

Dr Rubin Minhas  
BMJ Associate Editor

14<sup>th</sup> January 2017

**Re: BMJ.2016.035517 entitled "Active commuting is associated with lower risk of cardiovascular events: Evidence from a prospective cohort study of 264,337 UK Biobank participants"**

Dear Dr Minhas

We would like to thank the Editors and the Reviewers for their efforts in assessing the suitability of this manuscript for publication in The BMJ and the very helpful suggestions which have helped us to improve this paper. We are pleased that the Editors and Reviewers were supportive of this work and we have considered their comments carefully in revising the manuscript. We feel that our revised manuscript fully addresses the Editors' and Reviewers' concerns has been substantially improved, particularly by reporting commuting data for walking and cycling separately; by including data for mixed-mode commuting; and by exploring the dose-response relationship between walking and cycling commuting distance and health outcomes. In response to a comment from Reviewer 2, we have changed the paper title to "Association between active commuting (walking and cycling) and incident cardiovascular disease, cancer and mortality: Prospective cohort study of 264,337 UK Biobank participants". Our responses to the Editors' and Reviewers' comments are **outlined in red** below and changes to the text of the manuscript are also highlighted in red.

Thank you for your time in considering this paper for publication in The BMJ and we look forward to hearing your final decision in due course.

Yours sincerely



Dr Jason Gill and Dr Carlos Celis-Morales, on behalf of the authors

**The University of  
Glasgow Charity Number  
SC004401**

**Dr Jason Gill**

Reader

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Supported by



**Author responses in red.**

Dear Dr. Celis-Morales

Manuscript ID BMJ.2016.035517 entitled "Active commuting is associated with lower risk of cardiovascular events: Evidence from a prospective cohort study of 264,337 UK Biobank participants"

Thank you for giving us the opportunity to consider this paper, which we discussed at our editorial meeting \*\*\*. We are pleased to make a provisional offer of publication if you are able to revise it to address the points made by the referees and the editors. The referees' comments are available at the end of this letter, and the points raised by the editors are set out below.

We hope that you will be able to revise the paper and send it back to us within one month. When you resubmit, could you kindly ensure that you provide:

(a) A covering letter outlining how you have responded, or not responded and why, to both the referees comments and those of the editors.

**Author response: Thank you. Our point-by-point responses are outlined below.**

(b) A word count (excluding the references and words in boxes and tables). You should aim to keep this count below or very close to 2000 words.

**Author response: Thank you. We have now reduced the word count to 2086 words.**

(c) Please check that all the information required in the manuscript (see note below) is included in the revised manuscript.

**Author response: Thank you. We have checked and believe that we have provided all of the required materials with the original submission.**

To revise your manuscript, log into <https://mc.manuscriptcentral.com/bmj> and enter your Author Center, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision.

We hope that you will be able to revise the paper and send it back to us within one month.\*\* All accepted Analysis articles are published on thebmj.com, the canonical version of the journal. Please note that only a proportion of accepted Analysis articles will also be published in print. \*\*

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Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

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**IMPORTANT:** Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

I hope you will find the comments useful.

Best wishes

Yours sincerely

Rubin Minhas  
Dr Rubin Minhas  
BMJ Associate Editor  
[rm1000@live.com](mailto:rm1000@live.com)

Manuscript Meeting

Chair: Wim Weber

Doug Altman, John Fletcher, Joe Freer, Georg Roeggla, Rubin Minhas

1. Some people may have retired - were these people included or how were they dealt with?

**Author response:** Thank you for raising this important point. We only included participants in excluded participants who were in paid employment or self-employed who did not always work at home in our data. Thus, participants who had retired were excluded. We have now clarified this in the methods (lines 83-84).

2. It would be desirable to see data for walking and cycling separately, and also to see journey time analysed if this is not overly onerous.

**Author response:** Thank you for this very helpful suggestion. We have now reported data for walking and cycling separately, as well as data for mixed-mode commuting with a cycling or walking component. We have altered the methods (lines 110-117) and results (lines 151-176), and Table 1 and Figures 1-3 to reflect this change. We have also commented on this in the discussion (lines 179-208 and 221-225). This new analysis did reveal insights into differences between cycling and walking for some outcomes, with only cycle commuting, or mixed-mode commuting with a cycling component associated with lower risk of all-cause mortality and cancer outcomes, but both walking and cycling associated with lower risk of CVD outcomes. We are grateful to the reviewers and editors for requesting this change, which we feel has improved the paper's novelty and messaging.

We don't have data on time spent commuting. However we do have data on commuting distance and the number of times per week individuals commuted to work. From this we derived a weekly commuting distance variable and have analysed data by commuting distance. We have now reported this in the methods (lines 115-117) and results (lines 174-176), Figures 2-3, and in the

discussion (lines 181 and 194-196). These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was appeared a dose-response relationship with those with greater commuting distances having even lower risks of adverse outcomes compared those commuting lower distances.

