Author's response to reviews

Title: Comparing measures of comorbidity and functional status for risk adjustment to evaluate colorectal cancer surgery: a retrospective data-linkage study

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Author's response to reviews: see over
Dear Dr Peek,

Thank you for your correspondence of 5 December 2014 in which you invited us to revise and resubmit our manuscript in response to reviewers’ comments. Our point by point response follows.

Referee 1

1.1. The number of missing values for the ECOG and ASA scores is substantial causing a considerable risk of selection bias, especially since the ECOG scores are clearly not missing at random. Multiple imputation should be used to address this issue: a complete case analysis alone is not reliable.

We agree that multiple imputation could be used to include patients with missing data but we decided not to use this statistical method as this in itself could introduce bias into the results, particularly given the high level of missingness for ECOG (75%). The validity of results using multiple imputation depend heavily on the appropriateness of multiple imputation model and whether the assumptions underpinning this approach are met. Using imputed data, any difference in the performance of ECOG, ASA and Charlson scores could be due to real differences or could be confounded by the appropriateness of the multiple imputation model. One of the assumptions underpinning multiple imputation is that the missing data are missing at random (MAR),[1] which as the reviewer points out, we cannot assume in this case.

Therefore, we would prefer to leave the analysis as is but have raised this issue in our revised Discussion (Page 14, Para 2, Lines 8-10).

1.2. Co-morbidities are likely underreported in administrative data, causing the Charlson index to be systematically underestimated in this study; perhaps the same holds for the ECOG and ASA scores. Part of the underreporting can often be repaired by considering not only coded diagnoses but also looking at interventions and medication. For instance, cardiovascular disorders can often be established by looking at medication. Please consider extending your analysis with this opportunity, or explain why you did not use it. At the very least, include comprehensive lists of codes that we used to derive the scores (linking codes to the constituent parts of the scores), and give a detailed, descriptive account of your data in terms of the constituting elements of all three scores.

The purpose of our article was to explore methods to improve hospital risk adjustment models using routinely collected data, including statewide hospital episode statistics (the Admitted Patient Data Collection (APDC)), as these are the data most commonly used by clinicians, hospital administrators and various government organizations in Australia to compare the performance of different hospitals. Within the APDC, it is standard coding practice that only comorbid conditions which have an impact on the admission of interest are coded. Many comorbidities are inactive diagnoses of no contemporary relevance to the person’s care so these conditions are not coded in the record of the hospital episode. The approach taken in this paper ensures that we are dealing with currently active, clinically-relevant concurrent conditions but this method does indeed result in an under-estimate of the total prevalence of comorbid conditions in the patient cohort [2].
We have previously investigated the impact of including additional comorbidity information from previous hospital admissions in risk adjustment models to compare hospital cancer outcomes. [3] This previous work demonstrated that although Charlson scores were higher when more sources of comorbidity information were included, there was little change in the performance of Charlson score in the hospital risk adjustment models.[3] Thus, for comparison of hospital cancer outcomes, calculating the Charlson score from comorbidity information within the index admission was the most efficient approach, and the approach we used in the current paper. We acknowledge however that additional comorbidity information could improve risk adjustment models in other contexts, for example to compare individual patient outcomes.

We have now addressed this issue in our revised Discussion (Page 12, last paragraph, to page 13)

1.3. As I understand from the manuscript, all three scores were coded in categories (e.g. "0", "1", and "2 or more" for Charlson) in the regression models, which is motivated by sparsity of higher scores. Please clarify whether indeed this approach was used. I don't think it is good idea, because high scores are often very informative, all of which is lost through truncation. It is not necessary either: logistic regression can perfectly cope with covariates with skewed distributions. So, I advise to code these score numerically. If the assumption of linearity is considered problematic, a secondary analysis could use categorized scores. At the very least, include descriptive statistics of the raw (numerical) scores in the manuscript.

Yes, high Charlson scores were sparse so Charlson scores were categorized as '0' (ie no comorbidities), '1' or '2 or more'. The '2 or more' category comprises scores of 2 (38 patients; 6.6%); 3 (3 patients; 0.5%) and 4 (6 patients; 1%). As such, only 9 people (1.5%) had scores of greater than 2. There were no patients with scores higher than 4. We have now included this information in the Results (Page 11, para 4, lines 2-4).

1.4. Please give a more elaborate description of the peer groups (l. 108), such that this part of the analysis is more informative for readers outside NSW (or inside NSW but not familiar with the peer group definitions).

Hospital peer groups are based on the number of patients discharged each year, the role of the hospital (eg principal referral) and metropolitan or non-metropolitan location (Methods, Page 8, para 2). Peer grouping enables comparisons to be made between similar hospitals.

5. Why adjust for peer groups in the analysis (l. 143)? Probably these groups represent, to some extent, unmeasured confounding factors at patient level. Correcting for these groups is not useful in this study, because it will dilute the influence of co-morbidity and functional status.

