Author's response to reviews

Title: Evaluation of Easily Measured Risk Factors in the Prediction of Osteoporotic Fractures

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Version: 2 Date: 27 May 2005

Author’s response to reviews: see over
Dear Editors:

Please accept this revised manuscript for consideration for publication in BMC Musculoskeletal Disorders. The contents of the manuscript are original and have not been published elsewhere. The material and results outlined in this manuscript are of considerable value to clinicians and in the prediction of fragility fracture risk.

The following pages address comments made by the reviewer of this manuscript. We have attempted to clearly and concisely address all of these comments. If you have any additional comments please feel free to be in contact.

Yours sincerely,

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**MANUSCRIPT REVISIONS**

**Major Compulsory Revisions**

1.) The author's statement that the CANDOO database consists of over 10,000 men and women, however data is only shown for 3426. The authors do not inform us why the remaining subjects were excluded and do not discuss any bias implications.

- There are 10000 men and women in the CANDOO database—we only included: postmenopausal women over 55 years, those with a baseline visit, those with a follow up visit, and those with multiple fractures.
- This criteria left 3426 applicable subjects
- We have emphasized this more clearly in the 2nd paragraph of the methods section and have introduced the issue of gender bias.

2.) Subjects with multiple fractures were excluded - if the index fracture was included this would increase the numbers of fracture cases significantly. Can this data be added?

- This would definitely increase the number of fractures cases however it would make it difficult to group subjects into respective categories for analysis. For example, it would be difficult to place a subject in the hip fx group if that individual had multiple fractures at different sites.
- We assume that this is what you are referring to however if not then we have data available to clarify.

3.) No information is given regarding the follow-up period. Can information regarding the length of follow-up and how follow-up was achieved be added to manuscript?

- Patients in CANDOO had yearly follow-up assessments, although for a variety of reasons this did not occur for every patient
- These visits occurred at multiple clinical centres
- All included patients had an initial assessment and at least one follow up assessment collecting the same information. The majority of subjects had multiple re-assessments.
- We have clearly added this information to the 1st paragraph of the methods section

4.) Fracture status was based on self-reports and x-ray confirmation. However no numbers are provided for this. If the majority of cases were self-reported this will introduce a bias since it has been shown previously that recall data is not very reliable and differs by skeletal site.
The majority of cases for incident fracture were confirmed by x-ray. This has been made clear in the manuscript.

Although recall data has questionable reliability at times, a variety of data also exists to support the use of self-reported data in fracture analysis. Below are a list of references supporting its use:


5.) *The Fracture Index on which the analysis is based also contains a total score (with or without BMD) but this is not used in this analysis. It would be interesting to identify the sensitivity/specificity of the total score in this database with regard different fracture types.*

The purpose of our analysis was to examine some of the key risk factors from the Fracture Index rather than actually assess the usefulness of this tool specifically. In this regard we are not in a position to actually use the Fracture Index on the individuals in the database. Such results would indeed be interesting.

6.) *Why was hip, vertebral, wrist and rib fractures chosen? Many now accept that hip, wrist, vertebral and humeral fractures are "osteoporotic" fractures. Rib fracture are very difficult to confirm, but humeral fractures would be easier. Do you have data on fractures of the humerus?*

- It is very true that humeral fracture is easy to assess and now considered an osteoporotic fracture. However, the CANDOO database only has information on vertebral, hip, wrist and rib fractures.
- For this reason we focused only on these sites for new incident fractures.

7.) *T-score of the hip was included as a risk factor, however from Table 1 it appears that only 447 individuals had BMD assessment. Can you clarify this and make it clear in the manuscript that not all subjects had BMD assessment?*
This is correct…only 447 of the eligible candidates from CANDOO had BMD assessment information.

It has clearly been added to the methods, results and discussion sections that not all subjects had available BMD assessments and that this could be an important reason for the observed results with BMD.

**Minor Essential Revisions**

8.) **When giving the results of the multivariable regression it is stated that some risk factors were at "higher risk of developing a new hip fracture". These risk factors were not statistically significant. Can you make it explicit that these was simply a trend for higher risk, and these were not statistically significant.**

   - This has been corrected throughout the paper to reflect the increased trend towards higher risk.
   - We have also attempted to more clearly delineate those variables that were significant and those that were not.

9.) **In the figures can Family Hx Fx be changed to Maternal Hx Fx, as it is not family history but maternal history that has been used. The figures are also difficult to see especially the error bars. Can the figure background be changed so the data can be seen more easily?**

   - All figures have been changed to incorporate Maternal Hx Fx under the heading “Mat. Hx Fx” as the figures were space constrained.
   - The figure background and the font have been changed to make the data more clearly visible