3. Adjustment for leisure time activity preferable to sedentary behaviour.

**Author response:** Thank you. We have now adjusted the findings for time spent walking for pleasure, time spent undertaking strenuous sport, and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour). We have revised the methods (lines 134-139) and the legends to tables and figures accordingly. These adjustments did not materially change the findings.

4. The term "cancer event" is undefined and unfamiliar to cancer methodologists.

**Author response:** Thank you. We have now replaced the term 'cancer event' with 'cancer incidence'.

5. Need to be wary of saying no association when they mean no significant association.

**Author response:** Thank you. We have amended the text accordingly (lines 158-176).

6. What are the policy implications of this?

**Author response:** Thank you for this helpful suggestion, we have added the policy implications in the discussion section (Lines 184-187, 205-208 and 223-225). The statements included in the text are as follows:

Lines 184-187: "These results are important, because daily active commuting is an important contributor to total physical activity,<sup>3-6</sup> and thus facilitating active commuting, particularly cycle commuting, may be a viable approach to deliver physical activity-related health benefits at the population level."

Lines 205-208: This has important policy implications, suggesting that policies designed to affect a population-level modal shift to more active modes of commuting, particularly cycle commuting (for example cycle lanes, city bike hire and subsidised cycle purchase schemes, increasing provision for cycles on public transport), present major opportunities for public health improvement."

Lines 223-225: "The findings suggest population health may be improved by policies that increase active commuting, particularly cycle commuting, such as cycle lanes, hire/purchase schemes, and better provision for cycles on public transport."

Decision:

Put points

INFORMATION TO INCLUDE IN REVISION

Please would you also check that you have provided the following information

\* Competing interest statement (in the style explained at <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests>)

\* Contributorship statement + guarantor

(see <http://resources.bmj.com/bmj/authors/article-submission/authorship-contributorship>)

\* Copyright statement/ licence for publication (see <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse>)

\* Signed patient consent form(s), if the article gives enough personal information about any patient(s): - (see [http://resources.bmj.com/bmj/authors/editorial-policies/copy\\_of\\_patient-confidentiality](http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality))

**Author response:** Thank you. We included all relevant information in this with the original submission.

Reviewer(s)' Comments to Author:

## Reviewer: 1

Recommendation:

Comments:

Reviewer: Lars Bo Andersen

1. This study analyze a unique database from the UK Biobank with more than 250,000 participants. As such sthe study is unique. The study analyses all cause mortality and CVD and cancer specific mortality beside incidents of cancer and CVD. It is also a strength that they can analyze data with a short follow-up time making misclassification caused by changes in exposure during follow-up minimal. I consider this study very strong. However, there are also a number of limitations in the analysis. Many studies have confirmed that the benefit of cycling is substantial bigger compared to walking and with this huge database authors have sufficient statistical power to present the two active commuting modes separately. Also, I don't quite understand why they claim that mixed mode transport such as walking and public transport cannot be analyzed, because it was done in the article of Flint and Cummings based on UK Biobank published earlier this year in Lancet Diab Endocrinol.

**Author response:** Thank you for this very helpful comment. We have now reported data for walking and cycling separately, as well as data for mixed-mode commuting with a cycling or walking component. We have altered the methods (lines 110-117) and results (lines 151-176), and Table 1 and Figures 1-3 to reflect this change. We have also commented on this in the discussion (lines 179-225) This new analysis did reveal insights into differences between cycling and walking for some outcomes, with only cycle commuting, or mixed-mode commuting with a cycling component associated with lower risk of all-cause mortality and cancer outcomes, but both walking and cycling associated with lower risk of CVD outcomes. We are therefore very grateful to the reviewer for requesting this change, which we feel has substantially improved the paper.

Minor comments

2. I think the models should be adjusted for leisure-time physical activity rather than sedentary behavior or both (there is usually not co-linearity).

**Author response:** We have now adjusted the findings for time spent walking for pleasure, time spent undertaking strenuous sport, and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour) (lines 134-139). This does not change the findings.

3. It would be interesting to see how distance in people commuting to work relates to outcomes and correlates. You must have distance because you have residence and work addresses.

**Author response:** Thank you for this helpful comment. We used data on commuting distance and the number of times per week individuals commuted to work to derive a weekly commuting distance variable and have analysed data by commuting distance. We have now reported this in the methods (lines 115-117) and results (lines 174-176), and Figures 2-3, and in the discussion (lines 181 and 194-196). These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was a dose-response relationship with those with greater commuting distances experiencing a greater risk reduction.

4. How many had accelerometer measurements? Can a sensitivity analysis be done using only these and with adjustment for PA? How close was the association between objectively assessed PA and the different self-reported PA domains?

**Author response:** Thank you for this comment. Accelerometer data were available for 54,378 of the participants who had active commuting data. When we consider the subset of participants with accelerometer data (~20% of all participants with commuting data), there were too few events for us to obtain robust outputs from the outcome models. We have now included Supplementary Tables showing the differences in self-reported (Supplementary Table 1) and objectively-measured (Supplementary Table 2) total physical activity according to commuting mode. For both objective and self-report methods, there was agreement that physical activity was highest in cycle commuters, next highest in mixed-mode: cycling commuters, and next highest in walking commuters, with little difference between mixed mode: walking commuters and non-active commuters. The correlation between self-reported total physical activity and objectively measured PA was  $r = 0.18$ , which is broadly in line with other reports of the strength of association between self-report and objective physical activity methods (e.g. Sabia et al. (2014) *Am J Epidemiol.* 179:781-90).

