Author’s response to reviews

Title: Serum phosphate and social deprivation independently predict all-cause mortality in chronic kidney disease.

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Author’s response to reviews:

Dear Editor and Reviewers,

Thank you for your thorough review of our manuscript and for your valuable comments. We are grateful for the opportunity to send a revised version for your consideration.

We hereby provide a point-by-point response to the reviewer’s comments.

Reviewer 2 Dr Quinibi:

Regarding the Methods section:

1. Since their exclusion may have biased the results of our study, we agree that he 556 patients who had missing phosphate measurements, and therefore were excluded from the study, should be better described with regards to important properties, including distribution of CKD stages and Scottish Index of Multiple Deprivation (SIMD) quintiles, as well of death rate. In the revised version of the manuscript we have added a brief
description of these properties and now provide P values for the statistical differences between the group of excluded patients and the study cohort (Chi square tests). In more detail, the numbers/percentages are as follows:

a. Distribution of CKD stages (not significantly different from the study cohort; P=0.14):

i. CKD stage 1 and 2: 32.9% of patients
ii. CKD stage 3: 34.2% of patients
iii. CKD stage 4: 30.1% of patients
iv. CKD stage 5: 2.7% of patients

b. Death rate during follow-up: 13.7% of patients (not significantly different from the study cohort; P=0.54)

c. Distribution of SIMD quintiles (not significantly different from the study cohort; P=0.77)

i. SIMD quintile I: 30.3% of patients
ii. SIMD quintile II: 22.2% of patients
iii. SIMD quintile III: 16.9% of patients
iv. SIMD quintile IV: 14.3% of patients
v. SIMD quintile V: 16.3% of patients

2. The following traditional cardiovascular risk factors were included in the regression model (Model 3, Tables 4A-C): systolic and diastolic blood pressure, body weight, presence/absence of diabetes and/or coronary heart disease. In order to keep language consistent, we have added the term “traditional” (risk factors) to the explanation of the statistical models in the Methods section. Unfortunately, we were not able to adjust for other important cardiovascular risk factors including smoking habits, lipids and medication use.

Regarding the Results section:

3. and 2. We agree that follow-up period is relatively short. Also, unfortunately, we were not able to determine the cause of death in 121 out of 375 patients. We share the reviewers’ disappointment. As this was an unfunded study, using real world data, we were unable to access full death certificates, documenting cause of death issued for all patients, in particularly those dying at home or in other health boards, from the General Register of deaths. To access these requires appropriate funding, which we simply do not have for this study. The situation is exacerbated by our renal unit taking referrals from a wide geographical area, covering a number of health boards, using different clinical patient records systems. Whilst this extremely disappointing, we believe that this does not majorly detract from the messages contained in the paper.
Unfortunately, FGF23 has not been measured in this cohort. We agree that FGF23 measurements possibly would have added valuable information to our study.

Regarding the Discussion and Conclusion sections:

We agree that our finding of high phosphate as an independent predictor of mortality in CKD patients is not a novel finding. Moreover, it has previously been published that serum phosphate is higher in patients from deprived areas, and that socioeconomic deprivation is associated with higher risk of adverse outcome including premature mortality in CKD patients. Therefore, we acknowledge that the main value of our study is to confirm previous findings in a Scottish population, and we have slightly changed the Conclusion section accordingly. However, according to our knowledge, the lack of an interaction between serum phosphate and socioeconomic deprivation in their association with adverse outcome has not been published previously, and we believe this novel information may be of some additional interest.

We hope the changes we have done to our manuscript, as well as the responses we have given in this letter have been to your satisfaction, and that our article will be considered for publication in BMC Nephrology. We are happy to provide further information and make additional changes on your request, and we look forward to hearing from you.