Reviewer's report

Title: What is the real impact of acute kidney injury? Outcomes in a typical general hospital setting. A retrospective observational database study

Version: 2
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Reviewer: Catriona Shaw

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Bedford et al for BMC Nephrology

Thank you for asking me to review this interesting and informative paper. This paper addresses an important area in helping more clearly understand epidemiology and outcomes associated with AKI in the secondary care setting.

Summary of the paper

Bedford et al present findings from a population based study using data from linked hospital routine data including admission information, demographics, laboratory data, renal unit and ITU data in East Kent. Patients admitted to any of three hospitals between 1/2/09 and 31/7/09 were included in the analysis and followed up until 31/3/11. Patients on chronic RRT, maternity admissions and day case admissions were excluded.

Incidence and outcomes including mortality, in hospital mortality, LOS and ITU utilisation, re-hospitalisation within 30 days are presented by stage of AKI.

The paper is well written. I have some comments/questions which will potentially be easily addressed by some simple edits to the paper in particular in the definitions of the cohort, case ascertainment and outcomes but as they relate to interpretation of the data I have listed the queries under "major comments.

As the statistical methods used are quite complex I have suggested a statistician reviews the paper.

Major compulsory revisions

• Time of entry to the cohort: was this the date of admission for the individual, or the date of the AKI (date of the peak creatinine- including for the time updated analyses)? This potentially influences the interpretation of the analyses related to ITU admission and LOS and may raise the possibility of reverse causality. For example, it may be feasible that a patient who has a long LOS, has multiple health issues which increase the risk of AKI at some point in that stay, rather than the AKI event itself being antecedent and directly being associated with increased LOS. This query can be resolved by refining the case/cohort definition provided in the paper.

• I do not agree with the phrase “fully adjusted” used in relation to the multivariable models (e.g. page 9). Although the authors have used a range of co-variables in the analyses we cannot know that there aren’t other confounder
variables that have not been taken into account in the analyses that could explain some of the associations identified. For example, in patients with AKI3, severity of other concurrent multi-organ involvement/failure may explain some of the association with mortality. I would suggest this phrase is changed and a direct reference to the risk of confounding added to the limitations section.

• I think the potential for ascertainment bias needs discussing in relation to ascertainment of the AKI cases. For example, sicker patients may have had more creatinine measures, increasing the probability of detecting AKI.

Minor essential revisions

Methods:

• Exposure: There is a clear description of what methods were used for the baseline creatinine, however it is not clearly stated that which creatinine during any inpatient stay (presumably the peak) was used as the measure for comparison to calculate the AKI stage for that admission for an individual. For clarity this would be helpful to add.

• Outcome: How was mortality ascertained? Was this form a link with ONS? Was data on the outcomes of interest complete (e.g. place of discharge)?

• Was a competing risks framework used/considered e.g. for the outcome hospital re-admission analyses (all-cause mortality as a competing risk)?

• There is an error on page 7- the text currently reads “there were 20,464 admissions with no AKI and 5,521 admissions with AKI…Of these, 3,961…”. The breakdown (3961+1927+633) AKIN1-3 totals 6521 not 5521.

Results:

• I think it would add additional information and help interpretation of the regression model effect estimates if further descriptive stats were provided (potentially as an on line appendix/supplement if the word limit is a problem) e.g. baseline eGFR/CKD stage, categories of types of primary admission diagnosis, and place of residence prior to admission, and categories of primary diagnoses as part of the baseline descriptive characteristics.

Discussion:

• Is there any data which provides validation that the catchment population for this cohort is representative to the rest of England/UK? This would help the reader in terms of the generalizability of the papers findings.

Discretionary revisions:

These are mainly stylistic.

• Abstract: I would remove the word “actual” from “actual incidence” in the abstract. As the analysis is conducted using routine care data, not all individuals will be tested equally and this study reports the “detected” AKI incidence in a secondary care population.

• Consistency between the outcomes reported to have been selected (methods section “outcomes” and also in the stats section of the methods) and those
reported (table 4). In addition, the methods section says 3 models will be reported (9 unadjusted etc.), but in table 4, there are 4 models reported. In the results text presentation of the outcomes, as in the order presented in the methods may be neater.

• Statistical methods: it may improve the flow of the stats methods section to place the sentence “a time dependent risk analysis for survival was employed to allow adjustment for multiple admissions…” Is placed after the descriptive statistics section, and next to “Cox regression was used for…”.

• Statistical methods: a time updated analysis approach was used with the Cox model for all-cause mortality and it is stated that within patient correlation was addressed using a random effects approach for the outcome LOS. Re-wording of this paragraph so it is more clear how within patient correlation (if multiple observations per patient were used when available) was managed in the analyses for other outcomes (in patient mortality, re-admission etc) would be helpful for the reader

• Table 4-if the table needs to go on 2 pages, I suggest that the header for the table columns are inserted on the second page also for ease of reading.

• Table 3- 3 decimal places are probably not needed, 2 would suffice.

• In the discussion: the authors comment “the incidence of AKI… is significantly higher than previous estimates”. Do the authors have some explanation for why this is the case? Perhaps could this be due to increased testing of creatinine due to increased awareness? Change in definitions with AKIN criteria compared to other studies (they mention that there may some misclassification with cases of progressive CKD)? a true increase? I think their insights would be valuable addition to the discussion and also help the reader think about the generalizability of the findings.

• Discussion: The incidence reported here is in secondary care inpatients. A future area of interest would be to additionally try and understand more regarding community based AKI events in individuals who are not admitted to hospital.

Thank you once again for asking me to review this paper and please do let me know if I can be of further assistance.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests