Author's response to reviews

Title: Statistical power in parallel group point exposure studies with time-to-event outcomes: An empirical comparison of the performance of randomized controlled trials and the inverse probability of treatment weighting (IPTW) approach

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Author's response to reviews: see over
Dear editor,

Re: MS 2859949491635731 “Statistical power in parallel group point exposure studies with time-to-event outcomes: An empirical comparison of the performance of randomized controlled trials and the inverse probability of treatment weighting (IPTW) approach” by Peter Austin, Tibor Schuster, and Robert Platt.

We would like to thank you for inviting us to revise and resubmit the above-noted manuscript for consideration for publication in BMC: Medical Research Methodology. Our responses to the reviewers’ comments are described below. Note that reviewers’ comments are in bold type, while the authors’ responses are in regular type.

We have added text to the Authors’ Contributions section, stating that each author had read and approved the final manuscript.

Reviewer 1:
The revised study is helpful to understand the power of an observational study using IPTW compared to that of a similarly-structured RCT. The authors did extensive Monte Carlo simulation with different scenarios considering the levels of confounding, treatment effect and treatment proportion.

Major Compulsory Revisions:
No censoring remains an important limitation of the study. The authors mentioned in the cover letter that the purpose of this study “was to compare the power of an IPTW design with that of a similarly-structured RCT. Thus, the important issue was to compare the two designs when there was an equal amount of censoring (or an equal number of observed events)” However, censoring is a unique problem for survival analysis. Censoring in observational studies may be related to other confounders, i.e. variables that are related to both treatment assignment and outcome. On the other hand, censoring in RCT is not related to treatment assignment due to randomization. Therefore, censoring plays a different role in analysis power of observational studies compared to that of RCTs. So I do not agree with Line 436—442 (Page 21) that the results from these Monte Carlo simulations can be generalized in presence of censoring.
The lack of censoring is listed in the Discussion as a limitation of the study (line 434-442).

In summary, the merit of this study is that it showed how close we can approximate the power of an observational study using IPTW with that of a similarly-structured RCT. But it is important to mention the limitation of this study, and that power analysis should be specifically performed for each study with its unique condition of confounders and their association with treatment and outcome, the censoring mechanism, and the rate of events. The problem with conducting such a power calculation for an observational study that uses IPTW is that the weights are only known once the data have been collected and the treatment-
selection model has been fit. Thus, one cannot conduct an a priori power analysis or sample size calculation, since the weights are not known a priori. We use this fact to motivate our comparison of the power of an observational study that uses IPTW with that of a similarly-structured RCT (lines 140-149; 153-155). In keeping with the Associate Editor’s comment below, we have elected to not make modifications to the manuscript to address these comments.

**Reviewer 2:**
I have reviewed the revised manuscript. I am grateful to see that the authors considered feedback and did extensive revisions accordingly. Therefore, I would recommend that this manuscript could be acceptable.

Thank you.

**Associate editor**

The Associate Editor advises that it is at your discretion whether or not to incorporate the comment of referee 1.

Thank you for giving us this discretion. We have elected to not incorporate the comments of Referee 1. We have provided a justification for this in the paragraphs above.

All correspondence should be sent to Dr. Peter Austin, Institute for Clinical Evaluative Sciences, G-160, 2075 Bayview Ave., Toronto, ON, M4N 3M5, Canada. My e-mail address is peter.austin@ices.on.ca. My telephone number is (416) 480-6131, and my fax number is (416) 480-6048.

Sincerely yours,

Peter Austin, Ph.D.
Senior Scientist