We feel it does add value to the manuscript to include these baseline accelerometer data, to more robustly show differences in overall physical activity by commuting mode compared to self-report. However, as we cannot use these data with respect to our main outcome measures, we would equally be prepared to remove the accelerometer data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 118-126), but are happy to be guided by the editors on this issue.

5. CRF was assessed in >75,000 participants. This is a large sample and could be analysed according to active transport.

**Author response:** Thank you for this suggestion. We are in a similar position to the accelerometer data here. CRF data were available in 76,519 participants overall, but only in 39,022 participants who were included in our active commuting data set. We have now clarified this in the methods

(lines 118-126). When we consider this subset of participants, there were once again too few events to run the outcome models, similar to scenario with accelerometer physical activity data. Again we do feel that it adds value to the manuscript to show baseline differences in CRF by commuting mode (Supplementary Table 3), even though we cannot use these data in our analyses of the main outcomes. However, as for the accelerometer data, we would equally be prepared to remove the CRF data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 118-126), but are happy to be guided by the editors on this issue.

6. You adjusted models for BMI. Did you adjust for BMI as a categorical variable? BMI and all-cause mortality is U-shaped.

**Author response:** Thank you. Yes we considered BMI as a categorical variable in our adjustment. We have now clarified this in the methods (lines 135-136).

7. You wrote: The models for CVD events and CVD mortality were run excluding participants with a history of myocardial infarction, angina or stroke at baseline; similarly models for cancer were run excluding participants with a cancer diagnosed at baseline. I believe models of all-cause mortality should be with exclusion of all with chronic disease at baseline, because disease could be related to exposure and it is definitely related to mortality. It could be questioned if participants with diseases where an association with transport mode should not be expected, could be included and then adjust for the condition (such as hypertension and T2D without serious complications).

**Author response:** Thank you for this helpful comment. We have now excluded participants with cancer and CVD at baseline from the all-cause mortality models. Models for CVD outcomes exclude CVD at baseline and models for cancer outcomes exclude cancer at baseline. All models adjust for hypertension, diabetes and long-standing illness. This is described on lines 129-133.

8. It is surprising that more women use active transport. My guess is that this is only the case for walking and not cycling. If there is interaction here, you need to make the analysis stratified on transport mode. I would also like to see if difference in parameters such as fitness differ between cycling and walking.

**Author response:** Thank you. We have now stratified active commuting into walking, cycling and mixed modes including cycling and walking. In this dataset more women than men commuted by both cycling and walking. In the subset of participants for whom fitness data was available, cyclists were fitter than the walkers (Supplementary Table 3). These data are presented in Table 1 and results (line 151-154) and we have now commented on this in the discussion (lines 188-192).

Page 11, line 39. The 30% decrease is supported by Waththews et al 2007. The review by Oja et al 2011 also supported both the relationship with all cause-, CVD, and cancer mortality. Again, it's a guess because you haven't presented data, but if you analyze cycling and walking separately, you may find support for an association for cycling where you found nothing for total active transport. Your results are not in disagreement with Matthews et al, where no association was found for walking but a clear benefit for cycling.

**Author response:** Thank you for this helpful comment. We have now presented data for cycling and walking (and mixed modes) separately as suggested and indeed, our findings are findings are in line

with Matthews et al (2007). We have revised the discussion substantially to reflect these new analyses accordingly (lines 197-208 and 221-225).

9. Page 12, top. The meta-analysis had heterogeneous outcomes, but this was in my view not the main problem. It was rather the exposures where environments differed from study to study, which means that the proportion of cyclists compared with walkers differed.

**Author response:** Thank you for this helpful comment. We have now commented on this in the introduction where we first refer to this study (lines 69-70). In the revised discussion, which we needed to shorten to comply with the editors' suggestion to reduce the paper's overall length, we no longer make this specific comment about this paper.

10. Page 12, line 51. The association between transport mode and SES in the referenced study (by me) was relevant in the early 1980s where baseline measurements were done. Today it is reversed, so higher SES is more likely to cycle (and walk). The higher prevalence of active transport in low SES groups in UK is more likely caused by lack of infra structure and promotion of especially cycling. It is not comparable to Denmark. It is not wrong to cite the Danish study, but it has clearly been shown in Denmark that the key determinant of cycling is not SES. Cycling has increased 50% in Copenhagen since 1998 and it is mainly high SES individuals who have changed habits.

**Author response:** Thank you. This is another very helpful comment. In light of a comment from reviewer 2 and the editors' request for us to shorten the paper to as close to 2000 words as possible, we have now removed this paragraph from the manuscript.

