

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Association between subjective social status and cardiovascular disease and cardiovascular risk factors: A systematic review and meta-analysis
<b>AUTHORS</b>	Tang, Karen; Rashid, Ruksana; Godley, Jenny; Ghali, William

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Nancy Adler and Aric Prather University of California, San Francisco USA
<b>REVIEW RETURNED</b>	16-Oct-2015

<b>GENERAL COMMENTS</b>	<p>The present meta-analysis examines the associations between subjective social status (SSS) and measures of coronary heart disease (CAD) and CAD risk factors, including hypertension, dyslipidemia, and obesity. Analyses revealed increased odds of CAD and CAD risk factors among those low in SSS compared to those high in SSS. Consistent with the design of the SSS measure which asks individual's to place themselves vis-à-vis others in relation to the education, income and occupation, these associations were largely attenuated when adjusting for objective indicators of SES. The fact that there is a residual association suggests the value of assessing subjective as well as objective indicators.</p> <p>This study provides a valuable integration of prior evidence. Nevertheless, there are several methodological concerns that, if addressed, would strengthen the paper. Specific comments are below.</p> <p>Major Comments:</p> <ol style="list-style-type: none"><li>1. The rationale for including both community and societal ladder measures in the meta-analysis needs to be provided and some thought given to the implications of treating them as equivalent measures. Conceptually, one would expect that community SSS would operate differently than would societal SSS. For example, objective SES should be less strongly related to community status than to subjective SES. The instructions for indicating one's subjective SES explicitly point to income, education, and occupation while directions for completing the community SSS measure do not (it asks about where the individual stands in respect and status in their own community, and there is no reference to SES indicators). One approach, which would be more parsimonious, would be to limit this meta-analysis to only societal SSS. At the very least a sensitivity analysis where the community SSS data point was removed should be provided</li><li>2. A rationale for the inclusion of a dissertation in this analysis is</li></ol>
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	<p>needed. The findings from this source have not gone through peer review and it should not be equated with papers that have done so. At a minimum, it would be helpful to know if the associations hold upon its removal.</p> <p>3. More information is needed about how the outcomes were defined. For instance, how was dyslipidemia defined in each study? Did that vary by study? For studies that included CAD as an outcome, were these defined by self-report by the participant or were more objective measures available?</p> <p>4. Role of negative affect: To the extent that outcome measures were self-reported, it would be good to evaluate the association with and without adjustment for negative affect to evaluate the extent to which the associations between SSS and health are driven by excess negative emotion. It would also be helpful to note whether the outcomes are self-reported or not.</p> <p>Minor Comments:</p> <p>1. Introduction: Given the brevity of the introduction and the wealth of examples linking social status and health, the use of academy award seems somewhat tangential, especially since it did not replicate when using other categories of awards. Consider using a different example.</p> <p>2. Introduction: the authors note that the MacArthur ladder is one example of measuring social status hierarchy. If there are alternative measures used in any of the studies, it would be helpful to describe them. It would also be helpful to provide additional references for other measures that have been used and how the results match up.</p> <p>3. One of the interesting findings, which is consistent with earlier work, is that the subjective SES ladder does not work as well for some ethnic groups. It would be helpful to have a brief discussion of why that might be and how that could be tested.</p>
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<b>REVIEWER</b>	Dr. Jack Tu Institute for Clinical Evaluative Sciences, Sunnybrook Schulich Heart Centre University of Toronto Canada
<b>REVIEW RETURNED</b>	15-Dec-2015

<b>GENERAL COMMENTS</b>	<p>This is a well-written systematic review / meta-analysis of 10 articles examining the association between subjective social status (SSS) and the presence of coronary artery disease and/or risk factors (hypertension, diabetes, hyperlipidemia, obesity). The authors conclude that those with the lowest SSS are more likely to have these conditions even after adjusting for confounding factors such as socioeconomic status (SES) as compared those with the highest SSS. Specific comments are:</p> <p>1) The authors should provide more information about the MacArthur Scale of Subjective Social Status including a figure of the scale. This would allow readers who are not familiar with the scale to better understand it. It was also not entirely clear how they have defined those at the lowest vs highest end of the scale. Was it just the lowest and highest rungs? What was the sample size of participants at the extremes of the scales? Would it be possible to include a scatter plot of the distribution of people in each rung in each study?</p>
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	<p>2) The article should be reviewed by a statistician with expertise in meta-analysis of observational studies.</p> <p>3) Most of the studies included in the paper are cross-sectional in nature, and thus, causal inferences should be made cautiously.</p> <p>4) The lack of a significant relationship in non-Caucasians was an interesting finding, although the sample size was small.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Major Comments:

