the latter indication and in bipolar depression. These potential advantages account for an absolute 23% increase of these two drugs, the equivalent of the drops of the other medications listed.

Author response

We thank the reviewer for these helpful comments and have now altered the manuscript accordingly with additional references.

3) The slopes in table 2 are not likely to mean much to a non-specialist. They should be converted to percentages.

Author response

We thank the reviewer for this comment and have altered the manuscript to give greater clarification regarding their meaning. We hope this is now OK.

Quality of written English: Acceptable

Author response

Thank you for this.

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

Author response

Thank you for this

General

We have not added in an abbreviation section as all terms have been described in the manuscript.