Author's response to reviews

Title: The use of segmented regression in analysing interrupted time series studies: An example in pre-hospital ambulance care

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Author's response to reviews: see over
Response to reviewers' comments

Reviewer: Robert Penfold

This manuscript re-evaluates the impact of a collaborative intervention to improve quality in pre-hospital ambulance care for acute myocardial infarction (AMI) and stroke at 11 publicly funded ambulance organizations in England. In particular, the authors add a term to the regression analysis that accounts for the change in slope in the post-implementation period in order to appropriately account for both the overall secular trend and the impact of the intervention on the rate of increase in the outcomes (AMI performance, Stroke performance). I concur that the original study did not model the impact of the intervention correctly. A main advantage of the ITS approach is the ability to model both the secular trend and change in trend attributable to the intervention. However, I find the re-analysis incomplete, especially with regard to the AMI performance data. To be fair to the spirit of the original study and increase the educational value of the re-analysis manuscript, I believe that the re-analysis should present additional modifications.

First, the approach should consider the impact of censoring the “ramp-up” period in the all site (aggregate) analysis of AMI performance in order to account for the potential lag in time between implementation of the intervention and when the intervention reached “full-strength”. Such an approach has been used frequently by the Soumerai group and the authors appear to be familiar with their work (see also various papers in NEJM, BMJ, etc with Soumerai as senior author). It is uncommon for quality improvement programs to have an immediate impact on either the intercept or slope and the original authors should have noted this (and specified a “ramp-up” in the model appropriately). Similarly, the authors of the re-analysis should have examined this weakness. I believe the first 12 observations in the post implementation period should be censored. Technically, this is achieved by setting the first 12 post-intervention observations for the dummy variable “intervention” to missing. I think this approach will show that there was indeed an inflection in the slope but that this change was delayed until about 3 months after implementation. An alternative approach would be to include 2 index dates with the second index date beginning 3 months after the beginning of the intervention. That is, the segmented model would include 3 time periods: pre-intervention, implementation (12 weeks), and intervention. The possibility of these different specifications should be noted in the current manuscript under consideration. I will leave it up to the authors to decide which approach/result they show in figure 1.

A second consideration is the impact of censoring outliers, modeling them explicitly, and/or smoothing the time series. Power to detect a change in the weekly rate is significantly impacted by variability in the weekly rate. Measurements at weeks 7, 52, and 53 should be censored as part of a sensitivity analysis. A second approach would be to include dummy variables for individual observations (e.g., a dummy coded 1 for week 7 only). An third approach (probably best) is to smooth the rates with a moving average term in the model or aggregate to bi-weekly measurements. These 4 sensitivity analyses (censoring 12 weeks, specifying 2 index dates, censoring outliers, smoothing time periods) must be performed
We thank the reviewer for these excellent suggestions which we have carefully considered. Our article was intended as a commentary on an interrupted time series study which we believed had been analyzed incorrectly. As we did not have access to the complete dataset nor to details about the study beyond what was reported in the article, we did not want to undertake an extensive reanalysis of the data. However, we agree with the reviewer that there are several more sophisticated approaches that could have been considered. We have implemented one of the reviewer's suggestions (the one we regarded as most important) by accounting for a 3 month phase-in period. The results, which have been added as Table 2, do not differ substantially from our original results, and our conclusions therefore remain unchanged. In addition, we have added a discussion of all of the more sophisticated analytical approaches suggested by the reviewer, as well as several helpful references. We trust that these modifications meet with the reviewer's approval.

Other comments

The tone of the manuscript is not collegial. Remove comments referring to pre-publication history. Remove material about what the original paper did incorrectly. Rephrase all material in terms of ways to improve the analysis and alternate specifications that are likely to yield important new insights and new knowledge. You may find yourself in the very deep gratitude of the original authors if the re-analysis is presented helpfully. Rest assured that you will make a mistake at some time in your career and you will thank yourself for having been kind to your colleagues when it happens to you. For example: “In our opinion the authors failed to implement an analytical approach appropriate for an ITS design; therefore, we believe that the authors' conclusions may be misleading.” Becomes “We conducted sensitivity analyses under alternative model specifications in order to better understand the nature and scope of program effects.”

We are sorry that the article came across as non-collegial. It was indeed our intention to provide helpful suggestions to investigators considering interrupted time series studies. We have carefully reviewed the manuscript and removed all sentences that may be perceived as unfriendly. We have removed the comments referring to the pre-publication history, and tried to rephrase the entire article in terms of ways to improve the analysis and alternate specifications that are likely to yield important new insights. However, we did not completely remove material about what the original paper did incorrectly, as the key message of our paper was that the chosen analysis method did not match the design, which resulted in a loss of information and a potentially incorrect conclusion. We do not agree with the notion that segmented regression analysis is a "sensitivity analyses under alternative model specifications in order to better understand the nature and scope of program effects". By using this language, we risk suggesting to readers that was done in the original paper was acceptable, and we are just using different methods to investigate the same question. However, as stated above, we have expanded the discussion to note the different modeling approaches, and sensitivity analyses that could be considered.
A suggested title for the paper might be something like, “Alternate modeling approaches yield new insight regarding the implementation of improvements in pre-hospital ambulance care”. The current title is condescending and antagonistic.

We have modified the title to: The use of segmented regression in analysing interrupted time series studies: An example in pre-hospital ambulance care

I am guessing the page limit is 1500 words for a commentary. I suggest condensing the discussion of stratified analyses (i.e., by site) and removing any instruction on what the original authors should do.

As per the reviewer's suggestion, we have removed the discussion of analyses by site and removed any instruction on what the original authors should do.

Reviewer: Val Gebski

This is a commentary and re-analysis of the manuscript published in this journal by Siriwardena et. Al The re-analysis shows a potential problem in the original paper by using a segmented interrupted time series. The re-analysis is more powerful than simply fitting time as a continuous variable together with a complicated non-linear spline effect of age in that the ITS approach directly considers the impact of the interruption (ie intervention) as well as accounting for post intervention effect etc. The article is well written as I feel explains the problem clearly as well as offering a sensible alternative analysis.

We thank the reviewer for the positive comments on the manuscript.