Author's response to reviews

Title: Association of Health Behaviour with Heart Rate Variability: A Population-Based Study

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Author's response to reviews: see over
Dear Editor,

thank you very much for the invitation to resubmit a revised version of our manuscript.

We carefully considered the reviewer’s comments, responded to each suggestion in a separate authors’ reply to the reviewer (see below), and revised the manuscript accordingly.

We would be grateful if the editors could consider our revised manuscript for publication.

Thank you very much for your efforts.
Sincerely,

Alexander Kluttig (corresponding author)
Authors’ Reply to the reviewer’s and editor comments
(We cite the original reviewer’s comments in italics and numbered the individual
comments or questions consecutively. Authors’ responses are given after each
respective question / comment.)

Authors’ reply, general:
We thank the reviewer for the careful and thoughtful reading of our manuscript and
for the valuable comments, which help us further improve the quality of the
manuscript.

Reviewer 1:
- Please adjust in your analyses for age, sex, use of cv-medication (at least for
betablockers), prevalent disease (MI/ stroke/ CVD/ hypertension/ DM).

Authors’ Response:
In our analyses we identified potential confounders for adjustment based on directed
acyclic graphs (DAG) taking into account a priori assumptions about causal relations
among variables of interest in the source population. According to the resulting DAG,
only age had to be adjusted for in the analysis of the association of health behaviour
with HRV. However, especially in cross sectional studies as our study a clear
temporal classification of cause and effect is difficult. For example, in our cross
sectional design we cannot distinguish whether physical inactivity leads to diabetes
or vice versa. We therefore have undertaken analyses in healthy subgroups and
additionally have calculated models with adjustment for further potential confounders,
such as CVD, diabetes mellitus, heart rate, education, hypertension, body mass
index, beta blockers, ACE inhibitors, diuretic, calcium channel blockers, and anti-
arrhythmic agents, but we had not mentioned the results of these sensitivity analyses
in our manuscript yet since results were without relevant change compared to the
age adjusted models. However, we now have included a paragraph regarding these
results of the multivariate adjusted models (sensitivity analyses).

- Please move Supplemental table1 to the manuscript, Figure1 can be deleted,
Figures 2 and 3 should be designed less confusing (may be in table-format).

Authors’ Response:
We moved all three tables to the manuscript file as it was originally intended.
However, because we originally uploaded the tables files separately, these tables
were presented as supplemental tables by mistake. We have reformatted the Figures
2 and 3 in a table-format as suggest by the reviewer. Regarding Figure 1, we believe
that this figure is important for readers to understand the concept of a priori
identification of potential confounders by DAGs. We therefore want to keep that figure
in the manuscript.

Reviewer 2:
- Beside beta-blockers other drugs like digitalis, calcium antagonists and ivabradine
influence heart rate. Were the different subgroups of the study matched for these
drugs?

Authors’ Response:
In our primary analyses only age had to be adjusted for in the analysis of the association of health behaviour with HRV. However, as stated above (see statement to reviewer 1 comments) we have now added a paragraph in which we present the results of multifactorial adjusted models, including further drugs influencing heart rate (beta-blockers, ACE inhibitors, diuretic, calcium channel blockers and antiarrhythmic agents including digitalis). Because Ivabradine was approved in Germany in 2006 when our baseline investigation was already finished this drug is irrelevant for our analyses.

**Editorial comments:**
Please add a statement to the manuscript stating that participants consented to take part in the study. Manuscripts may be rejected if the editorial office considers that the research has not been carried out within an ethical framework, e.g. if the severity of the experimental procedure is not justified by the value of the knowledge gained.

**Authors’ Response:**
We added a statement to the manuscript stating that all participants were informed about the study and their written consents were obtained.

*We recommend that you copyedit the paper to improve the style of written English.*

**Authors’ Response:**
The manuscript has been updated linguistically by a professional copyediting service (International Science Editing).

*Please also highlight (with ‘tracked changes’/coloured/underlines/highlighted text) all changes made when revising the manuscript to make it easier for the Editors to give you a prompt decision on your manuscript.*

**Authors’ Response:**
All changes compared to previous version were highlighted.

*Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals).*

**Authors’ Response:**
We checked the revised manuscript regarding the journal style.