Additional Questions:

Please enter your name: Lars Bo Andersen

Job Title: professor

Institution: Sogn and Fjordane University College

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests> (please see BMJ policy) please declare them here: none

## Reviewer: 2

Recommendation:

Comments:

Thank you for the opportunity to review this manuscript which explored the temporal associations between active commuting and CVD events, CVD mortality, cancer events, cancer mortality and all-cause mortality. The findings revealed that active commuters were less likely to have a CVD event or die from CVD. The manuscript further explored socio demographic correlates of active commuting. As the authors note, this study is strengthened by its very large, representative sample, the fact that it controlled for a wide range of potential confounders and that it explored cancer and CVD (both events and mortality).

There are a number of limitations of this research however that I feel the authors don't adequately discuss. The first is the crude measure of active commuting. Previous work in the field is strengthened by the fact that the measure of exposure tends to be minutes spent in active commuting in a typical or past week. Not only do such measures provide a more accurate measure of exposure they are important for establishing whether there is a dose-response relationship (consistent with Hill's Criteria). Further, the measure did not allow for multi-modal journeys to be detected. As the authors allude to briefly in the discussion, because someone selects public transport or car as their 'main' mode of transport does not mean it is their only mode of transport. In fact, they may have accrued substantial and meaningful walking or cycling as part of their journey but because the total distance travelled is great, it was not the main mode of 'transport' used. I realise this limitation cannot be addressed easily but it should be clearly outlined as an important limitation of the research.

**Author response:** Thank you for making this very important point. We have now included mixed-mode commuting with a cycling component and mixed-mode commuting with a walking component in our analysis (as presented in Table 1) and have now reported this in methods (lines 110-117) and results (lines 151-176), Table 1 Figures 1-3 and commented on this in the discussion (179-225). We found that mixed-mode commuting with a cycling component was associated with lower risk of all-cause mortality and cancer outcomes. We have also used data on commuting distance and the number of times per week individuals commuted to work to derive a weekly commuting distance variable and have analysed data by weekly commuting distance in those who reported active commuting. These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was a dose-response relationship with those with greater commuting distances experiencing a greater risk reduction. This is now reported in the methods (lines 115-117) and results (lines 174-176), and Figures 2-3, and in the discussion (lines 181 and 194-196).

We were not able to use this weekly commuting distance variable in those reporting mixed-mode commuting as it was not possible to determine how much of the journey was undertaken using active transport, and have acknowledged this as a limitation in the discussion (Lines 216-217).

To my mind the second major limitation of this research is that analyses did not control for total or leisure time physical activity nor fitness. It is therefore highly possible that the associations that are seen reflect the fact that active commuters participate in greater overall physical activity (as the authors found). Controlling for other non-commuting PA is crucial for determining the specific impact that active commuting has on health. This should be addressed by the authors.

Because of these substantial limitations I think the authors need to temper their statement in which they write 'provides the most robust assessment of the association between active commuting and CVD outcomes'.

**Author response:** Thank you. This is another important point. We have now adjusted the findings for time spent walking for pleasure, time spent undertaking strenuous sport, and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour) (lines 134-139). This differential adjustment does not change the findings. We did not feel it appropriate to adjust for total physical activity, due to its collinearity with our main exposure variable. We are also unsure how we would interpret a finding of whether commuting mode was independent of total self-reported physical activity or not, as differences in the way that the questions for commuting mode and total physical activity were asked in UK Biobank does not exclude the potential for residual confounding in this analysis.

Fitness data were available in 76,519 participants overall, but only in 39,022 participants who were included in our active commuting data set. We have now clarified this in the methods (lines 118-126). When we consider this subset of participants, there were too few events to run the outcome models. We feel that these data add value to the manuscript to show at baseline cycling commuters had higher fitness than non-active commuters, even though we cannot use these data in our analyses of the main outcomes. However, we would equally be prepared to remove the CRF data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 118-126), but are happy to be guided by the editors on this issue.

A couple of other suggestions (observations):

The secondary aim to identify correlates of active commuting seems like an afterthought. No information is provided in the introduction and the method section seems focused on the first research question (no mention is made in the statistical analyses section and therefore the methods used to derive at the Figure are not clear). It is not clear why the papers focuses on two distinct research questions. Could the authors please revise the manuscript so that the exploration of socio-demographic and health correlates becomes a more legitimate focus, or alternatively remove it from the manuscript?

**Author response:** We felt that it was of value to try to understand correlates of active commuting to help characterising the profile of those who are active commuters. However, in light of your comment that this could be removed from the manuscript and the editors' direction that we should try to cut to manuscript to as close to 2000 words as possible, we have decided to remove this aspect of the work from the manuscript. If the editors and reviewer feel strongly that this aspect of the work should be retained and explored further, please let us know and we would be happy to reconsider, but this would be difficult to do within the newly imposed word limit.

I don't think the title accurately reflects the study. A mentioned aim was to explore the associations with cancer and this should be alluded to (whether the findings were significant or not).

