Author's response to reviews

Title: The Effect of Regular Physical Activity on Bone Mineral Density and Fracture Rate in Post-menopausal Women aged 75 and over: a retrospective analysis from the Canadian Multicentre Osteoporosis Study.

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Author's response to reviews: see over
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Editor,
BMC Musculoskeletal Disorders

To the Editor,

Please find attached one (1) copy of a revised manuscript submitted for consideration for publication in BMC Musculoskeletal Disorders. The manuscript, with the revised title of: "The Effect of Regular Physical Activity on Bone Mineral Density in Post-menopausal Women aged 75 and over: a retrospective analysis from the Canadian Multicentre Osteoporosis Study", carries the identification number: MS: 9810954448523464. As requested by Reviewer #2, a number of revisions have been made and are documented in this letter. Comments by Reviewer #1 were non-specific but have been addressed as part of the response to Reviewer #2’s comments.

Thank you for your continued consideration. Please feel free to contact me with any additional questions or concerns.

Best regards,

[Signature]

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Response to Reviewer's Comments

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Revised Title: The Effect of Regular Physical Activity on Bone Mineral Density in Post-menopausal Women aged 75 and over: a retrospective analysis from the Canadian Multicentre Osteoporosis Study

Author’s responses to reviewers’ comments in italics.

Reviewer #2:

This study is a sub-study of the Canadian Multicentre Osteoporosis Study (CaMos) consisting of 1169 women above the age of 75, utilizing data from the baseline investigation regarding physical activity level, fracture, and bone mineral density. The purpose of this study is to evaluate the association between moderate physical activity and bone mass and fracture, fractures occurring prior to the investigation and not prospectively. The authors find that an increasing amount of moderate physical activity is associated with higher bone mineral density at the hip. Prior fracture, however, is not associated with physical activity level. Additionally, the authors are evaluating other factors known to influence bone mineral density, such as anti-resorptive therapy, body mass index and age in relation to bone mineral density and fracture.

Despite being a potentially interesting report with data available for evaluating physical activity, the authors are not succeeding in focusing on their primary outcome. The paper as such is extremely long with numerous repetitious statements throughout Results and in the Discussion. Furthermore, the focus on physical activity is lost since other secondary factors are also analysed in conjunction with bone mass and fracture. Further difficulties lie in the fact that, despite noting that the CaMos study is a prospective study, all fracture data is retrospective and there is no information on time between fracture and the baseline assessment. With this it is extremely difficult to draw any conclusions of physical activity level which is evaluated as current or within the previous 12 months and fracture.

The paper needs extensive revision focusing on the main outcome and a major reduction in the text.

1. Title:
The title is not mirroring the design of the study and the findings. The effect of moderate physical activity suggests that it is a prospective study evaluating the effect on bone mineral density when it in truth is an association study. Furthermore, “fracture rate” suggests that fractures are reported prospectively which is not the case.

*The focus of the paper has been shifted to concentrate on the effect of regular moderate physical activity on bone mineral density only. The title has been altered and now reads: “The*
effect of regular physical activity on bone mineral density in post-menopausal women aged 75 and over: a retrospective analysis from the Canadian Multicentre Osteoporosis Study.”

2. Abstract:
Already in the Abstract it is unclear; even if stated that it is a retrospective analysis, it is not clarified that we are actually evaluating the association between physical activity, bone mineral density and fracture. The Abstract should also contain the actual study cohort consisting of 1169 women above the age of 75.
The time during which fractures may have occurred should also be clarified, whether it is from the age of 50 or over the entire lifetime.
Within a study of this size with over 500 patients with a history of fracture it needs to be clarified why it is not possible to report specific fracture types since they have been verified.

Information regarding fracture rate was deleted from the abstract. Anti-resorptive status, body mass index and age were clarified as confounding factors and their role in the analysis clarified.
The abstract now reads as:
“Physical activity is known to benefit many physiological processes, including bone turnover. There are; however, currently no clinical guidelines regarding the most appropriate type, intensity and duration of activity to prevent bone loss. To help address this gap in the literature, we performed a retrospective analysis of data from the Canadian Multicentre Osteoporosis Study (CaMos), a prospective cohort of 9423 adult patients, to determine the relationship between the amount of regular daily physical activity performed and bone mineral density. A total of 1169 female participants aged 75 and over provided information regarding their daily activity levels, including the amount of time spent each week performing physical activity at varying levels of intensity. Multiple and linear regression analyses were used to determine the effect of increasing amounts of this regular physical activity on bone mineral density. The results indicate that a step increase in the amount of physical activity performed each day resulted in a positive effect on bone mineral density at the hip, Ward’s triangle, trochanter and femoral neck (B=0.006 to 0.008, p<0.05). Possible confounding factors such as the use of anti-resorptive therapy, body mass index and age were included in the analysis and suggested that age had a negative effect on bone density while body mass index had a positive effect. Anti-resorptive therapy provided a protective effect against loss of bone density. The data indicate that a step increase in the amount of daily activity, using simple, daily performed tasks, can help prevent decreased in post-menopausal bone mineral density.

