Author’s response to reviews

Title: Osteoporotic fractures and obesity affect frailty progression: A longitudinal analysis of the Canadian Multicentre Osteoporosis Study

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Author’s response to reviews:

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Editor, BMC Geriatrics
Ian Cameron
https://bmcgeriatr.biomedcentral.com/

Dear Dr. Cameron,

We thank you for the provisional acceptance of our manuscript BGTC-D-17-00227 entitled “Osteoporotic fractures and obesity affect frailty progression: A longitudinal analysis of the Canadian Multicentre Osteoporosis Study“, for publication in BMC Geriatrics. We have revised our article and outlined our point-by-point response to each comment below.
We thank our reviewers Drs. Testa and Hewson for recognizing the value of our manuscript. We showed that incident low-trauma hip or vertebral fractures and obesity can significantly accelerate frailty in older adults. These high-risk groups ought to be considered in public health interventions aimed to reduce or reverse frailty and ensure optimal aging.

This manuscript has not been submitted elsewhere for publication. Preliminary results of our study were presented as oral and plenary poster presentations at the 2016 American Bone Mineral Research Meeting. Dr. Olga Gajic-Veljanoski was supported by the 2016 Hamilton Health Sciences postdoctoral fellowship and Osteoporosis Canada – CaMos Fellowship award. Dr. Courtney Kennedy was also supported by the Osteoporosis Canada – CaMos Fellowship award.

All authors listed have contributed sufficiently to the project to be included as authors, and all those who are qualified to be authors are listed in the author byline. At the end of our manuscript, as required by the BioMed Central Editorial Policies and Formatting Guidelines, we included Declarations related to: Ethics Approval and Consent to Participate, Consent for Publication, Availability of Data and Material, Competing Interests, Funding and Additional Acknowledgments.

We thank you for your kind consideration and look forward to your favorable reply.

Sincerely,

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Changes requested from Reviewer 1, Dr. Gianluca Testa, M.D., Ph.D.

Minor issues:

1. The introduction should be improved, in particular on how frailty progression has been studied and why the factors that might affect this progression are not clear.

Comment #1: We have revised background section to address this comment.

Page 4, lines 7 to 9:

However, understanding how frailty progression may be modified remains unclear. Cross-sectional studies have demonstrated the impact of risk factors such as physical activity [6-8]; but,
a gap persists regarding important modifiable and non-modifiable predictors of frailty change over time.

2. The 30-item CaMos Frailty Index (CFI) should be reported somewhere either in the manuscript or in the supplemental materials.

Comment #2: The development and validation of the 30-item CFI was published previously in Osteoporosis International. We have contacted The Editors of Osteoporosis International and sought the permission for copyright of Table 1 which contains all variables included in calculations of the 30-item. We are awaiting their response but we may not be able to get it by Nov 15, 2017.

We cited the reference #16 related to the 30-item CFI in our current manuscript.

Page 18, reference 16, line 11:


We have also added two sentences describing the variables included in the 30-item CFI, Method Outcome section, sentences 4 and 5, page 6. We would greatly appreciate if you accept this addition to the text.

Page 6, lines 9 to 15:

Thus, it included the following comorbidities: osteoarthritis, rheumatoid arthritis, thyroid disease, breast cancer, uterine/prostate cancer, inflammatory bowel disease, hypertension, heart disease (e.g., heart attack), stroke, thrombophlebitis, neuromuscular disease, diabetes type 1 or type 2, and kidney disease. It also included variables related to: general health, change in general health, feelings of having energy and tiredness, as well as deficits in: vision, hearing, walking, dexterity, cognition, pain, daily work, social activities, and limitations in: in moderate activities (e.g., moving table, vacuuming, golf, bowling), lifting or carrying groceries, climbing a flight of stairs, bending, kneeling, stooping, bathing or dressing.

3. In table 1, the authors report on lifestyle factors. These are mostly cardiovascular and respiratory risk factors. The authors should better describe, in the table and in the text, the cardiovascular, respiratory and kidney comorbidities.

We have added lines to describe better comorbidities included in the 30-item CFI Please see our response above and page 6 lines 9 to 15. Predictors are all defined on page 5, lines 14 to 28 and in Table 1.

Comment #3:

4. There are several typing errors.
Comment #4: Thank you. We proofread the article to correct typos in the text.

Changes requested from Reviewer 2, David Hewson

General comments:

1. This article is an extremely well written paper that provides important results with respect to potential risk factors for changes in frailty status over time. However, the article would benefit from changing the way in which the magnitude of the significant effects reported are interpreted. In the methods section, a mean rate of deficit accumulation per year of 0.04 reported in Kennedy et al. (2014) was cited as being a clinically important difference.

Yet in the present paper, although greater physical activity significantly decreased frailty over time, the reported change was only -0.00 (95%CI -0.00—0.00) in Table 3/Figure 3. It would be worthwhile discussing these findings considering a minimal clinically important difference for the CFI. Indeed, out of the 12 significant effects reported for women, only four reached an effect of 0.04, with only 6/14 significant effects for men reaching 0.04.

Comment #1:

a) Thank you. In prior manuscript version we rounded all estimates to the second decimal in Table 3. In this revised version (the main manuscript), we rounded all estimates to the third decimal. We also added a note under Table 3, page 24:

The estimates were rounded to the third decimal and may appear inexact.

b) We addressed your comment regarding our interpretation of the magnitude of the effects by revising the part of discussion. Please see additions on

Page 9, line 25 to 27:

Their effects on frailty progression were also clinically plausible because the rates of change were greater than a previously recognized minimal clinically important difference of 0.04 [16].

Page 10, lines 9 to 10:

Our analyses also showed that quality of life and physical activity protected against frailty; however, their impact might not be considered clinically meaningful because it is much smaller than the effect of fractures and obesity.

Specific comments:

2. Page 5, line 18. The plural of the noun analysis should be analyses (analyze is the verb).
Comment #2: Revised, thank you.

3. Page 6, line 12. Change "accumulated not saturated" to "accumulated but did not saturate"

Comment #3: Revised, thank you.

4. A pertinent point is made on page 11, lines 6-11. "Future studies should examine if culturally tailored psychosocial interventions improve older adults' well-being and their compliance to interventions aimed to decelerate physical frailty." Although this comment is likely to be true, it is unrelated to the rest of the article in which issues of compliance and culture are not mentioned.

Comment #4: We made no changes to this section. We analyzed altogether factors related physical and psychosocial components of frailty. Although the impact of HRQL or living arrangement may not be substantial in our analyses (please see results section: page 9, lines 4 to 10), we think that our results indirectly align with our recommendation for future research.