Author's response to reviews

Title: Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study

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Version: 5 Date: 16 March 2010

Author's response to reviews: see over
Dear Editor-in-Chief

Please find enclosed our second revised manuscript entitled: *Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study*

The authors are Jøran Hjelmesæth (corresponding author), Jo Røislien, Njord Nordstrand, Dag Hofsø, Helle Hager and Anders Hartmann.

The manuscript has been revised according to the reviewers’ comments and suggestions.

Please see our point-by-point replies to the reviewers’ concerns below.

We hope that the revised manuscript is acceptable for publication in *BMC Endocrine Disorders*.

Sincerely,

Jøran Hjelmesæth
Response to reviewers March 16, 2010

Reviewer’s report
Title: Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study
Version: 4 Date: 3 February 2010
Reviewer: Giorgio Bedogni

Reviewer’s report:
Major Compulsory Revisions
None

Minor Essential Revisions
1. Prevalence: I apologize for having been too synthetic in my comment. This is the – hopefully understandable this time – reasoning: if “prevalent T2DM” is the outcome, it follows that one wants to model the “prevalence” or “prevalence rate” of TD2M (0 = no; 1 = yes) – these terms are equivalent. The odds ratio is however not a prevalence ratio when the prevalence of the outcome of interest is > 0.10. The solution is very simple: one has just to write the “odds of T2DM” instead of “prevalent T2DM”. This is a semantic problem, yes, but with far-reaching methodological implications.

Reply: The term “prevalent” has been removed from the revised manuscript.

2. Calculating the 95%CI of Spearman’s correlation coefficient can be done using bootstrap. This is very easy to do in R and Stata but can also be done with few effort in SPSS. I am not using SPSS from many years but I have looked at the manuals and it seems quite easy to do the calculation. These references may help (checked on 03-February-2010):
http://gcrc.labiomed.org/Biostat/Education/Case%20Studies%202005/Session2/Hauk oos%20and%http://docs.google.com/viewer?a=v&q=cache:gHLtLJY4juUJ:support.sp ss.com/ProductsExt/Statistics/Please, note that I am insisting on this point just for the reason that a measure of effect without 95%CI is of doubtful clinical relevance even if admittedly this is not a major point of your paper.

Reply: 95% CIs have been calculated and implemented in the revised manuscript.

Discretionary Revisions
I am sorry to say that I am not still able to see the references in my PDF. This may be a problem with the web processing of the MS. Can you specify the software you used to program GAM? I supposed it was R but I may be wrong owing to the above considerations. Please, note that I cannot read references and do not know what ref 24 is.


Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests
Reviewer's report
Title: Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study
Version: 4 Date: 15 February 2010
Reviewer: Carlos Lorenzo
Reviewer's report:
This manuscript is a revision of a previously submitted paper on the relation of serum creatinine to prevalent type 2 diabetes among morbidly obese Caucasian women and men with eGFR >60 ml/min/1.73 m2. The results indicate that serum creatinine is associated with prevalent type 2 diabetes in Caucasian morbidly obese patients.
The paper is much stronger. Some variables and conclusions have been redefined and perfected, respectively. I am satisfied with the comments of Hjelmesæth et al. I do not agree with some of them, although I understand that the authors may validly hold their own.
In this regard, I have a few of comments:
1.- Measures of muscle mass are often absent in studies that relate body composition to insulin resistance and diabetic risk, but a potential relationship between skeletal muscle mass and insulin resistance is at least controversial. The authors described some studies in which a direct relationship is observed. Other studies, however, have described no relationship. Kuk et al. described no association between whole-body skeletal muscle mass and either glucose tolerance or insulin sensitivity in overweight and obese men and women (Appl Physiol Nutr Metab 2008;33:769). Similarly, Goulet et al. reported no relationship between insulin sensitivity and sarcopenia (loss of muscle mass) in healthy, non-obese, postmenopausal women (Appl Physiol Nutr Metab 2007;32:426).

Reply: Thanks for this interesting information. The paper by Kuk et al. has been referred in the introduction in the revised manuscript.

2.- In this study, there is not apparent relationship between creatinine and muscle mass. As suggested by reviewers 2 and 3, directly measured muscle mass may be necessary to properly assess muscle mass in the morbidly obese. Additionally, the authors indicate in page 8, para 2, line 2: “Serum creatinine does not correlate significantly with lean body weight (data not shown)”. I think it is simple to show the results by adding a couple of correlation coefficients.

Reply: We acknowledge the limitation of not having directly measured muscle mass and this is also addressed in the limitations section in the manuscript: “In addition, lean body weight, glomerular filtration rate, and creatinine clearance were estimated rather than measured with gold standard methods”. Thanks for the latter suggestion. The correlation coefficients are added to the revised manuscript.

3.- Age is used in the MDRD and the Cockcroft-Gault equations to estimate eGFR and CrCl respectively. In Table 1, men and women with diabetes do not differ from counterparts without diabetes in terms of CrCl, but differ in terms of creatinine. Individuals with diabetes are 8 to 9 years older than those without diabetes. This fact needs to be taking into consideration, because CrCl decreases with age. This could explain the relation of creatinine to prevalent diabetes and the absence of relationship between CrCl and prevalent diabetes.

Reply: We have addressed this issue in the discussion in the revised manuscript:” Although our diabetic patients did not have higher creatinine clearance than their
non-diabetic counterparts, they were on average 8 to 9 years older, and creatinine clearance tends to decrease with age. This could explain the apparent absence of association between creatinine clearance and diabetes in the present study, and, thus, ……..".

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests
Reviewer's report

Title: Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study

Version: 4 Date: 3 February 2010
Reviewer: Matthias Blüher

Reviewer's report:
All my comments have been successfully addressed in the revised version of the manuscript.

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

Quality of written English: Acceptable

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