Author's response to reviews

Title: Acute elevations in serum creatinine in primary care engender similar mortality risk to acute kidney injury in hospital

Authors:

Helen Hobbs (helen.hobbs@nhs.net)
Paul Bassett (paul@statsconsultancy.co.uk)
Toby Wheeler (t wheeler@nhs.net)
Michael Bedford (michael.bedford@nhs.net)
Jean Irving (jirving2@nhs.net)
Paul E Stevens (p stevens@nhs.net)
Christopher K Farmer (chris.farmer1@nhs.net)

Version: 3
Date: 31 October 2014

Author's response to reviews: see over
Dear Professor Haviv,

Re: Do acute elevations of serum creatinine in primary care engender an increased mortality risk?

Thank you for giving us the opportunity to resubmit our article to BMC Nephrology. We found the reviewers comments very useful and have incorporated their suggestions into this revised manuscript. We believe that these changes have strengthened the paper and thank you for reconsidering it for publication.

Yours faithfully,

Dr. Chris Farmer

Helen Hobbs
Paul Bassett
Toby Wheeler
Michael Bedford
Jean Irving
Paul Stevens

Response to reviewer’s comments

Reviewer 1: Farid Nakhoul
Comment 1. The paper includes several statistical designs, not all of them are familiar to the readers- it would be preferable to add a couple of sentences explaining these statistical designs.

Author’s response;
The methods section has been reworded to make the design clear to the reader.

Comment 2. The discussion and results chapter are not sufficiently clear and flowing. In the results chapter there is plenty of information, it would be worthy to simplify the numbers and add a few sentences explaining the results and what they represent

Author’s response;
The results section has been reworded to make it clearer and easier to read

Comment 3. Although this is an observational review, it would be interesting to add the writer’s hypothesis that would explain the connection between the rise in the patient's serum creatinine and the increase in the morbidity and mortality.

Author’s response;
The following sentence has been added to the text.
‘The hypothesis for the study was that acute elevations in the Serum creatinine measured in the community may represent episodes of AKI and therefore will be associated with increased mortality in the community compared to those who did not have acute elevations in the serum creatinine’

Comment 4. The first paragraph in the results contains the patient's characteristics—it is recommended to add a reference in the paragraph to Table 2 which summarises beautifully the patient's characteristics, which would make the text less clumsy.

Author’s response;
We have reworded the text and added a reference to table 2 in the first paragraph.

Comment 5. The graphs at the end of the text, there is no uniformity in the colours given to each AKIN group in pictures 2 and 3, AKIN3 is orange coloured, meanwhile in picture 4 AKIN2 is coloured in orange. It would be preferable to uniformly and consistently colour the groups, which would make it easier to follow the results.

Author’s response;
We agree that consistency with the graph would make the results easier to follow, we have asked the statistician to re-draw the final Kaplan-Meier graph unfortunately this has not arrived in time to meet this deadline. We hope to forward this on when we have received it.

Reviewer 2: Nicholas Selby
Reviewer's report:
Major: Comment 1; It is essential that the authors report the time between the baseline creatinine and measured creatinine used to determine presence of AKI. As well presenting mean/median data, they should include a frequency chart or histogram to show the proportion of patients in periods of time lapsed (e.g. 0-48hrs, 2-7 days, 8-28 days, 1-3 months, 3-6 months, >12 months). Without this, it is impossible to determine whether the authors are describing AKI or CKD, both of which can negatively impact outcome. In contrast to acutely unwell hospitalised patients in whom it is reasonable to suppose that an elevated creatinine (even with a gap between baseline and measured creatinine) is an acute change, the same cannot be said for a stable outpatient population.

Author’s response;
The logistic regression for model 7 and 8 now includes time in months to baseline as an independent variable to measure the size of the effect on outcome. The results are presented in Table 6

Comment 2; How many of the AKI stage 1 group were categorised only because of a rise in creatinine of 27micromol (with <50% rise), as the numbers of AKI stage 1 hugely outweigh the numbers in stage 2 and 3? It would also be important to know whether the associations with poor outcome held true for both groups within AKI stage 1 (i.e. those with >50% rise versus those categorised with only 27micromol rise).

Author’s response;
The results section now includes a second analysis looking at those defined with an absolute change in serum creatinine only compared with those with a relative change serum creatinine. The results are also displayed in figure 4 and in table 6
Comment 3; the authors have explained their decision to exclude patients with a rise in creatinine who also had a hospital admission during the study period. I understand that this group need to be analysed separately; however I would suggest that this group should be added to the manuscript and contrasts between the groups would be informative. Previously describing these data in a review article would not necessarily preclude their inclusion here. It is also misleading to discuss population based incidences when excluding certain subpopulations of AKI.

Author’s response;
Patients who had CA-AKI and were admitted to the hospital during the same time period were included in a different study. (Bedford, M., Stevens, P.E., Wheeler, T.W.K., and Farmer C.K.T., (2014), What is the real impact of AKI? BMC Nephrology 15:95 1-9). However in that study did not compare CA-AKI with HA-AKI therefore a direct comparison with our data set was not possible. However the patterns for outcomes between the studies have been discussed further in the discussion section.

Minor:
Comment 4; Please include the method used to measure serum creatinine (Jaffe or enzymatic) as this may have a bearing on precision of describing such small changes in serum creatinine

Author’s response;
This sentence has been added to the text ‘The enzymatic method for creatinine is standardized against NIST SRM 967 and thus is traceable to isotope dilution mass spectrometry (ID-MS). The assay was related to an ID-MS assay according to the equation: Abbott enzymatic = 0.982 (ID-MS) + 3.3 (n = 203). The assay is related to the Roche creatinine plus enzymatic assay (Hoffman-La Roche, Basel, Switzerland) used to re-express the MDRD equation according to the equation: Abbott enzymatic = 1.0338 (Roche enzymatic) + 0.98 (unpublished data, E.J. Lamb).’

Comment 5; The title is misleading and should be changed. There is no comparison with hospitalised patients; the title should reflect the study that has actually been performed.

Author’s response;
The Title has been changed to ‘Do acute elevations of serum creatinine in primary care engender an increased mortality risk?’


Author’s response;