**Author response:** Thank you. We have now amended that title as follows "Association between active commuting (walking and cycling) and incident cardiovascular disease, cancer and mortality: Prospective cohort study of 264,337 UK Biobank participants"

A possible explanation for the null findings that the authors did not allude to has been discussed in previous studies. That is, that in contrast to countries like China and Denmark with high rates of active travel (and where positive associations are often reported), the population levels of active commuting in England are not done at a level sufficient to provide health benefit. Given the crude measure of active commuting used, this could not be explored but it is a legitimate explanation.

**Author response:** Thank you for this thoughtful comment. We have now analysed the data in more detail – considering cycling and walking separately, as well as considering mixed-mode commuting – in response to your earlier comments and the comments of the other reviewers. When we do this, we do see beneficial associations between cycle commuting and all of our outcome measures, and beneficial associations for walking commuting and CVD outcomes. Beneficial associations were also seen for mixed-mode commuting including a cycling component for all cause-mortality and cancer outcomes. These findings are shown in the results (lines 158-173), and Figures 1-3 and we have commented on this in the discussion on lines 179-208. We thank the reviewers for their helpful comments which encouraged us to analyse our data in this way.

#### Minor comments

In the Discussion the authors write that 'because daily active commuting could be an important contributor to physical activity'. Much research exists to suggest that this more an 'is' than a 'could' and this evidence should be referenced.

**Author response:** Thank you, we have made this change and added appropriate references to support this (lines 184-185 and 188-190).

The authors also write that, 'For people with longer commutes.....'. This assertion does not seem appropriate in the context of these findings given that these people would be categorized as traveling by car and therefore, based on the data, not at a reduced risk of CVD.

**Author response:** Thank you, this is another helpful comment. We have now considered mixed-mode commuting, in response to your earlier comment. We found that mixed-mode commuting with a cycling component was associated with lower risk of all-cause mortality, CVD and cancer outcomes. We have also used data on commuting distance and the number of times per week individuals commuted to work to derive a weekly commuting distance variable and have analysed data by weekly commuting distance in those who reported active commuting. These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was a dose-response relationship with those with greater commuting distances experiencing a greater risk reduction. This new analysis has been reported in the methods (110-117), results (lines 158-176), Figures 1-3 and in the discussion (lines 179-208). The specific sentence that the reviewer refers to has been removed from the revised manuscript.

There appears to be a typo on line 52 in the Introduction

**Author response:** Thank you. We have now amended this.

Reviewer Name: Dr Shannon Sahlqvist

Additional Questions:

Please enter your name: Shannon Sahlqvist

Job Title: Lecturer

Institution: Institute for Physical Activity and Nutrition (IPAN), Deakin University

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests [http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='\\_new'](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new') (please see BMJ policy) [please declare them here](#): None declared

## Reviewer: 3

Recommendation:

Comments:

MS ID: BMJ.2016.035517

Title: Active commuting is associated with lower risk of cardiovascular events: Evidence from a prospective cohort study of 264,337 UK Biobank participants.

Thank you for the opportunity to review this interesting manuscript. In this paper, the authors have explored prospective data to examine the relationship between active commuting and incident

cardiovascular disease, cancer and all-cause mortality in adulthood. The authors have used data from the UK Biobank.

The use of prospective data to explore the possible relationship between active commuting and health outcomes is to be welcomed, and on the whole I believe this paper adds to the current evidence to explain why active commuting is associated with lower risk of cardiovascular outcomes. I do however have a few suggestions for the authors to improve this paper, and these are presented below.

#### Introduction

1) A strong case is made for considering the association of active commuting on the risk of health outcomes, independent of major potential confounders. I would however expect to see further explanation as to whether the association is modified by other domains of physical activity (leisure time, occupational and household) or cardiorespiratory fitness. I think the authors want to say something like ..... Active commuting contributes to overall physical activity levels thus might make an important contribution to the health benefit attributed to physical activity.

**Author response:** This is a very helpful comment, which has also been raised by the other reviewers. We have now adjusted the findings for time spent walking for pleasure, time spent undertaking strenuous sport, and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour) (lines 134-139). This did not affect the findings. Our data show that active commuters had higher levels of total physical activity than non-active commuters (Supplementary Tables 1 and 2). However we did not feel it appropriate to adjust for total physical activity, due to its collinearity with our main exposure variable. We are also unsure how we would interpret a finding of whether commuting mode was independent of total self-reported physical activity or not, as differences in the way that the questions for commuting mode and total physical activity were asked in UK Biobank does not exclude the potential for residual confounding in this analysis. We have now commented in the discussion (lines 184-187) that “These results are important, because daily active commuting is an important contributor to total physical activity,<sup>3-6</sup> and thus facilitating active commuting, particularly cycle commuting, may be a viable approach to deliver physical activity-related health benefits at the population level”.

Fitness data were available in 76,519 participants overall, but only in 39,022 participants who were included in our active commuting data set. We have now clarified this in the methods (lines 121-126). When we consider this subset of participants, there were too few events to run the outcome models. We have now mentioned this as a limitation in the discussion (lines 218-219). We feel that these data add value to the manuscript to show at baseline cycling commuters had higher fitness than non-active commuters, even though we cannot use these data in our analyses of the main outcomes. However, we would equally be prepared to remove the CRF data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 121-126), but are happy to be guided by the editors on this issue.

