PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Does healthy lifestyle behaviour influence the prognosis of low back pain among men and women in a general population? A population based cohort study.
AUTHORS	Bohman, Tony; Alfredsson, Lars; Jensen, Irene; Hallqvist, Johan; Vingard, Eva; Skillgate, Eva

VERSION 1 - REVIEW

REVIEWER	Professor Chris Maher The George Institute for Global Health, The University of Sydney
REVIEW RETURNED	17-Jul-2014

GENERAL COMMENTS	The strengths of this study are the large sample size and focussing on a composite measure of health. The limitations are the large loss to follow-up, the lack of clarity in the reporting of the methods and results, and the crude measure of prognostic outcome. Could you clarify if the statistical analysis plan was pre-specified (and better still published) and whether you have reported all analyses that were undertaken. Could you make clear what potential confounders stayed in the model. The study looked at predicting those with occasional low back pain who developed troublesome back pain (versus some other category). But to understand the sense of dichotomising back problems this way we need to know the scale used. I am unclear on the coding options you used to rate the degree of a back problem the participant had. At first glance this dichotomisation would pool people who improved or stayed the same and I wonder about the sense of that. If we knew the coding options for back pain and the counts in each category for both baseline and follow-up we could judge how sensible this approach was. I am not an expert in dealing with missing data but it seems to me sub-optimal to just analyse complete cases; particularly when the amount of missing data is so large. I think you should seek advice from a statistician on what is possible. This is potentially very interesting but the missing data and the lack of clarity in methods and results are major concerns. I think a statistical opinion re the missing data would be useful.

REVIEWER	Robert Grant

	Faculty of Health, Social Care and Education Kingston University and St George's, University of London UK
REVIEW RETURNED	18-Sep-2014

GENERAL COMMENTS	This is an important topic that is addressed appropriately with a well-designed study. The paper is very clear and I have little to add as a statistical reviewer. I would be interested to know more in the Discussion about the 34% who were lost to follow-up: how did they differ from those who remained. Also, another limitation I think worth mentioning in passing is that the study does not tell us what other relevant health services were accessed, e.g. physiotherapy. we know that healthy behaviour is associated with social class, and so is better access to healthcare (even simply through affording private care). This would be interesting to discuss briefly.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Professor Chris Maher

The strengths of this study are the large sample size and focussing on a composite measure of health. The limitations are the large loss to follow-up, the lack of clarity in the reporting of the methods and results, and the crude measure of prognostic outcome.

Dear Professor Maher, thank you for your thoroughly review of our manuscript. Below we will give our answer to your questions one by one. We hope that the changes and clarifications are satisfactory.

Comment 1: Could you clarify if the statistical analysis plan was pre-specified (and better still published) and whether you have reported all analyses that were undertaken.

Response: The statistical analyses was pre-specified but not published. The classification of the exposure (healthy lifestyle behaviour) and the outcome (LTLBP) was defined prior to the analyses. As low back pain is a common disorder we expected the outcome to be common why we decided, in advance, to present the result as relative risks (RR) rather than odds ratios (OR) something recommended in most biostatistical and epidemiological literature. All analyses were decided on in beforehand and all analyses performed are reported in the “Statistical methods” section:
1. We analysed men and women separately.
2. Both crude associations between the exposure and the outcome were analysed with generalized linear models with a binomial distribution and log function to calculate relative risk (RR) and the identity function to calculate risk differences (RD), with 95% CI.
3. To determine if a potential confounder should be included in the final model we included them, one at a time, into the crude model (outcome and exposure), and if the potential confounder changed the estimate by 10% or more it was included in the final adjusted model. The change in estimate (CE) method is recommended by several authors (see reference 29-33 in the manuscript).
4. In advance we decided to adjust for age which we did in all final analyses.
5. We used a likelihood ratio test to assess clinical relevant effect measure modifications between the exposure and potential confounders as well as between the confounders included in the adjusted analyses (SES and age in 10 year categories).
6. Wald test was used to test for potential trends in the association between exposure and outcome.
7. Chi-square tests were performed to see if the overall adjuster risk for LTLBP differed between men and women and to compare if the distribution of healthy lifestyle factors differed between the study sample and subjects lost to follow-up.

In the “Results” section we report the results for all statistical analyses mentioned above either in text or in table 2 and in figure 3.

Changes in the revised manuscript: We have clarified the assessment of clinical relevant effect measure modifications in the “Statistical methods” (row 11) and in the end of “Results”.

Comment 2: Could you make clear what potential confounders stayed in the model.