Hospital peer group was included in the model as the primary factor of interest. This has now been clarified in the revised manuscript (Methods, Statistical Analysis, Page 10, para 2, lines 2-4)

6. In addition to the rank correlations (l. 169) it would be valuable to see crosstables of the three scores. (Probably good to use truncated scores here!)

The cross-tabulations have now been included in new Table 2 as suggested by Reviewer #1.
Referee 2

Major Compulsory Revisions:

2.1 The results of the first objective of this study – to assess how frequently the ASA score and ECOG performance status can be obtained from population-based administrative data collections – is likely to vary considerably by region (particularly country-to-country, but also within countries that do not have a nationalised standard/requirement for the collection and reporting of particular measures. As such, those results which relate to the ‘completeness’ of this data are specific to one (albeit large) region – and the authors must acknowledge this as early as possible in the manuscript. I would suggest that the objective be re-worded to include ‘…in a large Australian population’ (or similar), and then address this more fully (with an extra paragraph) in the limitations section.

We have edited the Abstract (Background, line 6), last paragraph of the Introduction (Page 6, para 2, lines 2-3) and have added a sentence to the limitations section of the Discussion (Page 14, para 2, last 3 lines) of the revised paper.

2.2 Am I correct that your full cohort were limited to those for whom surgery was performed for curative intent? If so, this is important (in terms of applicability of your results to the wider colon cancer population), and needs to be stated more up-front.

The cohort was limited to patients whose who underwent a surgical procedure that was deemed as potentially curative by clinical experts (Methods Page 7, Data Sources para, lines 13-15).

2.3 The authors need to comment on the potential missing-ness of private hospital data. A recent study in the New Zealand context showed that a substantial proportion of colon cancer treatment data are missing from centralized collections, likely due to the high number of patients who seek treatment for this cancer in the private sector. (Gurney, Sarfati, Dennett, & Koea, 2013)

In NSW, the Admitted Patients Data Collection includes data for all hospitals, both public and private. Approximately half of all colorectal cancer resections take place in private hospitals, but these are captured in our hospital episode statistics. At present, the only routinely collected dataset that includes ECOG status are Local Health District Clinical Cancer Registries within the public sector. Thus we do not have ECOG status for patients in private hospitals. The question is whether the addition of ECOG or ASA status would change the performance of a risk adjustment model (that included Charlson score) differentially for patients in the private sector. Unfortunately, we do not have data to investigate. We acknowledge this issue in the Limitations section of the Discussion (Page 14, lines 4-6).

2.4 The authors need to comment more on the fact that their predictive modelling is necessarily minimised to those who have complete data. Is there anything conceivably ‘different’ about those patients for whom data was available, and how might this impact their results (if at all)? The patient characteristics supplied in Table 1 look highly-similar between the full cohort and those with ASA/ECOG data, but there may be other factors that the authors wish to comment on.

We address this issue in the limitations section of the Discussion (page 14, para 2, lines 3-10)

Minor Essential Revisions:

• Lines 110-112: This sentence is fragmented and should be re-worded.

This sentence has been split into two and reworded (Page 8, para 3 ‘Measures of patient health’, lines 1-3)

• Lines 116-117: Please state the ASA categories explicitly.
Done (Methods, page 8, last para).

• **Lines 119-121:** Please state the ECOG categories explicitly.

Done (Methods, page 9, para 1)

Discretionary Revisions:

• For completeness, the authors may wish to comment on the recently-published ‘C3 Index’, a cancer-specific measure of patient comorbidity (Sarfati et al., 2014) They may wish to comment on how the use of this measure may have influenced their results – particularly the inclusion and weighting of comorbid conditions which are colon cancer-specific (these are available in that paper). They may also wish to comment on the fact that the creators of the C3 Index found similarly-minor improvements in predictive model performance above that observable when using the Charlson Index alone. (This discussion would fit particularly well into the paragraph beginning at line 205.)

We have commented on this study in the revised Discussion (Page 14, para 1, lines 1-5 and new ref 23).

• Line 119-201: Your comment that resources put towards the general improvement of ECOG completeness may be a ‘stretch’ given a) the narrowness of your focus (i.e. colon cancer only, and a sub-set of that population for whom ECOG could be determined), and b) the usefulness of ECOG outside of the scope of population-level epidemiological investigations (e.g. in patient-level clinical care). I would suggest that this language is softened, or that more caveats (beyond that given in the next sentence) are added here.

This sentence has been deleted.

We have also reformatted the references and title page to conform to the journal style. Our revised article comprises an Abstract of 348 words, text 2939 words, 25 references and 4 tables.

Thank you for considering our revised manuscript.

Yours sincerely

Professor Jane Young
Professor in Cancer Epidemiology

References