PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Self-rated health and standard risk factors for myocardial infarction. A cohort study.
AUTHORS	Waller, Göran; Janlert, Urban; Norberg, Margareta; Lundqvist, Robert; Forssen, Annika

VERSION 1 - REVIEW

REVIEWER	Kuanrong Li German Cancer Research Centre
REVIEW RETURNED	10-Oct-2014

GENERAL COMMENTS	1. In Abstract, it is unclear to me whether the objective was to examine the relationship between self-rated health and standard risk factors for myocardial infarction, or to examine the association between self-rated health and myocardial infarction after adjustment for other known risk factors. The latter seems to fit the analysis more. I suggest the authors read the manuscript again and make it clear on what was the research question, what were the results, and did the results answer the question. 2. Is it plausible to treat the deaths due to MI as incident, fatal MI? If so, the definition of the disease outcome will become simpler. 3. More results should be given in Abstract. 4. Please confirm with a statistician on the use of "multivariate", "multivariable" seems to be the correct word and the two may not be interchangeable. 5. Why not further examine HDL and LDL? 6. By what means was the proportionality assumption was tested? 7. Please also show chi-square and ANOVA results in Table 1. 8. The Kaplan-Meier plot seems unnecessary indeed. It was even not described in Result. 9. In Discussion, the authors claimed that self-rated health is an independent predictor for MI. Then what is the possible underlying mechanism? Should we be confident to say that self-rated health is NOT merely a mediator between pre-existing health conditions and MI? This should be discussed. This study did control for blood pressure, total cholesterol, BMI, smoking etc. However, other possibly important risk factors such as psychological risk factors were not considered. This should be discussed as a limitation. The role of reverse causality should also be checked.

REVIEWER	Nicolas DANCHIN
	Hôpital Européen Georges Pompidou, Paris, France
REVIEW RETURNED	08-Dec-2014

| GENERAL COMMENTS | This paper by Waller et al. describes the correlation between a simple evaluation of the general health status and the risk of fatal or non-fatal myocardial infarction in a large Swedish cohort of presumably healthy individuals. Health status assessed by means of a very simple questionnaire appears to be an independent predictor of risk of AMI, on top of the conventional risk factors.

I must say that I really like the concept assessed by the authors, namely that a gross evaluation of the perceived health status represents a not negligible prognostic indicator.

The way the study is conducted is rigorous, although the statistical methodology would merit to be described a bit more extensively. As is usual in such studies, the authors have censored the patients who had an event in the year following inclusion, although there is no definite rule for the duration of censoring in such cases.

The results are presented clearly, and I think the authors make their point.

I have, however, a few remarks:

- The terminology "myocardial infarction/death in myocardial infarction" is impossible to understand. I think the authors mean fatal or non-fatal MI
- Table 1: please add the recruitment period (perceived health status might vary depending on the period)
- In the multivariate analyses (e.g. Table 3), BMI is used as a continuous variable. There is a lot of evidence that the relationship between BMI and outcomes is not linear, but rather presents as a U-curve. I think it would be more proper to categorise BMI and use BMI as sa categorical variable.
- In the discussion, I think the authors should expand on the potential mechanisms underlying their findings. For instance, what about the relationship between stress, depression and self-perceived health status? |
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VERSION 1 – AUTHOR RESPONSE

Reviewer Name Kuanrong Li
Institution and Country German Cancer Research Centre
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below 1. In Abstract, it is unclear to me whether the objective was to examine the relationship between self-rated health and standard risk factors for myocardial infarction, or to examine the association between self-rated health and myocardial infarction after adjustment for other known risk factors. The latter seems to fit the analysis more. I suggest the authors read the manuscript again and make it clear on what was the research question, what were the results, and did the results answer the question.
The research question has been put according to reviewers suggestion, in abstract page 2 and on page 5.
2. Is it plausible to treat the deaths due to MI as incident, fatal MI? If so, the definition of the disease

outcome will become simpler. This have been changed to fatal, non fatal myocardial infarction throughout the text.

