Reviewer’s report

Title: Evaluation of a multicomponent pathway to address inpatient delirium on a neurosciences ward

Version: 1 Date: 12 Sep 2017

Reviewer: Long H Ngo

Reviewer’s report:

The authors have been responsive to most of comments from my first review and have carried out a number of excellent sensitivity analyses. There are still several issues which I think the authors may want to address. These are rather more technical than clinical, and I feel, if addressed properly, would elevate the overall significance of this paper.

1) In my comment #2, I asked about the number of unique patients who contributed to the total number of visits. So there were 1501 unique patients who contributed to 1595 visits. The authors used all the visits which is the right thing to do because as the authors mentioned, it is not reasonable clinically to just use one visit per patient. In health services research, it is quite often that one encounters "repeated measures" data when a patient has multiple records, and therefore there are "within-patient" data that need to be handled properly. Now, the problem is when all visits data are used, the statistical assumption of "independence" no longer holds. This assumption of "independence" which was implicitly used by the authors in all statistical analysis work in this paper is not valid when all visits are used. "Independence" means that the probability of having delirium or any other outcomes measured here of one visit is independent from that of another visit; however, this cannot be true if the visits belong to the same patient. It is true only if there is one visit per patient. Visits of the same patient or "within-patient" visits are dependent on each other. This means that the probability of having delirium (or other outcomes) on the second visit of a particular patient is very likely related to the probability of having delirium on the first or third visit of this same patient. All the chi-square test, t-test, nonparametric test, and regression modeling used in Table 1, new Table 2, revised Table 3, revised Table 4 assume "independence" in the data. So the most glaring problem here in these analyses is that the unit of observations, the visits, are a mixture of dependent data (within-patient visits), and independent data (between-patient visits), and as a whole data set, one cannot simply ignore the dependency issue which if not properly accounted for tends to underestimate the standard errors and gives exaggerated p-values (i.e. reporting smaller p-values than they actually are). Now, the authors by doing the sensitivity analysis of looking only at unique patient data have partially responded to this important issue; however, to address this properly, they would need to use the correct analysis method for "repeated measures" or "longitudinal" method such as GEE (generalized estimating equations) or linear mixed-effects models. Ordinary methods of using chi-square test, t-test, multiple regression as used here are not valid for repeated measures data. A trained statistician in these areas should be able to assist the team to do these analyses properly.
2) As for the reporting of Table 1, there the percentage such as % of female should not be based on visits, but should be based on unique patients, because the currently reported descriptive statistics give more weight to subjects with more visits. For example, say there are only 2 patients A and B, A is female, B is male, so the percent of female is 50%. Now, if A has 1 visit, and B has 10 visits. Counting percent based on visits make the percent of female now 10/11=91%, a much biased estimate from the true percent of 50%! Same issue with continuous variables where means and SDs are reported. That is the problem right now with Table 1 where visits were used for patients characteristics. The p-values there using chi-square and t-test also assume independence which is again not valid when visits are used.

3) The same problem with the new Table 2 where visits were used, and not patients.

4) Same problem with Table 3 and 4 with descriptive data and p-values.

5) In the Statistical Analysis section, the authors mentioned about the goal of a reduction of delirium incidence from 12% to 8%, but then went on to use visits as units of observations as in "review of 1600 hospital admissions." Well, the definition of incidence is based on patients, and not visits, as units of observations so care needs to be taken to be precise. The incidence here for sample size should be based on patients, not visits. This is the kind of technical points as in item 1 to 4 above, that if corrected would make the paper's clinical contribution more credible and significant, and this reviewer strongly encourages the authors to consider correcting these points since the paper revision is well done with good additional sensitivity analyses, but these pending technical issues would severely diminish the importance and relevance of the paper which clearly would contribute to the field of delirium research.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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