

Author's response to reviews

Title: Risk factors for chronic kidney disease in Japan: a community-based study

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Version: 4 **Date:** 30 July 2009

Author's response to reviews: see over

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Version: 3 Date: 30 July 2009

Author's response to reviews: see over

July 30, 2009

Andrea Bucci, PhD.
Scientific Editor
BMC-series Journals

Dear Editor,

Thank you very much for the consideration to revise the manuscript 2055768486276548 entitled " Risk factors for chronic kidney disease in Japan: a community-based study " and consider it for publication in **BioMed Central - Nephrology**.

We appreciate the comments of the reviewers and have taken a great care to address their concerns. We have attached a revised manuscript incorporating the suggestions of the reviewers. Here is our response to reviewers' comments.

Sincerely,

Norimichi Takamatsu
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Reviewer's report

Title: Risk Factors for Chronic Kidney Disease in Japan: A community-based study

Version: 1 **Date:** 26 June 2009

Reviewer: Olafur Skuli Indridason

Reviewer's report:

The authors have made significant changes but I still have major concerns.

#1:

The definition of CKD in the guidelines they cited is eGFR less than 60 and/or other sign of kidney damage of more than 3 months duration.

Therefore when the authors talk about CKD stage 2 they are actually referring to a category of kidney function but not CKD. Moreover, the estimating equations are generally imprecise within the normal range of GFR and therefore it has been recommended that when the eGFR is >60, it should not be reported as a separate value but simply stated that it is >60.

>Answer: We thank the reviewer for the comments about the definition of CKD. We agreed and corrected the definition of stage 2 CKD in Tables 1, 2 and 5 according to the suggestion.

#2:

As I had suggested in my prior review, the authors should probably have only 2 categories, < 60 (CKD) and > 60 for their comparisons, just as they present in the abstract. Alternatively, they could talk about stages of kidney function rather than stages of CKD.

>Answer: We thank the reviewer for the comments about categories for comparisons. We agreed and mentioned stages of kidney function rather than stages of CKD in the revised manuscript.

#3:

The authors also have information on proteinuria (Uro-Paper) and albuminuria which frequently is used to define CKD. They should present how many subjects had proteinuria by recognized standards, as well as microalbuminuria (frequently defined as 30-300 mg/g) and macroalbuminuria (>300 mg/g). This allow for better comparison with other studies than using the 95th percentile for healthy subjects in the study. The 95th percentile could nevertheless be used for

the statistical analysis.

>Answer: We thank the reviewer for the comments about the information on proteinuria and albuminuria. We have now added the definition of proteinuria and albuminuria in method (page8, para2,3) and the data in Result (page12).

#4:

It is therefore not right to say that ACR is an independent risk factor for CKD as in this study it is associated with eGFR <60. It could be contributing to kidney damage or come as a result of kidney damage and not be a risk factor but rather a consequence of low eGFR.

>Answer: We thank the reviewer for the comments about “ACR is an independent risk factor for CKD “. We corrected these statements in abstract according to the suggestion.

Methods:

#5:

I still do not understand how the sample was selected. Were these subjects that came for an annual health examination and subsequently volunteered to participate in the study? This would probably explain why women outnumbered men on this scale.

>Answer: We thank the reviewer for the comments about the sampling. The population of this town was approximately 9300. We sent an official letter regarding an annual health examination and this program for the resident aged ≥ 18 at first. We then sent a second letter of invitation for the resident who had not rejected this program. Finally, a total of 1564 people aged ≥ 20 took part in the program and agreed to join the study. We have now added the statements in the Method section.

#6:

CKD was defined by the GFR criteria only, not by proteinuria. Someone that has eGFR of >60 and no proteinuria or other sign of kidney damage does not have CKD but lowered eGFR.

>Answer: We thank the reviewer for the comments about the definition of CKD. In this study, CKD was defined by the GFR (eGFR) criteria only, not by proteinuria. We have now stated the prevalence of proteinuria and albuminuria with low eGFR in the Results.

#7:

The authors should state the reference values for their creatinine measurement method.

>Answer: We thank the reviewer for the comments about the reference values for our creatinine measurement. The reference values were found to range from 0.8 to 1.3 mg/dL and from 0.6 to 1.0 mg/dL for male and female, respectively. We have now added the statements in the Methods.

Results.

#8:

I would like to see the mean eGFR for men and women separately in the first section.

>Answer: We thank the reviewer for the comments about the mean eGFR <60 for men and women. The mean eGFR for men and women was 80.8 and 80.0 mL/min/1.73m², respectively. We have now added statements in the Results.

#9:

In this section they also should state the prevalence of eGFR<60 for men and women separately and the prevalence of proteinuria, microalbuminuria and macroalbuminuria.

