Author's response to reviews

Title: Ethnic differences in the association between waist-to-height ratio and albumin-creatinine ratio: the observational SUNSET study

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Author's response to reviews:

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Dear dr Chap,

Thank you for the opportunity to revise our paper. We are grateful to the reviewers for their careful evaluation of our manuscript. We have revised our paper according to their suggestions. Below we have specified how each suggestion/comment was addressed. In addition, we have highlighted the textual changes in the revised manuscript.

Kind regards, on behalf of all authors,

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Reviewer 1

Van Valkengoed and co-workers presented interesting observation. They performed study in a large group of subjects, used correct methodology and found some interesting results. The results may have important implication for future clinical practice and research.

REPLY: We appreciate the reviewer’s positive assessment of our work.

Minor Essential Revisions:
There are some inconsistencies present. The authors should check numbers in table 2 describing in results (part with analysis of the association between waist-to-height ratio and the log albumin-creatinine ration).

REPLY: We apologise for these inconsistencies. We have checked the numbers in table 2. The numbers provided in the Table were correct. We have therefore changed the figures in the text to match those in the Table. The change to the text of the results section has been highlighted in yellow.

Discretionary Revisions:
Because of wide range of age of the enrolled subjects sub-analysis of age tertiles would be useful to determine possible statistically significant differences between central obesity and ARC in present ethnic group. These results could help us to define which age tertile of ethnic population is at highest risk for cardiovascular disease.

REPLY: We have checked whether the association differed across age groups, but found no significant interaction by age in the total population and in the separate ethnic groups (e.g. total population p=0.19). Therefore, we have decided not to add tables of the analyses of the smaller subgroups (further stratified by age) to the paper.

Reviewer 2
The study aims to compare the association between waist-to-height ratio and albumin to creatinine ratio (ACR) in different ethnic groups. Hindustani-Surinamese men and women had higher ACR than Dutch men and women. The prevalence of diabetes was higher in Hindustani-Surinamese subjects and the prevalence of hypertension was higher in Hindustani-Surinamese women. Type 2 diabetes and hypertension are wellknown causes of albuminuria and may explain the higher ACR in Hindustani-Surinamese subjects. I think the study should have been performed in subjects without diabetes or hypertension. It is known that this ratio varies with ethnicity and race in the United States. Creatinine excretion is higher in blacks and Mexican Americans than whites and this affects ACR. The authors did not find a significant difference in the association between the association of WHtR to ACR and ethnicity. So it is unclear how the results of this study could have further implications.

REPLY: We thank the reviewer for his critical review of our paper. We have specified how we have addressed the specific points of critique under major and minor compulsory revisions below. The changes to the paper as a result of these point have been highlighted in the text and tables in yellow.

Major Compulsory Revisions
Background. Please change abbreviation for waist-to-height ratio from WTH to
WHtR in order to use uniform abbreviations among studies. There is a published review that recommends using WHtR as a standard abbreviation. Please refer the following paper:

REPLY: As requested, we have changed the abbreviation from WTH to WHtR throughout the paper. In addition we have added the paper to the reference list.

Provide Company, site of production (city and country) for SECA mechanical scale and OMRON M4 sphygmomanometer.

REPLY: We have added the following information to the text:
- Omron Healthcare Europe BV, Hoofddorp, the Netherlands
- SECA gmbh & co, Hamburg, Germany

What is the meaning of “In” the last paragraph of Data Collection?
REPLY: We have changed this to ‘Indianapolis, IN’.

The name of the autoanalayzer was not provided for fasting glucose and urinary albumin and creatinine assays.
The name of the kits was not provided for urinary albumin and creatinine assays.

REPLY: The measurements were carried out at the Laboratory of Clinical Chemistry of the Academic Medical Center. We have specified this in the methods. In addition, we have added the information on the methods, as provided to us by the laboratory.

RESULTS: Characteristics of the study population: Dutch men and women had the lowest mean BMI. Where was the mean BMI presented? I do not see any BMI in the first column of Table 1.

REPLY: We thank the reviewer for pointing out this important omission. We have corrected this mistake: the mean BMI was added to Table 1.

RESULTS: Mean waist to height ratio and albumin-creatinine ratio:
Hindustani-Surinamese men had the highest median ACR of 0.36 (0.20-0.91), followed by the African-Surinamese 0.26 (0.16-0.46) and the Dutch 0.24 (0.16-0.45) mg/mmol (Table 1). I do not see these numbers in Table 1. A p value was not provided. Statistical significance cannot be determined from reading the test. I infer from the manuscript that an ANOVA test was performed on logACR
levels. The mean LogACR was not provided in table. The median ACR was provided in the text and that is fine and should not be deleted. The results of the post-hoc test were not provided. So the readers and I will not be able to understand which pair of logACR levels will be different. The results are not clearly presented. The reader should not make any assumptions or inferences to reach any conclusions.

REPLY: We agree with the reviewer that post hoc tests may contribute importantly to the interpretation of the results. We have therefore added post hoc tests (Hindustani Surinamese vs. Dutch and African-Surinamese vs. Dutch) as requested.

