Author's response to reviews

Title: Association between physical and mental health-related quality of life and adverse outcomes; a retrospective cohort study of 5,272 Scottish adults

Authors:

Zia Ul-Haq (z.ul-haq.2@research.gla.ac.uk)
Daniel F Mackay (daniel.mackay@glasgow.ac.uk)
Jill P Pell (jill.pell@glasgow.ac.uk)

Version: 4  Date: 12 October 2014

Author's response to reviews: see over
Ref: MS: 7237650401236466

Dear Jane

Manuscript Title: Association between physical and mental health-related quality of life and adverse outcomes; a retrospective cohort study of 5272 Scottish adults Zia Ul-Haq Daniel F Mackay and Jill P Pell

Thank you for forwarding the comments of reviewers. We have revised the manuscript to take account of these comments and we believe our manuscript is now much improved. Below is our point by point response to these comments.

Reviewer 1
Reviewer: Cyrille Delpierre
Reviewer's report:

This is an interesting paper aiming at studying the relationship between Health related quality of life (HRQoL) and subsequent health (mortality, incident cancer and CVD). Finding good predictors of health and mortality, easy to measure and use is an important topic for researchers involved in the study of health determinants. Because of the interest of the paper’s objective, I would have some suggestions to improve the message and the key findings of this article

Major comments
In the introduction it seems important to me to distinguish the several subjective health indicators that can be used and studied. As an illustration, self-reported health (SRH) and HRQoL are not identical, do not measure the same aspect of health and do not vary in the same way according to socioeconomic status (Delpierre et al. BMC Public Health 2012): in the third paragraph, authors talk about SRH and to me this is different of HRQoL. Thus this introduction should clarify that several indicators exist and that this paper analyses specifically HRQoL.

RESPONSE
We have now added the following para to the introduction:
‘There is an ongoing debate that if a single question such as, self-reported health (SRH) is available and is consistently reported to be a reliable measure then why to use a lengthy and multiple item questionnaires such as SF-36 and SF-12. However, health status measured by SRH, GHQ-12 and different measures of HRQoL are not identical (Delpierre et al 2012, Forero et al 2013). The SRH has clear advantage of reducing burden on respondents,'
particularly when the researchers are only interested for a broader view of overall health rather than a detail assessment. Nonetheless, SRH is a simple and reliable measure but it is at the cost of a detailed assessment on the individual domains of subjective well-being (Bowling 2005). A multi-item measure, such as SF-36 and SF-12 offer more precise and complete multi-dimensional information of the individual’s perception of their own health. Therefore, several indicators exist but they are not the same and should not be used interchangeably (Delpierre et al 2012). The focus of this study is the use of HRQoL as an indicator of future health outcomes”.

In the fifth paragraph it could be useful to precise how BMI is considered by authors: as a mediator between HRQoL and health or the opposite?

RESPONSE
We have now added the following sentences to the manuscript:
Introduction 5th para:
“Adiposity can act as a mediator in the association between HRQoL and adverse outcomes”.

Statistical analysis:
“We were interested in exploring whether sex or BMI could modify the relationship between HRQoL and outcomes, and thus influence the assessment of health outcomes and mortality by using HRQoL. Therefore we tested for statistical interactions between HRQoL summary scores and both sex and BMI.”

Discussion para 6-last 4 lines—
“It is possible that mental HRQoL and adiposity lie on the same causal pathway. It is not possible to be certain of the direction of effect. Poor mental HRQoL may impact on lifestyle and, therefore, increase the risk of adiposity. Conversely, adiposity may itself predispose to poor mental HRQoL”.

In Result, second and last paragraphs: I think that authors should be more specific regarding result for MCS (tables 1 and 3): for many variables (BMI, deprivation, education) the relationship with MCS is not linear but in U shape. Then people with high MCS and low MCS show similar proportions of obese, comorbid, not deprived and high educated people. This phenomenon could explain partly the fact that for cancer and CVD, people reporting lower MCS could have a lower probability of cancer and CVD that people reporting high MCS. The ageing, social, comorbidity and obesity gradients do not exist for MCS and should be presented.