Key Words: osteoporosis, physical activity, bone mineral density, post-menopausal”

3. Introduction:
The Introduction should highlight the focus that it is physical activity in the elderly that is the main purpose of the study. Furthermore it should be clear what the primary and secondary objectives are, the research questions addressed and the underlying hypothesis. Furthermore that the study is not limited to patients aged 75 and over but to women 75 and over.
The research question for this study was inserted into the final paragraph and the population being studied was changed as suggested. The final two paragraphs now read as:

“Patient compliance with exercise programs is a notoriously difficult area of clinical practice. Many patients do not follow their clinician’s recommendations and, as a result, risk worsening their condition (12). One method of combating this is to attempt not to prescribe new, unfamiliar exercises to patients but instead to suggest an increase in their normal activities of daily living.

With these difficulties surrounding the prescription of exercise for at-risk patients in mind, we undertook a study with the objective of determining what relationship, if any, exists between the amount of regular physical activity performed each day and bone mineral density. We sought to answer the research question: In post-menopausal women aged 75 and over, does an increase in the amount of regular physical activity performed, as compared to inactive controls, have a positive effect on bone density? Because the risk of fracture and the consequences associated with fracture increase with age (13), we limited our study to women aged 75 and over, in an attempt to focus on an at-risk demographic.”

4. Methods:

p 6: Already on this page the number of women involved should be reported and Figure 1 referred to.

Above changes have been made. Paragraph now reads as:

“The study population for this investigation is a sub-group of the CaMos cohort. Beginning with the initial CaMos cohort of 9423 participants, all participants aged 74 years and younger were deemed ineligible for this study, as were all male participants. As a result, 1169 women aged 75 and over were deemed eligible for this study (see Figure 1).”

p 7: Data Collection: Was information from the questionnaires reassessed and the questionnaire validated?

Details regarding questionnaire development and validation are described in detail in the paper summarizing the CaMos study and its development. The reference to this paper was expanded to address questionnaire validation. It now reads:

“The study methodology, questionnaire design and validation have been summarized previously (14).”

The questionnaire completed at study entry was used and further described as the “baseline” questionnaire in the Data Collection paragraph. The sentence now reads:

“Data collected at study entry comprised information gained from baseline questionnaires and from physical examinations.”

p 7: Assessment of Physical Activity Level: From this presentation it is still not obvious exactly how the various levels were determined. Neither is it clear whether a woman can be both in the moderate activity group and simultaneously also strenuous and vigorous groups. Are strenuous
and vigorous subgroups within moderate physical activity or not. Data in the table suggest the former.
It is also unclear what type of data is used for current activity level, what has happened during the past 12 months or the past week.

The paragraph has been altered to provide better clarification of the points raised by the reviewer. It now reads:
“Physical activity was assessed through self-reporting on the CaMos questionnaire. The current level of activity for each participant was assessed, i.e. participants were asked to indicate their level of activity, on average, during each week over the previous year. Activities were defined as either “moderate” (housework, brisk walking, golfing, bowling, bicycling on level ground), “strenuous” (e.g. jogging, bicycling up hills, tennis, racquetball, swimming laps) or “vigorous” (e.g. moving heavy furniture, loading or unloading trucks, shoveling, weight lifting). For each level of activity, participants were asked to indicate how many hours per week they spent performing those specific activities. Response options included: never, 0.5-1.0 hours, 2-3 hours, 4-6 hours, 7-10 hours, 11-20 hours, 21-30 hours and 31+ hours. Categories of activity were not mutually exclusive, i.e. a participant could indicate they took part in moderate, vigorous and strenuous activities over the course of a week if that was their typical pattern of activity.”

p 8: Assessment of Fracture: Fractures were self-reported but they were also verified. Hence it is unusual that it is not known when a reported fractures occurred. Were there any limitations in the questions suggesting that it should be fractures after a specific time or if it is lifetime fractures? Why was not proximal humerus fracture, a common fragility fracture, included in the study as a separate entity? Why is not the actual number of specific fractures reported since over 500 patients did have fractures? For example the number of hip fractures and distal forearm fractures, which are common at least prior to the age of 75.

The focus of the manuscript has been altered to focus on bone mineral density as the only outcome measure. As a result, this paragraph regarding fracture has been deleted.

p 9 Statistical analysis: The authors should further specify the definition of moderate physical activity. It is not obvious that the two other categories are excluded, this is reported only later in the text. There is a lack of clarity regarding confounding factors since the confounding factor anti-resorptive therapy, body mass index and age also are independently reported.

