Author's response to reviews

Title: Effect of comorbidity on health-related quality of life of injury patients in the first year following injury: comparison of three comorbidity adjustment approaches

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Concerning – resubmission revised manuscript “Effect of comorbidity on health related quality of life of injury patients in the first year following injury: comparison of three comorbidity adjustment approaches”

Dear Editor,

We would like to thank you for reconsidering our manuscript entitled “Effect of comorbidity on health related quality of life of injury patients in the first year following injury: comparison of three comorbidity adjustment approaches” under the condition that we revise it as recommended by the reviewers.

We have addressed all the reviewer’s comments, including revision of the title of the manuscript and we have performed new analysis in which we have added adjustments of the disability weights for age and sex.

We are grateful to Reviewer Janel E. Hamner for the valuable comments that we have addressed as follows:

Major essential revisions
1. We agree with the reviewer that the DALY generally refers to population based measures used by WHO and that the EQ-5D is usually used to calculate QALYs. However, injuries encompass a wide range of health outcomes. The currently available sets of disability weights, such as the set of disability weights derived or the Global Burden of Disease 1996 study and the set of Dutch Disability Weights, do not cover the large number of health outcomes caused by injuries. Therefore, researchers conducting burden of injury studies are using disability weights based on health-related quality of life measured by multi-attribute utility instruments such as the EQ-5D. These disability weights cover the complete
spectrum of health outcomes caused injuries allowing a more complete burden of injury estimate.

2. We agree with the reviewer that sex and age may affect the disability weights. Therefore, we have adjusted the disability weights for age and sex using the UK EQ-5D population norms (Kind et al., [1]), as described in the methods section (page 7, line 1-3). Dutch EQ-5D population norms are not available. The sample of patients was too small to assess whether comorbid diseases were associated with particular types of injury. Furthermore, we have performed linear regression analysis to determine the goodness-of-fit of the predicted comorbid disability weights using the three comorbidity adjustment methods (see methods, paragraph analysis, page 9, 11-13).

3. The reviewer asks whether the patients were restored from their injuries at 2.5 months after the injury, otherwise the estimation of the impact of injury may be diluted. In this study, patients not recovered from the injury at 2.5 months were included.

4. The percentage of injury patients that were restored from their injuries 9 months after injury was lower compared to the total sample of injury patients, of which 29% of the patients reported comorbid conditions. This percentage is comparable to the proportion of patients with comorbid disease found in previous studies. We have included this in the discussion section (page 13, 4-8).

5. The predicted disability weights were calculated for each injury patient separately. Figure 2, each data point represents a patient. We have included this in the results section (page 10, line 18-20).

Minor essential revisions

1. We removed the line “The adjustment approaches performed better in case of comorbid injury and severe chronic disease” from the abstract.

2. We removed the part in which the different types of comorbidity were discussed from the introduction section.

3. We adapted the color scheme of Figure 1. In the revised Figure 1 ‘injury’ and ‘disease’ have different colors, which look much better, thanks you!

4. The reviewer notes that in the paper, disease and condition were used interchangeably. We have replaced condition with disease throughout the manuscript.

5. The reviewer asks what criteria were used to establish ‘reasonable results”. We have removed the phrase from the manuscript.

6. We agree with the reviewer that the EQ-5D has large ceiling effects in the general population. These ceiling effects may also affect the measurement of health-related quality of life measured by EQ-5D among injury patients with mild short term injury. We have added this limitation of the EQ-5D in the discussion section (page 13, last 5 lines).

We thank Reviewer S. Shahraz for reviewing our manuscript. We are grateful to the reviewer for his suggestions. We have addressed them as follows:
Major essential revisions

1. We agree with the reviewer that assigning a disability weight by using the EQ-5D instrument has limitations. However, in this study, in order to use empirical data to test the comorbidity adjustment approaches, actual reported patient data are required. Therefore, we have used disability weights based on EQ-5D data. We have added this to the discussion section (page 13, last five lines and page 14, line 1-3).

2. The reviewer is right in that it would be valuable for the manuscript if we should not only describe the correlations between the 2 parameters, but also to value them. Therefore, we have used regression analysis to interpret the results of the correlation in terms of goodness-of-fit of the predicted comorbid disability weights. These sections are included in the results section (page 10, last 5 lines).

3. The response rate is indeed low and we agree with the reviewer that a missing data-analysis is crucial. However, a detailed description of the follow-up study and non-response analysis are presented in the publication of Polinder et al. [2].

Minor essential revisions

4. The reviewer notes that a good number of limitations of the studies have been mentioned.

5. We agree with the reviewer that backache is a symptom and not a disease and that arthrosis is an obsolete terminology. We have replaced arthrosis with osteoarthritis throughout the manuscript.

6. The reason for picking the six conditions is that they were asked specifically in the questionnaire items regarding the presence of one or more chronic disease(s) prior to the injury to assess comorbidity.

7. The reviewer notes that the assumption that injuries have no effect on the reported severity of functional loss of osteoarthritis after 9 months can easily be violated. However, the patients indicated in the questionnaire whether they still suffered from consequences or whether they were restored completely from their injuries.

8. We agree with the reviewer that not adjusting for sex and age is a major drawback. Therefore, we have adjusted the disability weights for age and sex using the UK EQ-5D population norms (Kind et al., [1]) as described in the methods section (page 7, line 1-3). Dutch EQ-5D population norms are not available.

9. We have removed the introductory explanations in the conclusions section.

We are grateful to Reviewer Pieter H. M. van Baal for his valuable comments that we have addressed as follows:

1. The reviewer states that comorbidity may complicate burden of disease studies for two reasons: a) frequency of disease combinations and b) impact of the disease combinations. We agree with the reviewer that this paper deals with the second reason. We therefore adjusted the title of the manuscript ("Effect of comorbidity on health related quality of life of injury patients in the first year
following injury: comparison of three comorbidity adjustment approaches”). Furthermore, we removed the part regarding the different types of comorbidity from the introduction section.

2. To clarify the methods section, we have changed parts of the methods section. Secondly, the analysis of the data has been revised. We have adjusted the disability weights for age and sex of the participant using population norm scores from the UK (Dutch EQ-5D norm scores are not available). Also, we have performed linear regression analysis to determine the goodness-of-fit of the predicted comorbid disability weights using the three comorbidity adjustment methods. Since the 9 months EQ-5D data was used as a proxy for pre-injury health-related quality of life in order to calculate the predicted comorbid disability weights, we do not think that a GEE analyses should be applied in order to account for the repeated measurements.

The article is revised on the Population Health Metrics web page. The specific revisions due to the review comments have been highlighted. In case of further queries we are most willing to help.

Kind regards,

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References