RESPONSE
We have now added the following sentences to the results section:
“There was a U-shaped relationship between BMI, level of education and socio-economic deprivation and higher MCS score (Table 1). Compared to the participants who were in the highest quintile of MCS (better mental HRQoL), those in the lowest quintile had similar proportions of obese, hypertension or diabetes, not socio-economically deprived, and
As a consequence, in the discussion, the difference concerning results observed with PCS and MCS should be discussed and argued. In particular the determinants of these 2 measures that could explain differences and also that could have been omitted in the analyses as confounders.

RESPONSE
We have now added a new Para (para 5) to the discussion:

“We did not explore the underlying mechanism by which HRQoL may impact on morbidity and mortality. Self-perceived health is more inclusive and provides additional information by incorporating both objectively measured and subjective assumptions of health risk (ref). HRQoL may identify accurate health status by covering those aspects of health which are difficult to capture by objective measurements such as subclinical disease, help-seeking behaviour and health system (ref). Better HRQoL may reflect an individual’s attitude towards improving health, and thus adopting preventive measures. In contrast, the low HRQoL may result in neglecting of the primary or secondary prevention such as healthy diet, physical activity, screening and taking regular medication for existing medical conditions which may eventually result in early death or disease incidence (ref). MCS was not associated with health outcomes. The exact mechanism is not known but there was a dose-response relationship between base-line BMI, level of education, comorbidity and socio-economic deprivation and low PCS. In contrast, there was a U-shaped relationship with MCS. Our current findings that comorbidity, ageing, social and obesity gradient do not exist for MCS could partly explain the fact that the participants with low MCS has lower risk of cancer incidence and CVD events, compared to the high MCS. Furthermore, one of the reasons of no significant association in MCS may be that SF-12 only detects the mental health wellbeing and not the severe mental disease.”

Minor comments:
In Methods: indicated classes built for alcohol consumption

RESPONSE
This is now provided to read as:
“alcohol consumption was categorized as never, previous, within limits (<21 units/week for men; <14 units/week for women) and excessive.”

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: no conflict of interest
Reviewer 3

Reviewer: Carlos Garcia Forero

Reviewer’s report:
The paper “Association between physical and mental health-related quality of life and adverse 4 outcomes; a retrospective cohort study of 5,272 Scottish adults” deals with the association between SF12 scores as predictors of health outcomes, both in the physical and mental components.

The paper is well-written and structured, but I’d like to point out some remarks for author consideration, mostly dealing with data analysis strategy.

Major compulsory revisions:

1) My main concern is the categorization of scores in the Cox models. While it is understandable that discrete categories using cut-off points are useful for clinical decisions, it is not necessarily so in population studies. In fact, it can lead to substantial power losses and misleading results (see, for instance, Royston et al. 2006, whose points can be generalized to any kind of regression model). In fact, the categorization of SF12 scores in quintiles might seem a bit arbitrary. Given that Cox regression allows mixing predictors of different measurement status, I’d recommend the authors to repeat the analysis treating PCS and MCS (and perhaps BMI and age) as continuous. I know that interpretation might be a bit more cumbersome as results in this case are hazard changes in 1-unit score changes, (however the score changes can be changed for more informative hazard scale changes), I believe that PCS and MCS results would greatly benefit from such treatment. I’d strongly recommend the authors to change the analysis strategy to continuous covariates for a stronger message. Otherwise, they must provide a stronger rationale for choosing the quintile discretization of SF scores, which seems a bit loose at the moment.


RESPONSE

We have now added to the methodology- inclusion criteria and definitions:
“For the ease of interpretation, PCS and MCS score quintiles were used in the analyses (Haring R et al 2011, Saquib et al 2013).”

Saquib et al. BMC Public Health 2013, 13:46

We have now acknowledged this as a limitation of this study and have added below to the discussion, last para

“Previous studies have also used the quintiles of PCS and MCS for the ease of interpretation (ref) but it may lead to considerable power loss and misleading results.”
Minor essential revisions:

2) While the SF12 PCS and MCS are the more commonly used scores for the SF12, they are not necessarily the only scoring systems (see for instance the RAND12 or multidimensional IRT models approximations for scoring the SF12). I understand that the authors chose a scoring system, and it is not necessary to repeat the analysis further, however, the existence of other possibilities and potential influences in results are recommended to be acknowledged in the discussion.