#### Methods

2) How exactly was the active commuting questionnaire validated – please provide more detail. Was it validated with objective measurement?

**Author response:** Active commuting was assessed by participant’s response to the following question: “In a typical day, what types of transport do you use to get to and from work?”. Four

possible answers were provided: a) car/motor vehicle; b) walk; c) public transport; and d) cycle, and participants could select one or more options. This was used to derive the following five commuting categories: 1) Non-active (car/motor vehicle and/or public transport only); 2) Cycling (cycling only and cycling plus walking); 3) Walking (walking only); 4) Mixed-mode: Cycling (Non-active plus cycling only, and Non-active plus cycling plus walking); 5) Mixed-mode: Walking (Non-active plus walking). For categories 2 and 3, a weekly commuting distance variable was derived from self-reported one-way commuting distance and the number of commuting round trips per week. Participants were then divided according to median values into groups with long and short weekly commuting distances for their commuting mode. This is a similar approach to that used as in other papers using UK Biobank to investigate other health outcomes, such as obesity (e.g. Flint et al 2016, *Lancet Diabetes-Endocrinol*, 4:420-435), except we used fewer categories to ensure sufficient power to detect differences in dichotomous endpoints. This has now been described in more detail in the methods (lines 110-117).

3) Please clarify if the measure of self-report physical activity is confined to leisure activities only and not work. One limitation of using a self-reported questionnaire is that reliability and validity may change as the population become better educated about the benefits of physical activity, a wide range of ages, and social desirability influences their responses.

**Author response:** In the original manuscript we reported total physical activity, as assessed by the short-form IPAQ, in Table 1, which did not distinguish between domains of physical activity. We did not adjust our findings for this due to collinearity with activity undertaken whilst commuting. We have now adjusted the findings for time spent walking for pleasure, time spent undertaking strenuous sport, and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour) (lines 134-139). This does not change the findings. This is reported in the methods (lines 134-139), Table 1 and Figures 1-3. We acknowledge the reviewer's comment about limitations self-reported physical activity and have included our inability to adjust for objectively-measured physical activity as a limitation in the discussion (lines 218-219). However, any effects of this on the study outcomes is likely to be relatively modest as for both objective and self-report methods, there was agreement that physical activity was highest in cycle commuters, next highest in mixed-mode: cycling commuters, and next highest in walking commuters, with little difference between mixed mode: walking commuters and non-active commuters (Supplementary Tables 1 and 2).

4) Please describe how many participants are asked to wear an accelerometer for the assessment of physical activity. What is the relationship between subjective and objective measures of physical activity?

**Author response:** Thank you. Accelerometer data were available for 54,378 of the participants who had active commuting data. We have now reported this in Table 1. There was a moderate correlation between accelerometer assessed physical activity ( $\text{milli-gravity}\cdot\text{day}^{-1}$ ) and self-reported total physical activity ( $\text{MET}\cdot\text{h}^{-1}\cdot\text{week}^{-1}$ ), at  $r = 0.18$ . We have now included Supplementary Tables showing the differences in self-reported (Supplementary Table 1) and objectively measured (Supplementary Table 2) total physical activity according to commuting mode and commented on this in the results (lines 151-154). For both objective and self-report methods, there was agreement that physical activity was highest in cycle commuters, next highest in mixed-mode: cycling commuters, and next highest in walking commuters, with little difference between mixed mode: walking commuters and non-active commuters. Thus, the findings on level of physical activity according to commuting group were broadly similar whether physical activity was assessed objectively or by self-report.

5) It is unclear if the mode of travel is the main mode or only mode.

**Author response:** Thank you for making this very important point. We have now included mixed-mode commuting with a cycling component and mixed-mode commuting with a walking component in our analysis and have now reported this in methods (lines 110-117) and results (lines 151-176), Table 1 Figures 1-3 and commented on this in the discussion (line 179-225). We found that mixed-mode commuting with a cycling component was associated with lower risk of all-cause mortality and cancer outcomes.

6) The authors should provide information on whether walking and cycling distance assessed. If this was not possible from the questionnaire, then the authors may like to state this limitation.

**Author response:** This is another very helpful comment: We have now used data on commuting distance and the number of times per week individuals commuted to work to derive a weekly commuting distance variable and have analysed data by weekly commuting distance in those who reported active commuting. These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was a dose-response relationship with those with greater commuting distances experiencing a greater risk reduction. This is now reported in the methods (lines 115-117) and results (lines 174-176) and Figures 2-3, and in the discussion (lines 181 and 194-196). We were not able to use this weekly commuting distance variable in those reporting mixed-mode commuting as it was not possible to determine how much of the journey was undertaken using active transport, and have acknowledged this as a limitation in the discussion (lines 216-217).

7) In the analysis section, the authors indicated that four incremental models were conducted, but only explained three (models 0, 1 and 2). The last one is missing (model 3).