1. The rationale for including both community and societal ladder measures in the meta-analysis needs to be provided and some thought given to the implications of treating them as equivalent measures. Conceptually, one would expect that community SSS would operate differently than would societal SSS. For example, objective SES should be less strongly related to community status than to subjective SES. The instructions for indicating one's subjective SES explicitly point to income, education, and occupation while directions for completing the community SSS measure do not (it asks about where the individual stands in respect and status in their own community, and there is no reference to SES indicators). One approach, which would be more parsimonious, would be to limit this meta-analysis to only societal SSS. At the very least a sensitivity analysis where the community SSS data point was removed should be provided

Our Response:

Thank-you for your feedback and comments. We agree that because community and societal ladders represent different concepts, we should not pool results from both ladders thereby treating them as equivalent measures. Of the ten studies, only one (the dissertation by Cross) used the community ladder. The other nine studies evaluated either the societal ladder alone, or both the societal and community ladders (see Table 1 of the manuscript). When both ladders were evaluated in the studies, we pooled results only from the societal ladder.

Given your valuable feedback, we have excluded the single study by Cross from our meta-analysis (though do include it for descriptive purposes to our systematic review). The pooled effect estimates and conclusions remain very similar, and are even slightly strengthened; the socioeconomic status (SES)-unadjusted odds ratio (OR) of hypertension comparing the bottom to the top of the societal ladder was 1.88 (95% CI 1.27, 2.79) compared with the previous OR of 1.77 (95% CI 1.29, 2.44) when including the Cross dissertation.

Given the exclusion of the Cross dissertation from the meta-analysis, Figure 1 (PRISMA flow diagram), Figure 2 (forest plots for SES-unadjusted ORs for each outcome), and Figure 3 (forest plots for SES adjusted ORs for each outcome), and Table 3 (stratified analysis) have been modified. The text of the results (pages 7 [20-22] to 8 [lines 1-4], page 11 [lines 6-7], page 15 [lines 5, 9, 15-16, 18-19], page 16 [line 2], page 18 [line 5 and last line], page 19 [lines 1-3], and Abstract [lines 12-13, 15-16]) have also been modified to reflect the exclusion of the Cross dissertation. The overall conclusions are unchanged with the exclusion of the Cross dissertation.

2. A rationale for the inclusion of a dissertation in this analysis is needed. The findings from this source have not gone through peer review and it should not be equated with papers that have done so. At a minimum, it would be helpful to know if the associations hold upon its removal.

Our Response:

Because the Cross dissertation was also the single study that evaluated community SSS alone, we have excluded this study from the meta-analysis as per our response to Comment 1 above. We believe that this change also addresses the concern of equating this non-peer reviewed paper with peer-reviewed papers.

We continue to include the Cross dissertation in the systematic review (though not the meta-analysis) as we wish to comprehensively describe the entire body of literature on subjective social status and cardiovascular outcomes, including sources in the grey literature. We highlight study quality concerns with the Cross paper in Table 4 (study quality criteria).

3. More information is needed about how the outcomes were defined. For instance, how was dyslipidemia defined in each study? Did that vary by study? For studies that included CAD as an outcome, were these defined by self-report by the participant or were more objective measures available?

Our Response:

We agree that the methods of measurement, and whether these were self-reported, represent important information. Therefore, we have added Table 2, which describes how each study defined and measured the outcomes. A summary of these methods of measurement is provided in the manuscript on page 13 (lines 9-14).

We have renumbered the original Table 2 (stratified analysis and meta-regression) and Table 3 (study quality criteria) to Table 3 and Table 4 respectively in the current manuscript given the addition of this new Table 2. To make room for this new Table 2, we have removed Figure 5 (funnel plots with and without trim and fill for the outcome of hypertension), for a total of 4 tables and 4 figures.

4. Role of negative affect: To the extent that outcome measures were self-reported, it would be good to evaluate the association with and without adjustment for negative affect to evaluate the extent to which the associations between SSS and health are driven by excess negative emotion. It would also be helpful to note whether the outcomes are self-reported or not.

