Author’s response to reviews

Title: Associations between ERα/β Gene Polymorphisms and Osteoporosis Susceptibility and Bone Mineral Density in Postmenopausal Women: A systematic review and meta-analysis

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Author’s response to reviews:

Dear Prof. Stavros Liatis,

We appreciate very much your encouraging decision and reviewers’ constructive and positive comments for our original manuscript entitled 'Associations between ERα/β Gene Polymorphisms and Osteoporosis Susceptibility and Bone Mineral Density in Postmenopausal Women: A systematic review and meta-analysis'. Based on the reviewers’ comments, we have further revised our manuscript and made itemized responses to the comments as below. The changes in the revised manuscript are highlighted in red. We would like to re-submit this revised manuscript to BMC Endocrine Disorders, and hope that it is acceptable for publication in the journal. Please do not hesitate to contact us with additional questions or concerns.

Looking forward to hearing from you soon.

Below are our point-by-point responses to the reviewers’ comments.

Responses:

Reviewer #1 (Patricia Canto):
1. This is a new version of the MS ID: BEND-D-17-00137R1. The authors have improved the previous version of the manuscript and answered my questions; however, I think the discussion continues to be very long and messy.

Answer: Thank you for your comments. We have rewritten our Discussion Section.

2. In conclusions, the authors mentioned "ERα/β gene polymorphisms were significantly associated with PMOP risk and BMD in postmenopausal women...." They must to write: … in Caucasian and Asian postmenopausal women, since they only analyzed these ethnic groups.

Answer: Thank you for your comments. We have revised it in our revised manuscript (Discussion section, line 412-415, page 19). ERα/β gene polymorphisms were significantly associated with PMOP risk and BMD in postmenopausal women, but each ERα/β gene polymorphism may have a distinct effect on PMOP risk and BMD in Asian and Caucasian populations.

Reviewer #2 (Torben Harslof):

The authors have complied with the issues raised in my review. They do, however, now write that there are "2400 million people with osteoporosis in the United States alone". This is obviously not true. Please correct.

Answer: Thank you for your encouraging comments. We have revised it in our revised manuscript (Introduction section, line 68-72, page 4). Postmenopausal osteoporosis (PMOP) is a common metabolic bone disorder characterized by low bone mineral density (BMD) and increased fracture risks [1-3]. It is estimated that osteoporosis affects approximately 10 million American adults, with another 34 million being at high risk due to low bone mass[4].

Editor:

1. Please represent authors’ names using their full initials, not their full name, in the Authors’ Contributions section. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors.

Answer: We have revised it.

Authors' contributions: HPZ and JNJ participated in the study design. QW and JZ made contributions to the data collection. LZ, YJX and TLM were responsible for the statistical analysis. HPZ and LYZ participated in the writing and LYZ was also responsible for the final proofing. All authors read and approved the final manuscript.

2. Please ensure that all authors meet the following criteria. An 'author' is generally considered to be someone who has made substantive intellectual contributions to a
published study. According to the ICMJE guidelines, to qualify as an author one should have:

a) made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; AND

b) been involved in drafting the manuscript or revising it critically for important intellectual content; AND

c) given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; AND

d) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Answer: We ensure that all authors meet the criteria.

3. Anyone who contributed towards the article who does not meet the criteria for authorship can be acknowledged in the ‘Acknowledgements’ section.

Answer: Thank you for your remind.

4. Please provide figure titles/legends under a separate heading of ‘Figure Legends’ after the References. If Figure titles/legends are within the main text of the manuscript, please move them.

Answer: Thank you for your comments. We have added it.

Figure Legends

Figure 1. Flow chart showing the process of selection

Figure 2. Forest plot describing the meta-analysis under the dominant model for the association between ERα G2014A polymorphism and the risk of PMOP (GA/AA vs. GG)

Figure 3. Forest plot describing the meta-analysis under the recessive model for the association between ERβ AluI polymorphism and the risk of PMOP (AA vs. GA/GG)

Figure 4. Forest plot showed that XX genotype of ERα XbaI was associated with increased femoral neck BMD compared with xx genotype

Figure 5. Forest plot showed that Pp genotype of ERα PvuII was associated with increased lumbar spine BMD compared with pp genotype
Figure 6. Funnel plot of the ERα PvuII polymorphism and PMOP risk.

5. Figure files should contain only the image/graphic, as well as any associated keys/annotations. If titles/legends are present within the figure files, please remove them.

Answer: Thank you for your remind.

6. Figures should be provided as separate files, and each figure of a manuscript should be submitted as a single file.

Answer: Thank you for your remind.

7. Please include the email addresses for all authors on the title page. The corresponding author should still be indicated.

Answer: We have revised it.

8. Please ensure that your manuscript is formatted as per the submission guidelines at https://bmcendocrdisord.biomedcentral.com/submission-guidelines/preparing-your-manuscript/research-article

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9. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Answer: Thank you for your remind.