Author's response to reviews

Title: Health-related quality of life after vertebral or hip fracture: a seven-year follow-up study

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Author's response to reviews: see over
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Authors’ response to referee 1: See following
Statements and answers related to the comments on our article. A point-by-point response to the reviewer’s suggestions is given below, with reviewer comments in black and our responses in blue. The main changes and additions, based on comments from the referee 1, are highlighted in yellow in the revised manuscript.

Referee 1

Reviewer's report
Version: 2 Date: 26 June 2009
Reviewer: Lisa Lix

Reviewer’s report:
The authors have made substantial revisions to this manuscript in response to multiple reviewer comments. Reviewer comments focused on issues of missing data, control for confounding covariates, characteristics of the reference group, and methods for assessing change over time.

Major Compulsory Revisions
The paired t-test analysis associated with objective (i) does not address a number of concerns raised by reviewers, including control for confounding covariates and bias due to missing observations. A paired t-test analysis is limited to individuals who have complete data at both the two-year and seven-year measurement occasions and cannot take account of any time-varying covariates (such as subsequent fracture) that may be associated with changes in quality of life. The authors have attempted to address the latter point by stratifying the data using information about fractures in the study observation period. However, by using paired t-tests and stratified analyses the authors have conducted multiple tests of significance without concern for the familywise error rate, the probability of making at least one Type I error in a family of tests. The authors should use a random-effects model with time-varying covariates to analyze these data; this would produce results for a single parsimonious model and allow them to test for differences between the two fracture groups in the change over time. As noted in the previous review, a random-effects model does not assume complete data for all subjects and allows for the inclusion of multiple covariates in the model of change over time.

Regarding the aim (i), to control for confounding covariates we also determined the mean value differences between hip and vertebral groups regarding change with ANCOVA. However, between the fracture groups there were no significant mean value differences in the change between two and seven years, or after controlling for covariates, age, new co-morbidity and new fracture. The ANCOVA analysis might have been reformulated as a random-effects model but in this case (restricting the analysis to the 67 patients who participated on both occasions) this would have yielded the same results.
The objective as well as the analysis have been limited to the two-year and seven-year follow-ups (as recommended by one of the reviewers). We believe there might be problems involved in including patients with missing data in the models, so we limited the analyses to the 67 patients with data from both occasions. Of course, it would be interesting to do some type of sensitivity analyses (testing different imputed values on missing observations, for example), but these are beyond the scope of this paper.

New text has been added to Statistical Analyses on page 12, and Results on page 14.

The t-test analyses reported in Table 3 involving the conduct of 16 tests of significance, each at the .05 level of significance. Assuming that the tests are independent, the probability of making at least one Type I error among these 16 tests is 0.56. The authors need to address the issue of multiple testing and control of the familywise error rate.

The partial correlation analysis conducted for objective (iii) and reported in Table 4 involves the assessment of statistical significance of 48 partial correlation coefficients. Consistent with my previous comment, the authors must address the issue of multiple tests of significance and control of the familywise error rate.

We agree with the reviewer; multiple testing increases the risk of obtaining a significant difference purely by chance. Therefore, the results should be interpreted with caution in this study. If a simple sequentially rejective multiple test procedure (Holm’s method) had been used, most of the results in the study would still be significant.

This information is now addressed in the discussion of limitations on page 22, in Discussion.

Furthermore, more precise p-values are now reported in Tables 2-5, for the reader’s own assessment.

Also, I am unclear why the footnote to Table 4 refers to “differences” between partial correlation coefficients.

Table 5 refers to partial correlation; we have changed the footnote and moved most of the information to Statistical Analyses, page 12.

The statement “differences between” is not correct in this sentence and context; we have thus removed this statement.

Minor Essential Revisions
Tables 2 and 3: I would recommend removing the symbol "(SD)" from each row header. Instead, include a table note indicating that values in parentheses correspond to standard deviations.

We have corrected this in Tables 2 and 3.
Table 4: The information about the association between the covariates and the SF-36 domains should be moved into the text of the manuscript rather than being included in a footnote.

The information has been moved to Results, page 15.

The symbol "(CI)" should be removed from each row header. Instead, include a table note indicating that values in parentheses correspond to 95% confidence intervals.

We have corrected this in Table 4.

Thank you for all the valuable comments!