3. More results should be given in Abstract. Abstract has been changed according to file. Numerical value has been inserted to HR of poor self-rated health in the multivariable analysis and confidence interval. All major results are put in text as before.

4. Please confirm with a statistician on the use of "multivariate", "multivariable" seems to be the correct word and the two may not be interchangeable. Our professor of Public Health, Urban Janlert declares the terminology being unclear in this respect, the terminology is not stringently used. Our statistician, Robert Lunqvist declares that from a statistical point of view the terminology should be "multivariable analysis". The terminology has been changed throughout the manuscript.

5. Why not further examine HDL and LDL? The simple answer is that data on LDL- HDL-cholesterol is missing for most participants. The more complex answer is that as data on total cholesterol of high quality is available it is of a minor concern to mention lack of LDL-cholesterol as a weakness in an epidemiological study. At a population level, total cholesterol has a well proven predictive value. Ref: Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J,Halsey J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from61 prospective studies with 55,000 vascular deaths. Lancet 2007;370: 1829_39.
Yes, HDL and LDL are important but more so when it comes to individual risk assessment. The sentence "The lack of data on HDL and LDL cholesterol levels could be seen as a limitation of the study." has been inserted on page 18.

6. By what means was the proportionality assumption was tested? It was tested by the log minus log plot. This is now stated on page 9, method section.

7. Please also show chi-square and ANOVA results in Table 1. P-values for ANOVA and Chis-square have been added in table 1.

8. The Kaplan-Meier plot seems unnecessary indeed. It was even not described in Result. The Kapla-Meier plot was used in preparation of the variables, as a means to explore the data behind the Cox-regression calculations. Referral to Kaplan-Meier has been removed from the manuscript.

9. In Discussion, the authors claimed that self-rated health is an independent predictor for MI. Then what is the possible underlying mechanism? Should we be confident to say that self-rated health is NOT merely a mediator between pre-existing health conditions and MI? A more lengthy discussion on these essential issues is inserted on page 19-20. Two new references are used, a seminal review of Jylhä and a newer reference by Chrisitian et al 2011, replacing the referenc of Lekande et al 2004. This should be discussed. This study did control for blood pressure, total cholesterol, BMI, smoking etc. However, other possibly important risk factors such as psychological risk factors were not considered. This should be discussed as a limitation. These items are dicussed on page 18 end of first paragraph, and on page 20.The role of reverse causality should also be checked. The issue of reverse causality is discussed on page 18, and results given on page 14.

Reviewer Name Nicolas DANCHIN
Institution and Country Hôpital Européen Georges Pompidou, Paris, France
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below This paper by Waller et al. describes the correlation between a simple evaluation of the general health status and the risk of fatal or non-fatal myocardial infarction in a large Swedish cohort of presumably healthy individuals. Health status assessed by means of a very simple questionnaire appears to be an independent predictor of risk of AMI, on top of the conventional risk factors.

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I have, however, a few remarks:

- The terminology "myocardial infarction/death in myocardial infarction" is impossible to understand. I think the authors mean fatal or non-fatal MI Changes have been made accordingly throughout the manuscript.
- Table 1: please add the recruitment period (perceived health status might vary depending on the period) Recruitment period is declared in all tables and figures.
- In the multivariate analyses (e.g. Table 3), BMI is used as a continuous variable. There is a lot of evidence that the relationship between BMI and outcomes is not linear, but rather presents as a U-curve. I think it would be more proper to categorise BMI and use BMI as sa categorical variable.
We agree. In the preparation of the manuscript we categorized BMI by one unit of BMI and related it to outcome. The results could imply a u-curve but the confidence interval for HRs were wide and did not warrant for a conclusion of non-linearity. After the remarks form the reviewer we did a sensitivity analysis, using BMI categorized if five categories in the multivariable analyses. This did not affect HRs. This is reported on page 9 and 14.
- In the discussion, I think the authors should expand on the potential mechanisms underlying their findings. For instance, what about the relationship between stress, depression and self-perceived health status?b This is discussed on page 19-20.