**Author response:** Thank you for this comment. We apologise for this confusion. We presented incremental models to show the effect of sequentially adjusting for different classes of co-variate on the outcome measures. However, in our results and interpretation of the data, we only considered model 2, which was the most adjusted model. Model 3 was similar to model 2 but excluded participants with comorbidities diagnosed at baseline. In practice, additional adjustments did not materially change the results and our data interpretation was all based on the fully-adjusted model. Thus, for clarity, we will now only present data for a single fully-adjusted model. We have clarified in the text (lines 134-139).

8) In the results section, how does controlling for additional variables in the model 3 in Figure 2 and Table S1? Does the model 3 is adjusted for model 2 plus physical activity and cardiorespiratory fitness? If yes, please clarify in details. It is important to know whether active commuting affects the health outcomes exclusively via some major confounder factors or also via physical activity and cardiorespiratory fitness.

**Author response:** Thank you for raising this important issue. As described in the response above, we have now presented a single fully adjusted model. This has been adjusted for the following physical activity-related variables: time spent walking for pleasure, time spent undertaking strenuous sport,

and time spent in light and heavy DIY, level of occupational physical activity and screen-time (as an index of sedentary behaviour) (lines 134-139). This did not affect the findings. We did not feel it appropriate to adjust for total physical activity, due to its collinearity with our main exposure variable. We are also unsure how we would interpret a finding of whether commuting mode was independent of total self-reported physical activity or not, as differences in the way that the questions for commuting mode and total physical activity were asked in UK Biobank does not exclude the potential for residual confounding in this analysis. It is clear from Table 1 that active commuters are more physically active than those who do not commute actively whether total physical activity is assessed by self-report or accelerometer. We have stated in the discussion that daily active commuting is an important contributor to overall physical activity (lines 184-196).

We have fitness data available for only 39,022 participants who were included in our active commuting data set. We have now clarified this in the methods (lines 121-126). When we consider this subset of participants, there were too few events to run the outcome models. We have now mentioned this as a limitation in the discussion (lines 218-219). We feel that these data add value to the manuscript to show at baseline cycling commuters had higher fitness than non-active commuters, even though we cannot use these data in our analyses of the main outcomes. However, we would equally be prepared to remove the CRF data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 121-126), but are happy to be guided by the editors on this issue.

We do note that the commuting groups with the highest levels of total physical activity and cardiorespiratory fitness appear to have the greatest benefits and have commented on this in the discussion (lines 188-196).

9) In Figures 1 and 2, please do not present the same data in both a figure and a table.

**Author response:** Thank you. In the revised manuscript there is no duplication of data in Figures and Tables.

Discussion

10) I would expect the authors to strength the discussion concerning the effects of physical activity and cardiorespiratory fitness on active commuting. Current study did not deal with the two variables in the incremental model, which could contribute importantly to adult's active commuting. If the physical activity and cardiorespiratory fitness have also been adjusted, will the same patterns be observed in Figure 2 and Table S1? The question will be how important the physical activity and fitness are to do with active commuting?

**Author response:** This is a very important point. We are not able to adjust our outcomes for cardiorespiratory fitness for reasons described above and similarly, we do not feel that it is appropriate to adjust for the measures of total physical activity that we have available to us. However, it is clear that the commuting groups with the highest levels of total physical activity and cardiorespiratory fitness appear to have the greatest benefits and have now commented on this in the discussion (lines 188-196).

Additional Questions:

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Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

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## Reviewer: 4

Recommendation:

Comments:

Overall this was a well written, strong study showing solid evidence for the relationship between active travel and CVD. I have a few recommendations and suggestions for clarification.

Abstract: line 26 Theses? These? This?

**Author response:** Thank you for pointing this out. We have corrected this typo.

Introduction: a mention of the relationship of mental health/psych well-being and active travel is worthwhile since stress is associated with CVD risk

**Author response:** Thank you for this very interesting comment.

Methods

Why is public transportation classified as as a non-active travel mode? There is literature supporting it in both directions- provide a rationale why you opted to classify it as non active travel.

**Author response:** Thank you for raising this very important point. We originally only reported participants' main mode of commuting, but in response to comments from all reviewers we have

now included mixed-mode travel including cycling and walking components in our analysis and have now reported this in methods (lines 110-117) and results (lines 151-176), Table 1 Figures 1-3 and commented on this in the discussion (line 179-208 and 221-225). Thus, participants who used non-active and active transport (walking or cycling) in their commute are now classified separately from those only reporting non-active transport. This would capture those who have an active commuting component alongside public transport. We found that mixed-mode commuting with a cycling component was associated with lower risk of all-cause mortality and cancer outcomes, although we did not observe a significant benefit on our outcome measures of mixed-mode commuting including walking. This may reflect the fact that the overall levels of physical activity in these commuters was not substantially higher than non-active commuters. We have now commented on this in the discussion (lines 188-196).

p5 line 8: how was mode of commute assessed? More details are needed. Was the number of trips/week by mode assessed? was it a "most of the time" categorical question?