>Answer: We thank the reviewer for the comments about the prevalence of eGFR <60 for men and women and the prevalence of proteinuria, microalbuminuria and macroalbuminuria. The prevalence of eGFR<60 for men and women was 6.6% and 9.4%, respectively. Proteinuria was defined as 1+ or greater measured by Uro-PaperII and the prevalence of proteinuria for men and women was 5.3% and 4.9%, respectively with the eGFR<60 level. Meanwhile, the prevalence of microalbuminuria for men and women was 23.7%, 10.9% respectively with the eGFR<60 level, and the prevalence of macroalbuminuria for men and women was 5.3%, 3.3%, respectively with the eGFR<60 level. We have now added statements in the Methods and Results.

#10:

In the Relationship between lifestyles and stages 3-4 CKD the authors say that several factors are significantly related to stage 3-4 CKD. Here they need to be more specific with regard to the direction of the association. For example those that drink are more likely to be in the control group. On page 16 in the discussion

this also needs to be clarified

>Answer: We thank the reviewer for the comments about the relationship between lifestyles and stage 3-4 CKD. We have now added statements in the Results and Discussion.

#11:

In risk factors for different stages of CKD the order of the OR for stage 2 kidney function is not right.

>Answer: We thank the reviewer for the comments about the order of the OR for stage 2 kidney function. We have changed these orders correctly.

#12:

There one can see that higher U-Col4CR is associated with normal kidney function. Moreover, in table 5 diabetes also has a borderline significant association in the same direction. Could this be related to the fact that many subjects with early diabetes may have hyperfiltration? The authors do not discuss this finding in any detail, see also discussion page 16.

>Answer: We thank the reviewer for the comments about the discussion in the association with U-Col4CR, diabetes in table 5 and kidney function. We have now added statements in the Discussion.

#13:

In the last paragraph of the results the authors state that the risk for developing CKD was dependent on ACR. This is not right but they could say that the risk of having eGFR <60 was associated with ACR.

>Answer: We thank the reviewer for the comments about the statement “the risk for developing CKD and ACR”. We corrected this statement according to the suggestion.

Discussion.

#14:

Page 16, they discuss results in table 4. Table 4 is somewhat confusing but if I understand right the insufficiency if exercise (+) means that there is insufficient exercise, exercise habit (+) means that persons sweat with exercise. For this and fatty meal and alcohol consumption, having the lifestyle is more common in the control group but the direction of the association is not discussed (see also

above)

>Answer: We thank the reviewer for the comments about the results in table 4. We have now added statements in the Discussion.

Conclusions

#15:

The authors are not studying the progression of CKD and the initial sentence therefore seems an overstatement.

>Answer: We thank the reviewer for the comments about the atatement in CKD progression. We agreed and corrected. We have now added statements in the Conclusions.

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

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests

Reviewer's report

Title: Risk Factors for Chronic Kidney Disease in Japan: A community-based study

Version: 1 **Date:** 7 June 2009

Reviewer: Paul Muntner

Reviewer's report:

This manuscript is much improved and I appreciate the authors' attention to most of the previous comments. However, there are concerns with the updated manuscript.

#1:

Most importantly, the definition of stages 1 and 2 CKD is not consistent with the K/DOQI guidelines. According to the K/DOQI guidelines, stage 1 CKD is an estimated GFR ≥ 90 ml/min AND microalbuminuria (≥ 30 mg/g) and stage 2 CKD is an eGFR of 60 to 89 ml/min/1.73m² AND microalbuminuria (≥ 30 mg/g). The definition of stage 2 CKD should be re-defined and the analyses corrected in Tables 1, 2, and 5. Alternatively, a more simple correction would be to change the terminology used (i.e., eGFR of 60 to 89 rather than stage 2 CKD) to reflect the study of eGFR levels rather than CKD stages.

>Answer: We thank the reviewer for the comments about the definition of CKD. We agreed and corrected the definition of stage 2 CKD in Tables 1, 2 and 5. We have used the terminology "eGFR levels" instead of stages 1 and 2 CKD in the revised manuscript.

#2:

Also, tables 3 and 4 would be much easier to read if percentages were presented rather than numbers. Could the authors explain how only 6 of 130 individuals with stage 3-4 CKD in table 3 have renal disease? I assume the prevalence of renal disease in this group is 100%? Is this a previous diagnosis of CKD? If so, could this be noted in the title and/or footnote?

>Answer: We thank the reviewer for the comments about the table 3 and 4. We agreed and changed these numbers to percentages. We have now added statements "Medical histories were previously diagnosed and self reported" in the footnote.

#3:

The reason for a lack of association between diabetes and anemia with stage 3-4 CKD remains unclear. Assuming "Diabetes" in Table 3 represents self-report diabetes, this was not associated with CKD. Also, it seems inconsistent with previous studies that <10% of those with CKD (Stage 3-4) have diabetes. This warrants a more full explanation in the discussion section of the manuscript.

>Answer: We thank the reviewer for the comments about the association between diabetes and anemia with stage 3-4 CKD. We have now added statements in the Discussion.

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.