Author's response to reviews

Title: Prospective association between self-reported life satisfaction and mortality: Results from the MONICA/KORA Augsburg S3 Survey Cohort Study.

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Author's response to reviews: see over
Dear editor and reviewers,

Thank you for your thorough assessment of our manuscript "Prospective association between self-reported life satisfaction and mortality: Results from the MONICA/KORA Augsburg survey 3 Cohort Study".

A point-by-point reply to each of your comments/critiques is provided below. Reviewer comments are identified in bold. New texts that have been introduced into the manuscript based on your suggestions are identified with "tracked changes". Their location in the manuscript is noted (section, paragraph).

We believe that the overall presentation of our study and results are significantly improved and look forward to your thoughtful assessment.

With best regards,

Maria Elena Lacruz, PhD
Issues addressed by Reviewer #1:

1. Background, paragraph 1: In the introduction, LS is defined as “trait levels of positive affect as well as cognitive assessments of the extent to which a person’s life matches his or her expectations”. Furthermore, the authors will “focus on life satisfaction because it reflects subjective perception ... and may be more stable than measures of positive affect”. This is an interesting approach; this study seems to contribute with important knowledge on how each individual’s subjective perception of their health, regardless of somatic and psychological health, affect mortality. However, in the rest of the manuscript this aspect is not emphasized. The results are rather discussed in relation to previous studies of positive well-being, which, according to the introduction, is less stable measure. 

To further emphasize our approach, the following paragraph has been added to the first paragraph of discussion:

"These findings suggest that regardless of an individual's somatic and psychological health, being satisfied with one's life is protective against mortality. This is in agreement with previous reports, which clearly show the association between a global subjective perception of one's own health and mortality. These studies also found a significant, independent association that persists even after adjustment for health status indicators and other relevant covariates {Idler, 1997 #64}.

2. I have some concerns regarding the relation between life satisfaction and other psychological measures. The concept of a single-item self-reported variable having significant influence on future life-length expectancy is tempting. Still, as expected, the analyses show that life satisfaction is closely associated with other psychological variables. Some of these variables are for this reader very similar to LS (e.g. self-rated health, health status), and the authors need to clarify why these variables need to be evaluated in the same Cox regression analysis. For me, it would be more clinical useful to evaluate the prospective influence by high LS adjusted by somatic, demographic and social factors, and psychological factors not very similar to LS. Indeed, the authors have done this (discussion, paragraph 3), when reporting high LS is independently associated with lower mortality if self-rated health is not added.
In conclusion, the possible clinical value of asking for subjective perceptions is preferable evaluated without adjusting for other measures of subjective perception. Alternatively, these two measures may be compared.

The possible clinical value of asking for subjective perceptions has been evaluated without adjusting for other measures of subjective perception (see crude model, cardiovascular risk factors, health and social determinants).

A comparison has been performed in two ways: 1) psychological model without self-rated health (see discussion, paragraph 4) and 2) inclusion of AIIC-information in Table 2, as suggested by this reviewer in point 11 (see below).

3. Methods, paragraph 3: Two of the references regarding previous use of this item in Norwegian studies are somewhat misleading. Reference 10 does not present validated data, while reference no 12 regards a selected sample of medical doctors, and is less relevant for a population-based study. Furthermore, in the referred HUNT-study this question was one of three items in a subjective well-being scale, in which the English translation is “When you think about the way your life is going at present, would you say that you are by and large satisfied with life or are you mostly dissatisfied?” Thus, the authors should clarify that this item, at least in the cited study, is one of several items in a well-being scale, and also consider referring to one of the following references:


-Moum, T., Næss, W., Sørensen, T., Tambs, K., & Holmen, J. Hypertension labeling, life events, and psychological well-being. Psychological Medicine, 1990; 20: 635–646.

Thanks for the important clarification. The references 10 and 12 have now been deleted.
4. The authors should consider presenting the two aims in the same order throughout all parts of the manuscript - i.e. 1) determinants of LS 2) prognostic influence by LS on mortality. Thanks for the remark. Now, throughout the manuscript these 2 aims are presented in the suggested order, except for in the discussion, where we decided to start with the most important result, that is the influence of LS on mortality.

