Author's response to reviews

Title: Bone densitometry and osteoporosis treatment after a fragility fracture in older adults: regional variation and determinants of use in Quebec

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Version: 2 Date: 30 March 2005

Author's response to reviews: see over
Sherbrooke, March 30th 2005

BMC Musculoskeletal Disorders
Submission of the revised manuscript: « Bone densitometry and osteoporosis treatment: regional variation and determinants of use in Quebec ».

To the editor,

On behalf of my colleagues, I am pleased to submit this revised draft, which I am confident will meet with your highest publishing standards. I want to thank Dr Cadarette for her invaluable and pertinent comments which formed the starting point for many of our changes. Below, you will find a detailed list of all the changes made in response to each the reviewer’s comments.

Should you have any further questions, please feel free to e-mail me at the address below. I look forward to hearing from you.

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RESPONSES TO THE REVIEWER SUZANNE CADARETTE:

General comments
This new version has been revised according to the reviewer’s comments and suggestions. The main changes made are the following: addition of osteoporosis (OP) treatment as an outcome of interest; addition of possible predictors to bone densitometry (BDM) and to osteoporosis treatment; removal of regression trees; removal of regional rates of deaths and incidence of fragility fractures.

Major Compulsory Revisions
1. Clarify OP drug availability vs. OP drugs covered by Quebec pharmacare.
   In Quebec, since 1996, almost all individuals 65 years and older are covered by Quebec Health Insurance Plan. We added this information in the method section (studied variables).
2. Include recent publications to strengthen background, methods and discussion...
   We read the three publications as suggested by the reviewer. They were not discussed in the earlier version because it was submitted prior to their dates of publications.
3. Missing important potential confounders/predictors available from claims data, e.g.: a) comorbidity; b) long-term steroid use; c) prior BDM test; d) Health services use and physician characteristics; e) see suggested references for others.
   We added some of the suggested predictors:
   a) We defined the comorbidity index as the total number of distinct prescription drugs dispensed during the year before the index date (Schneeweiss, et al. 2001). In order to take into account only comorbid conditions, we subtracted the number of OP related medications dispensed during that same period;
   b) We also included the long-term glucocorticoid use as extensive glucocorticoid therapy (at least 90 days in the 120 days before the index date) at a dose $\geq 5$ mg per day (Schneeweiss et al., 2001);
   c) We also added the presence of a prior BDM test in the 2 years preceding the index date was also added as a predictor of future BDM testing and as a predictor of future OP treatment;
   d) & e) Other predictors such as race and physician characteristics were not available in our data base.
4. Including treatment pre fracture and post fracture (within 30 days) has potential problems: mixes BDM for screening/OP diagnosis with BDM testing to monitor response to therapy, includes some but not all treatment prior to BDM testing.

We acknowledge that including OP treatment before and after the fracture as one single variable mixes BDM for screening/OP diagnosis with BDM testing to monitor response to therapy. We redefined OP treatment as treatment prior (1 year before) to fracture. OP treatments included bisphosphonates, HRT, calcitonine or raloxifene.

5. When comparing rates between regions: use small area variation statistics and comment on the stability of the reported rates.

We calculated the smoothed age-adjusted rates of BDM by a method developed by Fortheringham called geographically weighted regression (GWR). The model employed here was the regional rate of BDM as a function of gender, allowing the $\beta$ parameters to vary spatially. This method takes into account neighbouring regions into the modeling process; the resulting estimated rate provides a kind of smoothed estimated rate.

6. From what is presented in the paper, the benefit of regression tree analysis is not clear to me...

Regression tree is a method for which information on a data set is summarized by dividing the population into a number of subgroups, as homogeneous as possible but distinct with respect to the parameters to predict. The subgroups are identified by a tree-structured figure of binary questions on the predictors. The resulting classification is the most informative one with respect to the parameter in question. Tree-growing techniques are particularly suited to handling a large number of variables, and to investigating the interactions between those variables.

As suggested by the reviewer, we excluded the regression trees from the analyses. This kind of analyses will be the focus of another paper.

7. Sensitivity analysis: a) comment on adjusted results if exclude patients who die within two years...b) Prior BDM test, treatment: how do predictors change if exclude prior BDM testing and/or treatment prior to BDM test. This sensitivity analysis will help disentangle some of the predictors for screening to make treatment decisions vs. testing to monitor response to therapy.

In this revised draft, we analyzed data without excluding patients who died in the years following the fracture. When we did exclude them, we found results similar to those of the predictors of BDM testing and OP treatment, although the
magnitude of the odds ratios (OR) associated with the site of fracture was lower. In fact, a greater proportion of patients with a hip fracture died within two years post fracture than those with a fracture at any other site, which can cause a difference in the OR estimated.

In order to test the stability of the $\beta$ parameters, we excluded the variables: prior BDM testing and prior OP treatment. The resulting models show similar results between predictors and outcomes. The only predictor that seems to be affected by this removal is the long-term glucocorticoid use which can be explained by the fact that patients receiving a glucocorticoid therapy have had already BDM testing and/or OP treatment.

**Minor Essential Revisions**

1. **Broaden title/abstract or limit study to post fragility fracture BDM testing.**
   As suggested by the reviewer, we restricted the paper to BDM testing, i.e. we omitted fracture incidence and deaths rates by region. On the other hand, we added OP treatment as another important outcome. We changed the title accordingly.

2. **Clarify outcome of interest. What methods of BDM testing were considered? List all of the methods included, e.g. DXA, etc. If only DXA, then state this specifically and use this acronym instead of BDM.**
   We considered BDM by DXA only. In Quebec, all BDM testing are done with DXA. Other techniques (QCT, ultrasound etc.) are used for large population screening or are used in research centers. They are not covered by the Quebec Health Insurance Plan.

3. **p5: Osteoporosis Society of Canada instead of Canadian Osteoporosis Society**
   We changed it in the text.

4. **Excluding prior fragility fracture within 2 years is reasonable when examining post-fracture BDM testing. However, authors should acknowledge that this will not exclude all cases with prior fracture...**
   We acknowledge this in the discussion.

5. **Table 1: modify so specific to population under investigation, i.e. 65+ with fragility fracture.**
   We modified the titles of the tables in order to give more explicit information.

6. **Table 4&5: combine, omit p-values, present adjusted OR estimates as OR (95% CI).**
   We combined in the same tables the results from the logistic regression models for the 2 outcomes of interest, namely, BDM testing and OP treatment. We also
omitted the p-values, but the significance ranges now appear in the footnotes of the tables.

7. **Add limitation of using BDM testing as the end point to examine care gap to discussion.**
   Hard to know if care gap vs. different management strategies in regions if don’t also examine treatment.
   
   We recognize that BDM testing can be very different from one geographical region to another because of the limited access to BDM in some regions. By adding the outcome OP treatment, we see that there is regional variability in OP treatment. However, this is not as important as for BDM.

**Discretionary Revisions**

1. **Include treatment rates by region.**
   We included regional OP treatment rates 1-year post fracture.

2. **If all OP drugs open listed, consider OP treatment (or combination BDM testing/OP treatment) as the outcome.**
   We added this as an additional outcome.

3. **Given hierarchical nature of the data, consider multilevel analysis.**
   Since we did not have information on treating physicians from the administrative data base, we could not consider this kind of analyses.

4. **Omit figures 1, 4 & 5.**
   We omitted the figure 1 explaining the cohort selection since it was already explained in the text. We also excluded all regression tree analyses so that the figures 4 & 5 we removed.

**Quality of written English: Needs some language corrections before being published.**

This new version of the manuscript has been revised for language quality.