Response: In the final adjusted models age, in 10 year categories, and socio-economic status (SES) were included. We decided to adjust for age in advance and SES was the only potential confounder that changed the estimate by 10% or more of the 17 potential confounders tested. We believe that we clearly stated what potential confounders stayed in the model already in the original manuscript; 1. In the “Statistical methods” part we stated that “All final models were adjusted for age categorized into 10 year intervals”. 2. Footnote b in table 2 says, “Adjusted for age in 10 year categories and socio-economic status (SES) in six categories” and in the same table we have presented Age and SES in the parenthesis in the “Adjusted” column. 3. In the end of the “Results” part we have stated that SES was the only variable found to be a confounder why the final analyses were adjusted by SES and age in 10 year categories. Furthermore we believe that we have clearly presented the adjusted measures of prognostic outcome in the text (Results, after table 2) as well as in table 2. We hope that you find this clarification satisfactory why we haven´t made any changes in the revised manuscript according to this comment.

Comment 3: The study looked at predicting those with occasional low back pain who developed troublesome back pain (versus some other category). But to understand the sense of dichotomising back problems this way we need to know the scale used. I am unclear on the coding options you used to rate the degree of a back problem the participant had. At first glance this dichotomisation would pool people who improved or stayed the same and I wonder about the sense of that. If we knew the coding options for back pain and the counts in each category for both baseline and follow-up we could judge how sensible this approach was.

Response: Thank you for this valuable comment. We agree that this need to be clarified why we have made some changes in the revised manuscript:
• We have included the questions used to define occasional low back pain at baseline in 2006 and long duration troublesome low back pain at follow-up in 2010 in a new appendix (Appendix 1) and refer to the appendix in the “Methods” paragraph.
• The counts for the outcome LTLBP are already presented for each category of the exposure in both men and women in the original manuscript (table 2) why we hope that this is enough.
We have included the counts for the different coding options at baseline defining subjects with and without occasional LBP in the flow chart (figure 1).

Further, we fully agree that this dichotomisation results in an outcome variable that compare participants with occasional LBP at baseline that have developed long duration troublesome LBP (LTLBP) at follow-up to participants who could have improved, stayed the same or even got slightly worse from baseline to follow-up. We find this perfectly sensible when this is in line with our research question.

Comment 4: I am not an expert in dealing with missing data but it seems to me sub-optimal to just analyse complete cases; particularly when the amount of missing data is so large. I think you should seek advice from a statistician on what is possible.

Response: We agree that the missing data are a weakness in our study which we have stated in the original manuscript. During the analyses of the data we were supported by a statistician (see the acknowledgement) but following your advice we have in addition discussed the matter of imputation compared to the use of complete cases with another statistician. As a result of this consultation we decide to keep the analyses as they are since we believe that they are appropriate in this context. Since we agree that attrition and loss to follow-up are weaknesses in the study that we need to address more carefully, we have extended the discussion about the selection bias that might be present due to this in the Discussion part of the revised manuscript (last paragraph of "strength and limitations"). Further we have changed the conclusion of the study from "Healthy lifestyle decreases the risk…" to "Healthy lifestyle seems to decrease the risk…"

This is potentially very interesting but the missing data and the lack of clarity in methods and results are major concerns.

I think a statistical opinion re the missing data would be useful.

Reviewer: Robert Grant
This is an important topic that is addressed appropriately with a well-designed study. The paper is very clear and I have little to add as a statistical reviewer.

Dear Mr Grant, thank you for your kind comments on our manuscript. Below we have tried to address your comments one by one and we hope that you will find them appropriate?

Comment 1: I would be interested to know more in the Discussion about the 34% who were lost to follow-up: how did they differ from those who remained.

Response: As this is a study regarding aetiology we consider the difference in the exposure between the study sample and the drop-outs being the most important but due to your comment we have included some more information regarding the 34% missing. Further, we have expanded our discussion, in the Discussion part of the revised manuscript, about how the difference in the exposure may have affected our results (last paragraph of "strength and limitations").

Comment 2: Also, another limitation I think worth mentioning in passing is that the study does not tell us what other relevant health services were accessed, e.g. physiotherapy. we know that healthy behaviour is associated with social class, and so is better access to healthcare (even simply through affording private care). This would be interesting to discuss briefly.

Response: We agree that information on the use of health services would have been an interesting potential confounder to assess. Unfortunately we did not have this information as the data was derived from a Public Health Questionnaire not concerning health care. Further, we agree with your opinion concerning the association between healthy lifestyle behaviour, social class and the access to healthcare. We have analysed several potential confounders probably associated with social class, e.g. disposable income, education, financial stress and SES. The latter was included as a confounder in the adjusted analyse. Even though information about the use of health services is a potential unmeasured confounding factor we believe that information on health care access would not have changed our conclusions as we have tested other potential confounders probably associated to that. We hope that you can agree with us. Nevertheless, to clarify this, we included "for example information on health care services" in our discussion about unmeasured confounding (first paragraph of "strength and limitations").

VERSION 2 – REVIEW

REVIEWER	Prof Chris Maher The George Institute for Global Health, Australia
REVIEW RETURNED	31-Oct-2014

GENERAL COMMENTS	I think the authors have done an excellent job of considering reviewer comments and revising the manuscript accordingly. I have no further revisions to request. I look forward to seeing this paper in print.