5. Abstract: The authors analyze the data with respect to how LS in the highest tertile compared to the lower tertiles influence on mortality, and which factors determinate high LS. This should be reflected in the aims (i.e. which variables determine high LS et.c.)
Thanks for the remark. The following changes have been incorporated into the Abstract, first paragraph:

"Aims: To identify factors which determine high life satisfaction (LS) and to analyse the prognostic influence of LS on mortality."

6. Absolute risks are asked for in aims, but not mentioned in the results section.
The following sentence has been incorporated into the results section of the abstract:

"Participants with higher LS (n=721, 27%) benefited the most with respect to absolute mortality risk reduction (higher LS=67; mid = 98; low = 140 per 10,000)."

7. “Confirmed” is perhaps not the correct statement when it was not hypothesized in the aim. Furthermore, the second sentence in the conclusion does not state in which direction high LS influence on long-term survival.
The following changes have been done in the conclusion of the abstract:

"Baseline assessment demonstrated that psychological, social and life-style factors, but not somatic co-morbidities, were relevant determinants of LS. Moreover, the analysis showed that men with higher LS have a substantial long-term survival benefit."
8. The abbreviation for LS should be given when first mentioned.
Thanks for the remark. Correction has been done in the 1st paragraph of background.

9. In line with comment 1; After contrasting the term LS from the terms well-being and positive affect in paragraph 1, paragraph 2 mainly comment on well-being or positive affect, and not on LS, which is somewhat confusing.
The terminology has been revised to avoid confusion.

10. The first sentence in paragraph 3 imply that there is a a-priori hypothesis of the effect by LS on mortality, which is lacking in the last sentence in the same paragraph (page 4). Clear hypotheses or statements in the introduction would improve the readability.
There was no a-priori hypothesis, thus the term "protective" has been deleted to improve readability.

11. The authors have used C-statistics to explain the determinants of LS. They may also consider using C-statistics comparing regression models including somatic and demographic variables with and without various psychological variables when evaluating the mortality risk. In my opinion such comparisons of the additional mortality risk contributed by LS (or similar measures as mentioned in comment 2) would improve the clinical significance of including self-reported measures in prognostic evaluations.
Thanks for the very helpful remark. We have now incorporated in Table 2 (HR) Akaike information criterion (AIC).

Thanks for the correction: "coronary heart disease" has been changed throughout the paper to "cardiovascular disease".

13. Paragraph 6 (and table 2): The text literary says that the gender-specific analyses was adjusted for gender.
Thanks for the remark. It has been clarified (footnotes Table 2).
14. Paragraph 7: I am not convinced that all CVD risk factors and health factors are confounders, as several of these are not associated with LS in crude analyses (suppl. table 1). At least, the authors should consider provide hazard ratios for all variables in the regression analyses, in order to ascertain which factors are possible mediators (e.g. as a supplementary table).

Thanks for the remark. Additional supplementary tables have been done to add information for all variables in the Cox-regression analyses for all participants (suppl. Table 2), women (suppl. Table 3) and men (suppl. Table 4).

15. Paragraph 8: Supplementary table 1 mentions that LS is associated with angina pectoris, which most often reflect coronary heart disease.

It has been changed to (Results, paragraph 8):

"There are clear trends in the direction of an association between self-reported, pre-existing cardiovascular disease and lower LS (supplementary table 1)."

16. The conclusion should reflect the aims, and state the direction and magnitude of effect by high LS on mortality.

Thanks for the remark. Changes have been made in the conclusion:

"In summary, our cross-sectional analysis suggests that LS is essentially a subjective construct associated with social roles, psychological characteristics, and health perception, but not somatic factors. Moreover, in men LS has a substantial impact on long-term survival. Participants with higher LS benefited the most with respect to absolute mortality risk reduction (higher LS=67; mid = 98; low = 140 per 10,000). Furthermore, higher LS was independently associated with survival in men (HR 0.55, 0.37-0.81) but not in women."

17. Methods, paragraph 2: Is the question asked by a researcher in an interview or answered by the participants in a questionnaire? The abstract states that there was an interview, it is mentioned as a questionnaire.

Thanks for the remark. It was a questionnaire. The abstract has been corrected:

"data collection was"
18. Methods, paragraph 8: The number of end-points registered is also stated in the results section. We thank the reviewer for noticing this redundancy and have made appropriate changes (Methods, paragraph 10):

"The study population was followed for an average of 12 years (S.D. 2.1)."