We suspect that the point concerning 'mean logACR not provided' may perhaps have been related to a print error (see point about A4 printing below), as the median ACR, percentage albuminuria and mean log ACR were given in the last 3 rows of Table 1. We had also indicated in the footnote that “Bold= difference between ethnic groups p#0.05”.

As the reviewer indicates, differences in the mean log ACR were indeed evaluated by performing an ANOVA test. This was specified in the Methods section. We have now further clarified this in the footnote under the table.

RESULTS: Mean waist to height ratio and albumin-creatinine ratio: The prevalence of albuminuria was lowest among the African-Surinamese. I do not see the frequency of normoalbuminuria, microalbuminuria and macroalbuminuria in men and women from the three different ethnic groups under study. The result of a chi-square test is not provided to support the conclusion of “The prevalence of albuminuria was lowest among the African-Surinamese.”

REPLY: Statistical differences were indicated by bold highlights in the table. We have now clarified the tests used in the footnote, and have added information on post-hoc tests. Moreover, we corrected the text to indicate that among men there was not statistical difference in albuminuria between groups (the difference was found among women only).

Due to the low numbers, persons with microalbuminuria (total n in all groups combined=60) and macroalbuminuria (total n in all groups combined =22) were grouped together. This was indicated in the footnote underneath the table. We have now also specified this in the Methods section.

RESULTS Association between waist-to-height ratio and logACR: In the total population, the logACR increased by 0.353 (0.272-0.435) for every 0.1-point increase in the WTH (Table 2). I do not see this number in table 2; instead the unadjusted correlation was given as 0.359. Please provide clarification for differences in correlation in the text 0.353 and 0.364 and in table 2. No clarification is needed for table 3.

REPLY: The numbers in Table 2 were accurate. We have made the appropriate
corrections in the text.

DISCUSSION Association WTH and logACR: However, the results are in contrast another study that reported no association between the waist circumference and microalbuminuria among South Asian origin subjects with type 2 diabetes in India [25].

The authors performed a study on diabetic and nondiabetic subjects but reference 25 was performed only in diabetic subjects. These two studies are not comparable. I also looked into reference 25 and I could not see a correlation coefficient between waist circumference and ACR.

REPLY: Unnikrishnan et al. described the univariate association between the presence of microalbuminuria and the waist circumference: in Table 2 the authors report a Waist circumference (cm) among Normoalbuminuria 90 ±10; Microalbuminuria 91 ±10; Overt nephropathy 89 ± 14, with a p-value for trend of 0.864. We have clarified in the text that the authors reported the univariate association only.

We agree with the reviewer that our study population may not be completely comparable to the population in that study, as we have also included persons without diabetes. We have clarified this in the discussion.

REFERENCES: References were given as a mixture of full journal names and abbreviated journal names. Please use a uniform style.

REPLY: We have changed all journal names to the abbreviated version.

Table 1. The log ACR was not given,

REPLY: The mean log ACR was given in the last row of Table 1. We have now highlighted the label in bold.

Table 1 BMI is missing.

REPLY: BMI was indeed removed between the previous and the final version of the paper. This was corrected (also see point above).

Table 1 A post-hoc test was not given so I cannot ascertain which two groups are different from each other, indicate different groups with superscript letters.

REPLY: The reviewer raises an important point. We have therefore added post-hoc tests to Table 1.

SUPPLEMENT: 2nd column 7th row; I believe it should be WHtR

REPLY: Thank you for pointing this out. This was corrected.
Minor Essential Revisions

Background - 4th paragraph, 1st sentence: change to between waist-to-height ratio and the ACR

REPLY: We have added ‘and’ between ratio and the.

METHODS Data Collection: add comma: Before the physical examination,
METHODS Data Collection: change veryfief to verified
METHODS Data Collection: Put a dot after physical examination.
METHODS Response and participation: Addresses/km². 2 should be superscript.

REPLY: We apologise for these errors. We have corrected the text, as indicated.

METHODS Statistical analysis: As far as I remember SAS Institute Inc. is located in Cary, North Carolina

REPLY: We have changed ‘Cary, USA’ to ‘Cary, NC’.

DISCUSSION Association WTH and logACR: Please remove the extra parenthesis at [[16-17, 26-27].

REPLY: The redundant ‘[’ was removed.

Please correct reference 7.
Reference 11: Add comma after Froelich M,
Reference 13: space is missing in VishwanathaJK
Reference 22: Correct as Annals of Internal Medicine or its correct abbreviated form.
Reference 34. The name of the paper is not in bold style.

REPLY: We have made the appropriate corrections to the references.

Table 1 is misaligned. The rows for education is not aligned properly, please correct it. Also it did not fit to A4 paper when I printed it.

REPLY: The extra spaces were removed. Unfortunately we cannot explain why the document would not print on A4 paper. We have checked the settings of the document, these were: A4 with 2.5 cm. margins.

Table 2. Please change Sexe to Sex

REPLY: This was corrected.

Figure 1 is very similar to Figure 1 of reference 20. Reference 20 can be cited in
the legend of the figure or in the text.

REPLY: We have added the following text to the figure legend: The inclusion in SUNSET was reported previously [21].