This section was re-written to provide clarification. References to “moderate” physical activity were deleted, as the findings regarding participation at varying levels is discussed in the following paragraphs. References to fracture rate were also deleted from the statistical analysis section. The section now reads as:
“Statistical Analysis
To determine the relationship between the amount of regular physical activity performed and bone mineral density and fracture rate, two approaches were used.
Initial demographic analysis determined the general features of the cohort, including average age, height, weight, body mass index and similar descriptive statistics. Physical activity levels were analyzed and the cohort examined for frequency patterns.

To determine the effect of physical activity on bone density, regression analysis was used. Linear regression analysis was used to evaluate the effect of varying levels of physical activity at each of the five individual sites. Multiple regression analysis was used to determine the relative effect of increased amounts of regular activity on bone density, taking into account possible confounding factors such as the use of anti-resorptive therapy, body mass index and participant age. All analyses were performed using SPSS 19 (Chicago, IL).”

5. Results:
In general each section in the Results is repeating parts from the methodology and it can be extensively abbreviated. Furthermore, much of the information available in the Tables is also repeated in the text. Certain sections are using more extensive descriptions than necessary, for example on p 11 regarding physical activity. Additionally, most of what is said regarding secondary factors is a repetition of Methods and should be extensively abbreviated and put into context.

References to fracture rate in the results section have been deleted.

The first two paragraphs were altered to address the reviewers concerns. They now read:
“Figure 1 is a CONSORT diagram summarizing the eligibility criteria for the sub-group in question. Following exclusion of ineligible participants, a total of 1169 participants from the initial cohort of 9423 participants were selected for inclusion in the study.

Demographic and anthropometric data for eligible participants was collected. This data is summarized in Table I. Body mass index (BMI) was calculated as per the World Health Organization recommendations. The mean BMI of 26.2 ± 6.5 (median BMI: 26.0) of participants in this study equates to a classification of “overweight”, according to the World Health Organization classification (17).“

In the third paragraph, the descriptions of activity levels were deleted.

p 13 The Effect of Secondary Factors on Bone Mineral Density: This is section purely addresses other factors associated with bone mineral density and not at all physical activity which is the main focus of the paper. As before it is repetitious in relation to Methods and the Tables.

Data from Table III (demographic info sub-grouped based on fracture status) was added to Table I (general demographic and anthropometric data). “Secondary Factors” are now referred to as “Possible Confounding Factors”. Demographic and confounding factor data were reorganized to allow the Methods section to flow more easily. Data regarding fracture status was deleted.
p 15 The Effects on Fracture Rate: The title for this section is problematic since the report utilizes current (or 12 mo) physical activity, while we know nothing about when fractures did occur. Hence it is clearly association with previous fracture and current physical activity level and that needs to be obvious from the analysis in this and the following section.

Sections relating to fracture rate have been deleted from the manuscript.

6. Discussion
The Discussion is 11 pages long. This is an extremely long Discussion and partially it is related to it being repetitive and unfocused as to the primary purpose of the paper. Generally it is describing effects on bone mineral density and fracture where it really is an association study using retrospective data and it is not a prospective study which is acknowledged in the limitations. They should also be mirrored in the Discussion. There is also an unnecessary reporting of data within the Discussion.

p 23: It is said that it is an important finding of the study that bone mineral density decreases with age. This is well known.

This section has been deleted.

p 25: The authors are speculating extensively on the use of anti-resorptive therapy and the marginal effect of anti-resorptive therapy, whereas their second explanation not knowing when fractures had occurred is more likely that fracture patients or high risk patients are receiving appropriate treatment.
The reference by Gerdhem P et al. Osteoporosis Int (2003) on physical activity and bone mineral density in elderly women should be included in among the references.

The Discussion was largely re-written to address the concerns raised by the reviewer. Specifically, sections regarding fracture rate have been deleted. The section summarizing the activity level of women over age 74 has been significantly shortened. Data that was summarized in the Results section but re-stated in the Discussion was deleted.
The retrospective nature of the study was more plainly acknowledged, with the fact that this was not a prospective study discussed in the limitations section.
Reference to and discussion of the findings of the Gerdhem study have been added.

7. Conclusions
The Conclusions should be abbreviated and focusing on the findings.

The Conclusions section has been shortened and more focussed on the findings.

8. Tables
Table 1: Height, weight and BMI: The number of decimals should be reduced.

Changes made as suggested.
Table 2: It should be clarified exactly how the groups are stratified and that it is current or up to 12 months regarding physical activity. It appears from the Table that those who are reporting strenuous and vigorous activity are also included among those reporting moderate exercise. The moderate group totals 1168, hence it appears that one person is missing.

*The table was altered to minimize confusion, as requested. Totals were double-checked and altered as needed.*

Table 4: Please define anti-resorptive therapy. This group includes both bisphosphonate and HRT and/or combination therapy? For how long had any of the women been using any of the therapies?

*The reference to “anti-resorptive therapy” was removed as it was included participants undergoing HRT or taking bisphosphonates and was therefore redundant.*

Table 5: Ward’s triangle can be excluded from the report.

*Reference to Ward’s triangle in Table 5 was deleted.*