RESPONSE
We have now added below sentences to the discussion:
“We have used the SF12 PCS and MCS scoring system for the SF-12 but the alternative scoring systems are also available such as RAND-12 and multidimensional item response theory (MIRT) models (Forero et al 2013, Forero et al 2014). It is suggested that these alternatives models may have more power to detect the true differences and can also provide more reliable and intuitive scoring, particularly when the SF-12 is used to assess the mental health status (Forero et al 2013).”

3) A limitation section in the discussion should be included. Using retrospective designs has its own caveats, but there are others depending on the nature of the analysis (for instance, what could be the results if a non-proportional hazard model had been used, or —if the authors stick to the categorical predictor approximation, it should be mentioned as a strong limitation of this work).

RESPONSE
We have now added the below limitation section to the discussion;
“The advantage of retrospective cohort study includes readily access to data but it is at the cost of lack of control over the data collection. By treating PCS and MCS as ordinal data we were able to examine whether there were evidence of a dose relationship. Previous studies have also used the quintiles of PCS and MCS for the ease of interpretation (ref) but it may lead to considerable power loss and misleading results.”

4) Table 1 is nice, but I miss a table with sample characteristic information and the overall distribution information in the full sample (and not just by quintiles)

RESPONSE
We have now added a supplementery table (Supplemental Table 1) for the overall distribution.

Discretionary Revisions:
The MCS results could have been related to adverse mental outcomes (such as incident severe psychopathology, suicidality). Did the authors have access to such information? It is not a heavy criticism and more like a personal curiosity, but it is out of doubt that this would
be a quite relevant information, and I’d love to see some results or comments on the issue, where they available either in this or future papers.

RESPONSE
Thank you for this very good suggestion. Unfortunately, we do not have access to adverse mental health outcomes at this stage but we are considering this in our upcoming research.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests

Reviewer 2
Reviewer: Chiara de Waure
Reviewer's report:
The paper "Association between physical and mental health-related quality of life and adverse outcomes; a retrospective cohort study of 5,272 Scottish adults" deals with the impact of HQoL on the occurrence of CVD, cancer and death. This topic is quite interesting and up to date but, in my opinion, is deeply biased. In fact, HQoL is related to well-being and, actually, it is highly predictable that the lower the HQoL the higher the risk for chronic diseases and deaths. This is also demonstrated by the results that Authors got. In fact, the occurrence of CVD, cancer and death was shown to be associated to PCS but not to MCS. It is clear that a low PCS is due to physical impairments and that the latter could explain the exceeding risk.

RESPONSE
Conventionally, health is measured narrowly using symptoms, physical signs and objective measurements, such as laboratory tests, to indicate the presence or absence of disease. Although health makes an important contributor to overall “quality of life”, the latter is also influenced by many other aspects of life, such as education, housing, employment, leisure time, neighbourhood and social belonging. HRQoL may identify accurate health status by covering those aspects of health which are difficult to capture by objective measurements such as subclinical disease, help-seeking behaviour and health system use. However, our knowledge about the self-perception of health and its association with long-term outcome is still in its early phase and more scientific research is needed. This research which was adjusted for important baseline risk factors, including diabetes and hypertension may strengthen the growing evidence that HRQoL provides additional information and is predictive of future morbidity and mortality. Individuals with poor HRQoL are a higher risk group who may merit closer surveillance and earlier intervention.

Establishing relationships between HRQOL with adverse outcomes may encourage the inclusion of self-perceived health assessment to the daily clinical consultation as a screening
tool and also encourages the doctors to inquire about the detailed aspects of patient’s health and well-being. Self-perceived health is an important indicator of both health and health risk and its routine use may enhance individuals and community health.

Alongside this major concern that impairs the originality and relevance of the paper, there are further major concerns to be addressed.

