Author’s response to reviews

Title: Assessing a modified-AJCC TNM staging system in the New South Wales Cancer Registry, Australia

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RE: BCAN-D-19-00587

Dear Editors,

We thank the editors and peer reviewers for reviewing our article. Our responses to all reviewer comments are provided below. Please note the manuscript page and line numbers refer to the non tracked changes version of the revised manuscript (we provided two versions: tracked changes and non tracked changes).

Formatting corrections were also made according to the BMC Cancer Editorial Office.

We have also provided a Declarations section with the mandatory sub-sections within the manuscript.

Please let us know if there are any issues with our re-submission.

We look forward to hearing from you.
Yours sincerely,

Sheena Lawrance,
Manager, NSW Cancer Registry

Reviewer 1

General comments

Including stage into population based cancer registries is an important goal. Therefore this presentation is of great value as it compares different grouping methods with the AJCC-SG and additionally with survival data. The authors want to contribute with their work to the discussion about stage grouping at a population level, especially beyond the pure epidemiological readership into clinical researchers.

Comment 1

I fear that the paper in its present form will be hard to read for this broader audience and thus the authors will not hit their point. The presentation would be more understandable when

1) It would be more instructive shown (perhaps by graphs) how the data were gained and

Authors’ response

We added a diagram (Figure 1) to show how stage data was obtained. We also added more detail around stage data collection in the NSWCR (in terms of staging procedure and workload) in response to comments from Reviewer 2: Discussion section, Page 14-15, Line 317-353.

2) When we would get an information about the total number of cases (as it is shown for the prostate cancer cases, but placed in the part discussion).

Authors’ response

We added the total number of cases both in Table 1, and to the text in the Results section. A breakdown of non-applicable and missing cases was also added to the text.
Results section, Page 9, Line 203-210: “A total of 25,299 NSW cases were identified as eligible for RD staging as of 15 June 2018 and extracted from the NSWCR for analysis. These included 3,890 melanoma cases, 7,223 prostate cases, 4,770 colorectal cases, 4,798 breast cases and 3,618 lung cases (Table 1). Of these we found 1,860 cases could not be RD staged due to missing information (N= 1,142) or staging was non-applicable (N= 718). There were 2,097 cases without a TNM stage due to missing information (N= 2,071) or staging was non-applicable (N= 26). There were 3,280 cases without a DoS value due to missing information (N = 3,175), or staging was non-applicable (N = 105).”

Results section, Page 11. Total number of cases were added to Table 1. As noted in the Table 1 footnotes, we removed non-applicable cases when calculating the percentages shown in the table.

Comment 2

Page 7, line 37: "as lung and colorectal cancers have a poorer prognosis". Poorer than what? Correct at lung cancer, but what is meant in colorectal carcinoma?

Authors’ response

Colorectal cancers generally have poorer prognosis compared to prostate, breast and melanoma cancers. We have added an explanation to make this clearer in the text.

Methods section, Page 7-8, lines 184-190: “Prostate, breast and melanoma cancers generally have high 5-year survival rates (ranging from 90.6% to 95% based on Australian cancer data, 2010-2014) compared to lung and colorectal cancers (lung cancer 5-year survival in men and women in 2010-2014 are 14.5% and 19.6% respectively, whereas colorectal survival rates in men and women are 69.0% and 70.0%). Only lung and colorectal cancer were chosen for the 4-year survival analyses as we expected higher numbers of deaths to occur in these patients compared to prostate, breast and melanoma.”


Comment 3

Page 7 "Benjamin and colleagues". Citation missing?

Authors’ response
Methods section, Page 8, Line 194: The correct citation has been added and the author name has been corrected.

Comment 4

Page 14, line 40: Here we first get numbers of cases. This is part of "results" but not discussion.

Authors’ response

We added the total number of cases both in Table 1, and to the text in the Results section (see previous comment 1).

Comment 5

Page 15 "HR". abbreviation missing.

Authors’ response

The abbreviation has been added. Discussion section, Page 14, Line 293.: “…hazard ratios (HR) to more clinically relevant …”

Abbreviation list, Page 19. Abbreviations were revised.

Reviewer 2

Comment 1

The authors explained the reason for examining RD-stage or a similar simple staging system in the manuscript as availability of TNM values obtained from notification sources routinely provided to PBCRs and derived by applying simplified AJCC business rules developed by the VicCR. However, the other countries are not familiar with RD-stage and have no access to TNM information necessary for RD stage.

Authors’ response

Discussion section, Page 16, Line 372-390. Reviewer 2 raises an important point regarding limited information availability in other countries – this has been added into our discussion. Further comments around this were added to the discussion (see also our response to Comment 4 below).
Comment 2

The readers may not understand if the conclusions tell that RD stage may substitute for AJCC in the other countries as well, or simply declare that Australian PBCRs will use RD stage because of information availability.

Authors’ response

Conclusion section, Page 18, Line 427-433. We have revised our conclusions to more clearly indicate our recommendations to other PBCRs:

“RD-staging may assist other PBCRs to record stage aligned with AJCC-TNM…While a TNM-based staging system would be preferable, simplified staging systems such as DoS and Essential TNM may suffice for certain tumour groups or where PBCR resources and notifications are lacking”

Comment 3

I hope that the manuscript contributes to the researchers and the tumor registrars in the world to develop their cancer registries. Please explain more about RD-stage in terms of staging procedure and workload compared with AJCC-TNM.

Authors’ response

More detail around RD-stage in terms of staging procedure and workload compared with AJCC-TNM was added.

Discussion section, Page 14-15, Line 317-353. “RD-staging in the NSWCR – procedure and workload compared to AJCC-TNM and DoS

Both RD-stage and AJCC-SG data were derived from T, N and M values which were sourced from manual review of pathology reports by NSWCR coders (as part of the RD-staging project), and/or manual review of hospital in-patient notification and other clinical information sources by Cancer Information Managers (CIMs) (as part of routine NSWCR data collection). The RD-staging project, conducted in 2017, involved manual collection of T, N and M values from pathology reports of melanoma, breast, prostate, colorectal and lung cancer cases diagnosed in 2011. This exercise not only provided the RD-stage data, but also resulted in a substantial increase in AJCC-SG data coverage. While a formal comparison of procedure and workload for RD-staging and AJCC-TNM staging cannot be performed, we can provide comments around (i) routine data collections and (ii) data collections performed specifically for the RD-staging project.
Routine TNM data collections in the NSWCR are performed by CIMs and involve transcribing data from reports held in either data extracts from cancer treatment centres, or reports held at point of care in the NSWCR. Complete population coverage is not possible as CIMs generally collect data from public (as opposed to private) hospitals and treatment centres. When there are data inconsistencies or when data is missing, CIMs review clinical documents from cancer treatment centres and all inpatient hospital notifications sourced from hospitals. This can take years to get through full review due to the volume of inpatient notifications generated. The proportion of missing data is variable, however generally data completeness is poor across the board. It is also worth noting that even when the CIMs manually review 100% of patients in a period, recovering and providing TNM values for 100% of those patients is not possible primarily due to data governance (e.g. private consult notes cannot be provided and public treatment referral letters miss key information), and also due to TNM not being essential to some treatment decisions in some treatment modalities and/or protocols. Collection of DoS is conducted routinely within the NSWCR and is part of coding a cancer case. DoS collection adheres to published IARC categories 13 and is comparatively straightforward for the tumours staged in this study. Generally, there is higher stage data completeness for DoS compared to collection of T, N and M data.

The RD-staging project involved extensive training of NSWCR coders to recognise and assign T, N and M based on review of available pathology reports in the NSWCR. Where T, N and M values were not able to be transcribed – information in reports were reviewed and interpreted by coders to assign T, N and M. We estimated NSWCR coders completed manual TNM staging of 16,007 cases within 61 working days. The time spent on the RD-staging project however impacted on routine coding procedures – for other PBCRs where additional resourcing is not available, collection of stage data may not be worthwhile.”

We also provide additional comments regarding pathology reporting practices in Australia. Page 17, Lines 406-410. “In light of the move toward Structured Reporting of Cancer nationally and internationally, the The Royal College of Pathologists of Australasia (RCPA) has issued a Position Statement 29 advising its Fellows to implement AJCC Staging (8th edition). In general, Australian pathologists have historically used AJCC staging in practice and NSWCR implemented Business Rules for AJCC accordingly.”

Comment 4

The readers may expect the authors to mention the Essential TNM, one of the simplified staging system, as well. Could you develop the discussion in a more "worldwide" way?

Authors’ response
We provide some additional discussion around AJCC’s Essential TNM procedure: Discussion section, Page 16, Line 372-390: “A limitation of RD-staging is that other countries are not familiar with RD-stage and have no access to TNM information necessary for RD stage. In 2018 the Union for International Cancer Control (UICC) released Essential TNM a process for collecting stage data in PBCRs in low and middle income countries where there are insufficient resources to derive complete TNM data. 25 Essential TNM is aligned with the UICC staging system, not AJCC –differences between the two systems have previously been documented.26 While a comprehensive formal mapping of Essential TNM to AJCC TNM and DoS was outside the scope of this study, we provide some brief comments based on the Essential TNM User Guide. 27 Generally, Essential TNM aligns more closely with DoS: DoS 1 (and DoS 6) would equate to L1/L2, DoS 2 would equate to A1/A2, DoS 3 and 7 map to R+, and DoS 4 map to M+. Examining the staging of prostate cancer in more detail – Essential TNM, like DoS, defaults N+ tumours to Stage III, which we found to map across AJCC SGs III and IV. T4 N0 M0 also maps to AJCC SG IV but aligns with DoS 2 and would align with Essential TNM TA (locally advanced). Given the simplification of T staging and the assumption of Stage III disease for node-positive prostate cancer, DoS and Essential TNM are likely to align in under-staging AJCC-SG IV cancers as well as resulting in a higher number of unknown stage cases for biopsy-only cases. It would be reasonable to consider DoS as a staging system for PBCRs in low and middle income countries given there is documentation available for most tumour groups (not just breast, cervix, colon and prostate cancer) 13.”

Comment 5

Most of the other countries PBCR collects DoS information in the database. The authors mentioned that DoS remained useful for epidemiological studies, by citing several previous studies. We expect to have a little more comments, perspectives or proposition of future update on DoS for these countries.

Authors’ response

Please see the response to comment 4 above regarding DoS and Essential TNM.

Reviewer 3

General comment

The manuscript compared the use of different staging systems in NSWCR population-based level cancer registration. The found RD-staging provided greatest stage data completeness and alignment to AJCC-TNM for prostate cancers. Whereas for colorectal cancer, summary stage from DoS was an equivalent surrogate staging system to both AJCC-TNM and RD-stage. The
paper was well written. And the analysis may inform potential implementation of a new stage data field in population-based cancer registries.

Authors’ response

We thank Reviewer 3 for this feedback.

FORMATTING CHANGES:

1. Figure legends - Please provide figure legends under a separate heading of 'Figure Legends' after the References. If legends are present within the figure files, please remove them. Figure files should contain only the image, as well as any associated keys/annotations.

Authors’ response

We added a section titled ‘Figure legends’, page 25. The figure files only contain the image and associated keys/annotations.

2. Figures should be provided as separate files, not embedded in the main manuscript file.

Each figure of a manuscript should be submitted as a single file that fits on a single page in portrait format.

Authors’ response

Figures were removed from the main manuscript file. Figures were rotated so that they fit on a single page in portrait format.

3. Please rename Materials and methods to Methods only.

Authors’ response

This title has been corrected.