Author's response to reviews

Title: Study protocol: a randomized double-blind placebo-controlled trial of Classic Yin and Yang Tonic Formula for Osteopenia

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Author's response to reviews: see over
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Dear Editors and reviewers:

We would like to resubmit our manuscript “Study protocol: a randomized double-blind placebo-controlled trial of Classic Yin and Yang Tonic Formula for osteopenia” (MS: 1725176005228941) to the Trials for consideration for publication. We have carefully addressed all questions raised by reviewers and modified the manuscript (marked in blue). We have also provided ‘point-to-point’ replies to reviewers’ comments (please see the appendix). In addition, we have changed the author order, there is no conflict of interest for all authors involved in the author list.

Sincerely,

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Appendix: (reply marked with blue)

Reviewer: Marissa Lassere

Reviewer's report:
I would suggest the following modifications:
1. Abstract. "Discussion" should be "Discussion".
2. Page 7 line 5 "wrost" should be "worst".
Reply: Thanks for reviewer's comment. We have already modified the manuscript and corrected the English grammar (marked in blue).
3. References 1 and 2 are in the incorrect order. Reviewer 2 has indicated this as well.
Reply: Sorry, references 1 and 2 are in the incorrect order. We have corrected them.
4. Discussion: Please reference the sentence "it is well documented......vertebral fracture".
Reply: After carefully reviewing literatures, we have changed" it is well documented that low BMD, among all clinical risk factors, is the major determinant of vertebral fracture" to" Low bone mineral density (BMD) is a
known risk factor of fracture and a strong predictor of new vertebral fracture”, and added reference 10,11.

5. Also change "is THE major determinant" to "is A major determinant".
NB Neither BMD nor morphometric vertebral fractures are clinical endpoints. Clinical endpoints are how a patient "feels, functions or survives".
Reply: Yes, so we think BMD is not the clinical endpoint but primary outcome in this article.

6. Could confidence limits be provided around the odds ratios (reference 10). Reply: After carefully reviewing the reference, we have added the confidence limits.

Reviewer: Kent Johnson
Reviewer's report:
The re-write of the manuscript (MS: 1725176005228941) is much improved. I have only a few suggestions, some referring to clarification of the content and others to style.
Page 1, Abstract, line 6: REPLACE “evaluate the efficacy and safety” WITH “evaluate the effect on BMD and the safety”,
Page 2, last line: REPLACE “attractive” WITH “possible”
Page 3, line 7: INSERT “The” at sentence beginning with “present study”
Page 3, line 12: REPLACE “identified partially” WITH “partially identified”
Page 3, line 15: REPLACE “This trial will be” WITH “Subjects will be”
Page 3, lines 15, 16: REPLACE “to Shanghai” WITH “with Shanghai, & “to Fudan” WITH “with Fudan”
Page 3, line 20: DELETE “And” at beginning of sentence
Page 4, line 6: REPLACE “HbA1 cover” WITH “HbA1c >”
Page 4, lines 12-13: REPLACE “will be cause for exclusion” WITH “are also exclusion criteria”
Page 4, line 15: DELETE “consideration for the”
Page 4, line 16: DELETE “be”
Page 4, line 22: REPLACE “this” WITH “these”
Page 4, line 24: DELETE “placed”
Page 5, line 1: REPLACE “are” WITH “is”
Page 5, line 3: Should this be reference [1]? REPLACE “based on symptoms help” WITH “is based on symptoms and helps”
Page 5, line 20: neuro-endocrine should not be capitalized
Page 4, line 27: Clarify – Is everyone blinded? If not, who is not? State in text
Reply: The treating physicians, subjects, investigators and statisticians will be blinded to treatment assignment.
Page 7, line 16: Reference [7] does not seem to be a reference about statistics
/sample sizes. Define in text what the variables in the formula are. Sigma =, alpha=, beta =, etc Page 7, line 18: Do you assume the SD of the BMD may be improved 0.125, or do you assume the mean of the BMD may be improved 0.125?
Reply: After carefully reviewing literatures, we have changed the reference about statistics /sample sizes and defined the variables in the formula. We assume the SD of baseline BMD may be 0.125.
Page 8, line 20: REPLACE “endpoint efficacy” WITH “interest”
Reply: we replace “endpoint efficacy” with “primary outcome”.
Page 2, line 1: please describe how “kidney deficiency in TCM” is defined
Reply: In traditional Chinese medicine (TCM), kidney deficiency syndrome is a general term for deficiency conditions of kidney and Neuro-endocri-no-immune network, The symptoms mainly include: low back pain, soreness and weakness of the lumbar regions and knees, dizziness, fatigue, spontaneous sweating, a hot or cold sensation in the palms, soles and chest, dysphoria, insomnia, The pulse is weak, the tongue is red and covered without fur or bulky, moist, and covered with white fur.
We have added this part to Patients Population and Recruitment Procedure.
Reply: we have changed the order of reference [1] and [2].