19. Results, subtitle and first sentence paragraph 2: Consider revise the language. Following correction has been done:

"Differences in socio-demographic, somatic and psychological factors between subgroups of LS.
Supplementary table 1 shows the differences in CVD risk factors, life-style and co-morbidities, socio-demographic variables and psychological factors between high, medium and low subgroups of LS."

20. Table 2: Please consider to revise the caption to reflect that LS is dichotomized in high vs. medium/low.
Changed to:

"Predictors of all-cause mortality in participants with high vs. medium/ low life satisfaction:"

21. There are several misprints and grammatical errors throughout the manuscript (e.g. “interviews were conducted on..” (abstract), “..but generally, they indentify.. (background) “the association of all previously mentioned factors on... (methods), “...more capable of coping with psychic distress” (discussion)
Misprints and grammatical errors have been corrected. An English native-speaker has revised the manuscript.
22. Abstract: The first sentence is aims rather than background, and should be a full sentence.
It has been changed from background to aims and it is now a full sentence.

23. Abstract: Considering the third sentence in the result section, the second sentence is redundant.
Second sentence has been changed to incorporate results on absolute risk reduction.

24. Methods, paragraph 5: The order could preferably be changed so that blood sampling is mentioned first. Additionally, spell out CVD when first mentioned.
Thanks for the suggestion. The order has been changed and CVD has been spelt out.

25. Methods, paragraph 7: I believe the common term is food frequency questionnaire rather than food frequency test.
Thanks for the remark. The term has been changed from "food frequency test" to "food frequency questionnaire".

26. Results, paragraph 7: The first part of the second sentence repeat the first sentence in the same paragraph, and may be omitted.
We appreciate this remark; it made us aware of the fact that this was misunderstood, so it is now rephrased:

"The fact that even after adjustment for cardiovascular risk factors or health factors, the relationship between mortality and LS remained significant (HR 0.61; 0.41 – 0.91 and HR 0.58; 0.39 – 0.86 respectively), suggests that both CVD risk factors and health factors are confounders in the association between LS and mortality."

27. Discussion, paragraph 7: The term DEEX-scale is not mentioned in the methods.
Thanks for the observation. We have included a sentence in Methods, paragraph 8:
"Depressive symptomatology, measured with the DEEX-scale …"
28. References: Please check the references 5, 23, 30.

Thanks again for the remark. All references have been checked and corrected.
Issues addressed by Reviewer #2:

1. The literature review is limited, in particular the rather substantial literature on the role of depression / negative affectivity in mortality is mostly disregarded (see literature cited in e.g. Bjerkeset et al. 2007). This is particularly important since measures of negative affectivity are employed by the authors, and may appear to play an important role, also in the present study.

   Thanks for the remark. The aim of this study is to analyse the effects of positive affect, therefore we centred on life satisfaction. Nevertheless, a new sentence has been added with references to reviews of the above mentioned literature.

   "Much research has been done on the prospective associations between negative affective states, physical health, and total mortality [1-3]. In contrast, there has been little research linking well-being with physical health, although limited evidence points to the association of well-being with greater health and longevity [4-6]."

2. The statistical methods applied are adequate, but the modelling and some of the interpretations of results leave much to be desired. The interpretation of results when “psychological determinants” are controlled for (final sentence of second para on p. 12) is clearly inaccurate: when the association between LS and mortality disappears (and the hazard ratio even turns slightly positive for women (Table 2)), this indicates that the psychological determinants are indeed confounders of the association between LS and mortality. Suggesting a “mediator role” assumes that depression etc. are intervening variables between LS and mortality, which would be a very unusual assumption in this field. It seems far more reasonable to assume that the various psychological determinants are causes of LS, and if mediation should occur, the result would be that the association between mortality and “psychological determinants” disappears when LS is controlled for. The said pattern should be evaluated within the context of the prospective relationship between depression / negative affectivity and mortality. True, the authors do report results from ancillary analyses in which “self-rated health” is removed from the model with psychological determinants (Table 2), finding that the association between LS and mortality is then restored. This suggests that self-rated health acts as a
confounder, but it would be far more informative if all the candidates within the “psychological determinants” had been evaluated and results reported. In any case, the interpretation of results for “psychological determinants” should focus on confounding, not on mediation. The upshot of this discussion is of course that a direct and causal role of LS on mortality has not been established, contradicting the authors’ assertion that “. . . LS has in men a substantial impact on long-term survival” (abstract).