**Author response:** Thank you for making this very important point. In response to comments from all reviewers, we have refined our data analysis and have now included mixed-mode commuting with a cycling component and mixed-mode commuting with a walking component, as well as non-active commuting, cycling commuting and walking commuting. We have now reported this in methods (lines 110-117) and results (lines 151-176), Table 1, Figures 1-3, and commented on this in the discussion (lines 179-208 and 221-222). This new analysis did reveal insights into differences between cycling and walking for some outcomes, with only cycle commuting, or mixed-mode commuting with a cycling component associated with lower risk of all-cause mortality and cancer outcomes, but both walking and cycling associated with lower risk of CVD outcomes. We found that mixed-mode commuting with a cycling component was associated with lower risk of all-cause mortality and cancer outcomes. This is now reported in the results (lines 158-173), Figure 1, and in the discussion (lines 181-182, 191-196 and 221-222).

We have also now used data on commuting distance and the number of times per week individuals commuted to work to derive a weekly commuting distance variable and have analysed data by weekly commuting distance in those who reported active commuting. These data indicate that for cycle commuting significant dose-response trends were observed between commuting distance and all outcomes, and for walking commuting significant trends were observed between commuting distance and CVD incidence and CVD mortality. In other words, the data show for outcomes where an association was observed between an active commuting mode and the health outcome, there was a dose-response relationship with those with greater commuting distances experiencing a greater risk reduction. This is now reported in the methods (lines 115-117) and results (lines 174-176) and Figures 2-3, and in the discussion (lines 181 and 194-196). We were not able to use this weekly commuting distance variable in those reporting mixed-mode commuting as it was not possible to determine how much of the journey was undertaken using active transport, and have acknowledged this as a limitation in the discussion (lines 216-217).

The inclusion of dietary outcomes was curious. What is the hypothesis behind this? Is there other literature to support investigating this relationship?

**Author response:** Thank you. Dietary intake data was not an outcome measure in this study. We reported dietary data in Table 1, which reported descriptive characteristics of participants, included dietary variables as co-variates in our statistical models, to ensure that any associations we observed

between mode of commuting and our outcome measures were not confounded by differences in diet between the groups. We think adjusting for diet is an additional strength of this study.

Sedentary behavior is mentioned in the results- was this captured in the IPAQ or the accelerometer data?

**Author response:** Sedentary behaviour was captured as a self-reported measure of screen-time. We have now clarified this in the methods (lines 138 and supplementary materials).

What outcomes came from the accelerometer data?  
how many people wore the accelerometers?

**Author response:** Thank you for this comment. Accelerometer data were available for 54,378 of the participants who had active commuting data. We have used these data to describe baseline physical activity levels in participants, to supplement the self-reported data we have for the entire cohort. These descriptive data are presented in Table 1 and formal statistical analyses of differences in physical activity according to commuting mode are now included in Supplementary Table 1 for self-reported and Supplementary Table 2 for objectively measured total physical activity. For both objective and self-report methods, there was agreement that physical activity was highest in cycle commuters, next highest in mixed-mode: cycling commuters, and next highest in walking commuters, with little difference between mixed mode: walking commuters and non-active commuters. Unfortunately, when we consider the subset of participants with accelerometer data (~20% of all participants with commuting data), there were too few events for us to obtain robust outputs from the outcome models.

We feel it does add value to the manuscript to include these baseline accelerometer data, to show differences in overall physical activity by commuting mode when a more robust assessment of physical activity was used than self-report. However, as we cannot use these data with respect to our main outcome measures, we would equally be prepared to remove the accelerometer data to ensure that the paper gives a clear unambiguous message. We have left these data in with further clarifications (lines 118-126), but are happy to be guided by the editors on this issue.

p6 line 28 finesse? fitness?

**Author response:** Thank you for pointing out this typo. We have now corrected this.

Discussion

The finding that women were more likely to be active commuters was interesting and contrary to many of the other studies - the authors should comment on this.

**Author response:** Thank you. This is an interesting comment. We originally considered all active commuters in a single group. However in response to reviewer comments, we have now considered cycle and walking commuting separately. In our data set, women were more likely to engage in both cycling and walking commuting (see Table 1).

Please expand on the implications of the study- how could the information be used? Community, environment or policy approaches to address the findings?

**Author response:** Thank you for making this very important point. We have now expanded on this in our discussion (Lines 184-187, 205-208 and 223-225). The statements included in the text are as follows:

Lines 184-187: “These results are important, because daily active commuting is an important contributor to total physical activity,<sup>3-6</sup> and thus facilitating active commuting, particularly cycle commuting, may be a viable approach to deliver physical activity-related health benefits at the population level.”

Lines 205-208: This has important policy implications, suggesting that policies designed to affect a population-level modal shift to more active modes of commuting, particularly cycle commuting (for example cycle lanes, city bike hire and subsidised cycle purchase schemes, increasing provision for cycles on public transport), present major opportunities for public health improvement.”

Lines 223-225: “The findings suggest population health may be improved by policies that increase active commuting, particularly cycle commuting, such as cycle lanes, hire/purchase schemes, and better provision for cycles on public transport.”

Additional Questions:

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A fee for organising education?: No

Funds for research?: No

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