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

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Reviewer: Raymond Hsu

Reviewer's report:

This is a somewhat straightforward descriptive study assessing the population incidence of AKI in a defined catchment area in East Kent, United Kingdom. The strengths include the large sample size and seeming completeness of data available to the researchers. However, the findings of this study are not really that novel, and for audience outside of the UK, it's difficult to appreciate what's so innovative about the accurate depiction of AKI incidence in a "district general hospital setting."

Critical comments as follow:

MAJOR COMPULSORY REVISIONS

1. The authors's main goal is the describe the population incidence in this area. They elected to study adult patients only, having excluded patients <18 years from analysis (numerator ascertainment). However, in their calculation of incidence (or more accurately, the incidence rate), they used the total population of East Kent, approximately 720,000, as the denominator. Authors cannot claim that their "per million person-year calculation" is correct if the denominator used is that of the entire population including children. In addition, 720,000 seems a fairly rough estimate. The authors need to cite specific census source(s) for their population counts, and describe whether the census year matched their study year.

2. Additionally, for the incidence calculation, the authors should be more transparent in their explanation of how they derived 12,394 pmp/yr. It seems to me that they took 4462 patients that had AKI, multiplied by 2, then divided by the 720,000 population count. First, this method should be spelled out more explicitly in the Methods. Second, the assumption of this method is that the 4462 cases from February through July of 2009 is representative of the whole year, but there may indeed be seasonal variation in the incidence of AKI (ie related to flu season, related time of the year when more pts may undergo surgery, related to skill level of practitioners/trainees). The study would be stronger if authors could conduct the analysis on the entire calendar year so that a more accurate incidence rate can be calculated. If this approach is not do-able, authors should explain why they picked the study period and address the inference of incidence rate from only 6 months of data as a major limitation of the study.

3. If the authors are able to address Comment # 1 above, then it would seem that
the calculated incidence would be even greater than 12,394 pmp/yr (ie once they remove patients under 18 from the denominator of 720,000). As they pointed out in the first paragraph of Discussion, the incidence here is "significantly higher than previous estimates." This may be in fact the most novel finding of the entire study, as the regression outcomes showing associations between AKI stage and death, LOS, resource utilization are all very well established already. The authors should expand upon their finding of significantly higher incidence and postulate as to REASONS WHY this may be. Is there something specific about this "district general hospital" setting that is distinctively different from other studies cited, such as the Scottish Grampian region study cited? Or, are we seeing a temporal trend, i.e. incidence has greatly increased since the prior studies? Or, is the increased incidence due to the changing definitions being used? This is really the heart of the paper, and unfortunately the authors currently offer no hypotheses for this interesting finding.

4. The use of the lowest serum creatinine in the 12 months following discharge to determine AKI stage (for those without pre-hospitalization creatinine) seems problematic. I am not aware of this method being previously used in other studies. If it has been used, please cite prior example(s). The assumption that AKI must have occurred if serum creatinine improved following admission by greater than 26.4 may not always be correct. For examples, pts may lose great muscle mass during prolonged hospitalizations, leading to decrease in serum creatinine; pts may have undergone a kidney transplant (authors do not mention excluding transplant pts) leading to decline in creatinine; a patient who required dialysis-requiring AKI who subsequently remain dialysis-dependent (or a patient who became dialysis-dependent in the months following discharge) can easily have a lower creatinine than the peak hospital creatinine. I think the study would be stronger if this method was not used altogether. Alternatively, authors can perform sensitivity analysis excluding the number of patients whose AKI was ascertained using the post-discharge creatinine, to see if the incidence changes significantly. (Again, as the authors give no explanation as to why their incidence is so high, I wonder if it is partially due to ascertainment bias here.)

5. There is a discrepancy between what the authors described as a 3-stage method of regression analysis in Methods and what is presented in the Results (where in Table 4 there appears to be 4 models). It seems that the authors should perform 1) adjusted model, 2) gender & age-adjusted model, 3) gender, age, and "other covariates" (as listed in Table 1, including Charlson co-morbidity Score). The whole point of the Charlson score is to define the burden of baseline conditions, so I don't see the need to perform a fourth model with the individual co-morbidities.

MINOR ESSENTIAL REVISIONS:
1. In the Data Extraction section of Methods, authors should further define how patients who had AKI and required dialysis are extracted. Authors later describe how RRT was abstracted from the renal data system in Outcomes, but inpatient dialysis for AKI is a main predictor here. Also, would make sure that authors did not only look for dialysis in patients meeting AKIN stage 3 creatinine criteria, as it
is very possible a large subset of patients had less substantial delta creatinine before requiring dialysis.

2. It is unclear how baseline CKD stage was defined. I am unclear what is the "baseline pathology data" (in Independent Variables, under Methods). Is the CKD stage obtained using the "baseline creatinine" from the same methodology as described in the previous paragraph (under Data Extraction)? Did authors also use the post-discharge nadir creatinine to define CKD for the subset of patients without pre-hospitalization creatinine?

3. In the 3rd paragraph of Results, they write: "Co-morbidity was over represented in patients with AKI, but this was not related to AKI stage...deprivation was not related to AKI stage." These statements imply some sort of trend testing was performed, yet no methods or results of any statistical tests were shown. Looking at Table 2 last two rows, it DOES look like there is a trend of more co-morbidities with increasing stage of AKI.

4. In Table 4, all of the outcomes listed are binomial outcomes (ie Risk of Death, In-Hospital Mortality, Readmission) except Relative Length of Stay and Relative ITU Length of Stay. As the authors provide odds ratios here, I wouldn't really know how to interpret the OR's in those two columns without further explanation.

DISCRETIONARY REVISIONS:

1. Too many figures/tables. I think Table 1 can be eliminated and placed into the text. In fact, the paper would be stronger if the authors had a separate paragraph in Statistical Methods describing the co-variates used in multivariate regression analysis, and WHY those co-variates were chosen. For example, cite prior literature supporting why you picked Weekend Admission as a factor.

2. Table 2 also contains perhaps some uninformative information. I don't think it's necessary to list every single co-morbidity extracted, as these are all presumably code-based. I think showing the Charlson Index scores would be sufficient. If authors wish to keep all the rows, they should explain, for example, what constitutes "Renal Disease" in their data extraction. It may actually be more informative to show the co-variates used for regression analysis (currently listed in Table 1) by AKI stage.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.