We appreciate these important comments and considerations which have led to a vivid discussion in our group. We definitely agree with the reviewer that the use of the term “mediator” is set incorrectly. Therefore, we have omitted this term and, following the reviewer’s suggestion, have replaced it with the term “confounder”.

The following sentences have been incorporated:

- (Results, paragraph 7): "A different effect of psychological factors on the relationship between LS and mortality was observed, whereby the strength, significance and in the case of women, the direction of the effect of LS on mortality was changed when psychological factors were accounted for in the model. This effect modification suggests a confounding role of psychological variables in the effect of LS on mortality."

Furthermore, we analysed the confounding impact of all factors incorporated in the psychological model.

- Discussion, paragraph 4: “Our data suggest, as previously reported, [6] that LS has a favourable effect on survival in healthy and disease populations, which was lost after adjusting for other psychological determinants. The fact that LS lost significance in the psychological model, could have been caused in part by the well-established association between self-rated health and mortality [26], that may have weakened the relation between LS and mortality. Indeed, only when either self-rated health or social network index were excluded from the psychological model, the LS association with mortality is restored (data not shown). The exclusion of none of the other variables from the "psychological model" (including depressed mood) modified the association between LS and mortality."
Supplementary tables 2 to 4: with hazard ratios for each of the variables for each model (CVD risk factors, health, psychological and social). Clearly shows that only self-rated health and social network are relevant confounders in the relation between LS and mortality.

3. Effect sizes: Since the distribution of independent variables is not known, it is hard to evaluate effect sizes in Table 1. One might consider adding a column with effect sizes. In supplementary Table 1 p-values are used as proxies for effect sizes, but since many of the associations are so strong, we are unable to distinguish between the strong and extremely strong effects. Adding (linear and non-linear) effect sizes (using risk factors etc. as dependents in a series of logistic regressions) would be helpful.

Thanks for the remark. In order to address the first part of the reviewer's comment, we have incorporated in Table 1 the Cohen's effect size index. The reviewer is right, we thought about giving effect sizes also for supplementary Table 1 but decided to keep it without as this table has only descriptive purposes and is aimed to give just an overview about the data for the reader.

4. The unusual, very strong, inverse association between LS and age should be further commented upon. The comments on top of p. 16 does not reflect the vast literature on this topic and the discrepancy between current results and those of the majority of relevant studies on the subject. Why are results so unusual in the present study? Could it be that the very specific focus on health and health-related factors are responsible for this association? What about the association between self-rated health and LS, do we find a similarly strong association there?

Thanks for the important remark. Following has been introduced in the discussion, paragraph 5:

"How LS changes with age is an intriguing question, especially in light of prior findings that it improves from middle age onward, even in the face of physical health decline; little is known about the determinants of this pattern {Blanchflower, 2008 #78}{Stone, #79}. The decline in LS across life span for men and women could be partially explained by the fact that older people are more often ill and health-related
factors play an important role in LS. Indeed, when the analyses are repeated only for “healthy participants” (sensitivity analysis) we can see the previously reported U-shape pattern with lowest LS levels in middle 50s for both men and women {Stone, #79} (data not shown)."

5. There seems to be a “not” lacking in the 6th line of para 2 on p. 9. Supposedly it should say “… health factors are not confounders..”
Thanks for the remark. It has been changed.

6. The comments in the final sentence of the second para on p. 16 does not seem to make sense. Should be clarified.
Thanks for the remark. The final sentence from paragraph 6 in the discussion has been changed:

“Interestingly, although some co-morbidities (angina, insomnia, acute illness last week) were associated with differences in LS, none of these variables were relevant determinants of LS according to the logistic regression analysis.”

7. There are some lapses of grammar, syntax and spelling that need correcting (e.g. “loose” rather than “lose”, “worse health as”, the word order in the final sentence of the abstract).
Misprints and grammatical errors have been corrected. An English native-speaker has revised the manuscript.