Our Response:

Of the nine studies included in the meta-analysis, only one study by Demakakos et al. (2012) considered psychosocial factors when modeling the association between subjective social status and health outcomes. In this study, the hazard ratio of developing incident diabetes for men was 2.60 (95% CI 1.46, 4.64) for the lowest SSS quartile compared to the highest SSS quartile, when adjusting for age, comorbidities, marital status, employment, cardiovascular and non-cardiovascular comorbidities. The HR was only minimally lower at 2.54 (95% CI 1.38, 4.67) when additional adjustment for psychosocial factors was performed (specifically for depressive symptoms, social support, social relationships, sense of control in life and at home). Similarly, adjustment for psychosocial factors mildly attenuated the HR for women, though the same trend remained where lower SSS is associated with higher risk of developing diabetes (HR 1.98, 95% CI 1.05, 3.70 without adjustment for psychosocial factors compared with HR 1.63, 95% CI 0.84, 3.14 with adjustment for psychosocial factors).

Operario et al. specifically examined the question of whether negative affect mediates or confounds the association between SSS and health outcomes.[1] If low SSS adversely affects health through worsening negative affect – that is, if negative affect acts as a mediator of this association -- then it may not be conceptually appropriate to adjust for negative affect given its role in the causal relationship. However, if negative affect acts as a confounding variable, then such adjustment would be necessary. Operario et al. were able to demonstrate that negative affect did diminish the association between SSS and self-reported health outcomes, but also equally diminished the association between objective socioeconomic factors (such as income and education) and these same outcomes. Negative affect likely acts as a mediator rather than a confounder in the association between objective SES and health (as negative affect should not affect how individuals report their income or education). Therefore, because a similar reduction is seen in the association between SSS and health when accounting for negative affect, negative affect does not seem to uniquely confound SSS and health but rather also acts as a potential mediator in this pathway. Adjustment for negative affect may therefore result in an underestimation of the association between SSS and health.

Because the question of the role of negative affect on the association between SSS and health is a pertinent one, we have added our inability to assess this to our limitations on page 25 (lines 1-6).

Reviewer 1

Minor Comments:

1. Introduction: Given the brevity of the introduction and the wealth of examples linking social status and health, the use of academy award seems somewhat tangential, especially since it did not replicate when using other categories of awards. Consider using a different example.

Our Response:

Because the seminal Whitehall II study and the studies citing the neuroendocrine effects of low social status adequately illustrate our point that the association of SES on health is not entirely explained by resource deprivation, we have simply removed the Academy award example. Our Discussion section also describes the income inequality and Macaque monkey social status literature, which provide indirect evidence of the association between social status and health; these examples were not reiterated in the introduction.

2. Introduction: the authors note that the MacArthur ladder is one example of measuring social status hierarchy. If there are alternative measures used in any of the studies, it would be helpful to describe them. It would also be helpful to provide additional references for other measures that have been used and how the results match up.

Our Response:

We have added descriptions of other measures of SSS, with references, to the Introduction on page 5 (lines 13-17). The results of studies using these other measures are remarkably consistent with the results from this systematic review and meta-analysis. This information has been provided on page 25 (lines 11-15).

3. One of the interesting findings, which is consistent with earlier work, is that the subjective SES ladder does not work as well for some ethnic groups. It would be helpful to have a brief discussion of why that might be and how that could be tested.

Our Response:

Thank-you for this comment and suggestion. We have added a discussion (page 23 last line to page 24 line 9) about why the subjective SES ladder may not work well for some ethnic groups (such as if they derive social status and self-worth not from income, education, or occupation, but rather from other values that are not defined by the MacArthur ladder). We have made suggestions about further research and how to take this into account (page 24, lines 9-13).

Reviewer 2 Comments:

1) The authors should provide more information about the MacArthur Scale of Subjective Social Status including a figure of the scale. This would allow readers who are not familiar with the scale to better understand it. It was also not entirely clear how they have defined those at the lowest vs highest end of the scale. Was it just the lowest and highest rungs? What was the sample size of participants at the extremes of the scales? Would it be possible to include a scatter plot of the distribution of people in each rung in each study?

Our Response:

Thank-you for this feedback. We agree that a visual of the actual subjective social status ladder would be helpful for those who are not familiar with the scale. For this reason, we have obtained the written permission from the Program Coordinator of University of California, San Francisco (UCSF) Center for Health and Community to reproduce the exact images of the MacArthur Scale of Subjective Social Status for our paper. We have attached these figures as Appendix 1, and refer to it at the first mention of this ladder on page 5 (line 20).

We did define those at the bottom of the ladder as those on the lowest rung. The top of the ladder included those on the highest rung. This has now been explicitly stated on page 9 (line 13 and last line). When individual studies did not present effect sizes using these two comparisons, the effect size using this comparison (bottom rung versus top rung) was calculated, per the methods, "Data Analysis" section (second paragraph).

Though we agree that a scatterplot or description of the distribution of respondents on each rung of the ladder would be interesting, this information cannot be provided as it was not consistently available across studies. For example, four of ten studies (Cross 2011, Frerichs 2014, Reitzel 2013, Subramanyam 2012) reported the mean SSS ranking only without demonstration of the distribution across the ten rungs. Two studies (Demakakos 2008, Woo 2008) showed histograms of the proportion of males and females (stratified) on each rung. One study (Demakakos 2012) divided the 10 rungs into 4 groups and provided a distribution for these four groups. Two studies (Adler 2008, Singh-Manoux 2003) divided the 10 rungs into 5 groups and provided a distribution for these five groups. Given the variability in how the data were presented in each study, it was not possible to include a scatter plot of this distribution. However, because the mean SSS ranking was available and widely reported across all studies, this information was included in Table 1.

2) Most of the studies included in the paper are cross-sectional in nature, and thus, causal inferences should be made cautiously.

Our Response:

We agree that because of the cross-sectional and observational nature of the included studies, we should not imply causality of the associations between low subjective social status and cardiovascular risk. We have carefully reviewed the manuscript and have ensured that such causal inferences have been modified to state associations only, such as on page 22 (line 12-13), page 23 (lines 1-2), and page 26 (second last line).

3) The lack of a significant relationship in non-Caucasians was an interesting finding, although the sample size was small.

Our Response:

To enhance the discussion of this finding, we have added further detail and implications to research in our discussion section. Please see our response to “Minor comments #3” from Reviewer 1 above.

References

1. Operario D, Adler NE, Williams DR. Subjective social status: Reliability and predictive utility for global health. *Psychology & Health* 2004;19(2):237-46.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Nancy Adler University of California, San Francisco USA
<b>REVIEW RETURNED</b>	02-Feb-2016

<b>GENERAL COMMENTS</b>	The revised manuscript was responsive to earlier reviews. It is clear and informative. My only remaining concern is about possible overstatement in the discussion. While it is fair to say that the findings provide some of the strongest evidence to date that psychosocial factors are involved in the association of SES and health, it is not accurate to say that the paper provides DIRECT evidence since it does not directly test psychosocial variables. It would be helpful to clarify how primate studies support a psychosocial explanation, especially in terms of the importance of perceptions of status, not just one's placement in a hierarchy. Finally, the last suggestion in the discussion that the SSS scale be modified to measure perceived status without reference to objective socioeconomic measures ignores the fact that this is what the "community" ladder does. These are minor points but they detract from an otherwise strong paper.
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<b>REVIEWER</b>	Jack Tu ICES Sunnybrook Schulich Heart Centre University of Toronto
<b>REVIEW RETURNED</b>	26-Jan-2016

**GENERAL COMMENTS**

I am satisfied with the authors changes in response to my original comments.

**VERSION 2 – AUTHOR RESPONSE**

## Comment 1:

The revised manuscript was responsive to earlier reviews. It is clear and informative. My only remaining concern is about possible overstatement in the discussion. While it is fair to say that the findings provide some of the strongest evidence to date that psychosocial factors are involved in the association of SES and health, it is not accurate to say that the paper provides DIRECT evidence since it does not directly test psychosocial variables.

## Response to comment 1:

Thank-you for this comment; we agree entirely. We have modified our statement to reflect that the primate and income inequality literature does not measure perceived social status directly but infers that it exists as a contributor to health outcomes. Our study therefore advances knowledge by examining explicitly-measured (rather than inferred) social status and its association with cardiovascular risk. We have removed the statement indicating that our study provides direct evidence that psychosocial factors contribute to health outcomes. These changes were made on page 23 (lines 8-10).

## Comment 2:

It would be helpful to clarify how primate studies support a psychosocial explanation, especially in terms of the importance of perceptions of status, not just one's placement in a hierarchy.

## Response to comment 2:

We have elaborated on the primate literature, as suggested, on page 22 (lines 15-23) and page 23 (line 1).

## Comment 3:

Finally, the last suggestion in the discussion that the SSS scale be modified to measure perceived status without reference to objective socioeconomic measures ignores the fact that this is what the "community" ladder does.

## Response to comment 3:

The reviewer has made an excellent point. We have modified our suggestions for future research in non-Caucasian ethnicities to take into account that the community ladder does exactly what we are suggesting (that is, it measures perceived status without reference to objective SES measures). These changes were made on page 24 (lines 20-23) and page 25 (lines 1-3).