**Introduction**
- the Authors did present the results of a retrospective cohort study on the same topic. Why did they perform the new study? Is not a duplicate?

**RESPONSE**
As pointed out by Reviewer 1 that “In the introduction it seems important to me to distinguish the several subjective health indicators that can be used and studied. As an illustration, self-reported health (SRH) and HRQoL are not identical, do not measure the same aspect of health and do not vary in the same way according to socioeconomic status (Delpierre et al. BMC Public Health 2012): in the third paragraph, authors talk about SRH and to me this is different of HRQoL. Thus this introduction should clarify that several indicators exist and that this paper analyses specifically HRQoL”.

In response we have added below to the introduction;
“There is an ongoing debate that if a single question such as, SRH is available and is consistently reported to be a reliable measure then why to use a lengthy and multiple item questionnaires such as SF-36 and SF-12. However, health status measured by SRH, GHQ-12 and different measures of HRQoL are not identical (Delpierre et al 2012, Forero et al 2013). The SRH has clear advantage of reducing burden on respondents, particularly when the researchers are only interested for a broader view of overall health rather than a detail assessment. Nonetheless, SRH is a simple and reliable measure but it is at the cost of a detailed assessment on the individual domains of subjective well-being (Bowling 2005). A multi-item measure, such as SF-36 and SF-12 offer more precise and complete multi-dimensional information of the individual’s perception of their own health. Therefore, several indicators exist but they are not the same and should not be used interchangeably (Delpierre et al 2012). The focus of this study is the use of HRQoL as an indicator of future health outcomes”.

**Methods**
- Operational definitions are not all provided (e.g. category of alcohol consumption: what did the Authors mean with "within limits" and "excessive"?).

**RESPONSE**
This is now provided to read as:
“alcohol consumption was categorized as never, previous, within limits (<21 units/week for men; <14 units/week for women) and excessive.”
• Comorbidity is not investigated in deep. The Authors speak about hypertension and diabetes but what about the information collected through saliva and urine samples? According to me it is not right to say that results are adjusted for comorbidity if they took into account only hypertension and diabetes.

RESPONSE
“Comorbidity” is now changed to hypertension and diabetes throughout the manuscript.

• In statistical analysis, Authors described how they tackled interactions. But why did They choose to study only interactions with BMI and gender?

RESPONSE
We have now added to the statistical analysis;

“We were interested in exploring whether sex or BMI could modify the relationship between HRQoL and outcomes, and thus influence the assessment of health outcomes and mortality by using HRQoL. Therefore we tested for statistical interactions between HRQoL summary scores and both sex and BMI. “

We have mentioned in Discussion para 6:
“It is possible that mental HRQoL and adiposity lie on the same causal pathway. It is not possible to be certain of the direction of effect. Poor mental HRQoL may impact on lifestyle and, therefore, increase the risk of adiposity. Conversely, adiposity may itself predispose to poor mental HRQoL”.

Results
• Looking at PCS and MCS classes, there are overlapping (e.g. as for PCS, score 51 is included in the second and third classes and score 55 is included in the third and fourth classes; similarly, as for MCS, 53 is included in the second and third categories and 56 in the third and fourth ones).

RESPONSE
This is now corrected

• There are some significant results for MCS which are not elaborated on at all.

RESPONSE
We have now added this in response to the reviewer 1 comment (Result 2nd and last para)

Discussion
• Authors stressed that the results of their study are applicable to the general population and that this distinguishes their study from previous ones. Notwithstanding, specific populations may be included in the general population and Authors did not try to make sub-analysis excluding them.
RESPONSE

Our claim that the results of this study are applicable to general population is based on the use of the Scottish health survey. We have now added below sentences to the discussion, para 8;

“The Scottish health survey has rigorous methodology and maintains the overall higher response rate of 60% or above from the eligible households. The age and sex proportion of the adult respondents is externally validated with the General Registrar Office for Scotland mid-year population estimates. The Scottish health survey used weighting to take account of the underrepresentation of the large households responses and non-response biases. It is also considered to be representative of the Scottish population in terms of the SIMD quintiles (Lawder et al. 2010; Gray et al. 2010).”

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests