Reviewer's report

**Title:** Prediction of fractures using low-frequency ultrasound - comparison with DXA-based BMD

**Version:** 1  **Date:** 24 December 2013

**Reviewer:** Albrecht Popp

**Reviewer's report:**

The authors aimed to evaluate whether and to what extent fractures were associated with axial ultrasound velocity measurements at the tibia combined with or without clinical risk factors compared to BMD measured with DXA at the femoral neck and in a cohort of elderly women. The cohort was followed for fractures between 1997 and 2010. The clinical risk factors were collected in 1997, their association with hip fractures has been published by most of the authors in this journal last year (Määttä et al. BMC Musculoskeletal Disorders 2012, 13:173).

The current study design is a mixture of a case-control study (1997-2006) and a prospective study (2006-2010). All incident fractures as well as hip fractures were regarded separately. After the direct comparison between DXA and ultrasound measurements, the predictive value of ultrasound measurements was improved by adding clinical risk factors but their weighting has been specified elsewhere.

Confusing is the focus on the low number of hip fractures: Regardless the model applied, it is hard to believe that any measurement at any skeletal site other than the hip (i.e. tibia) should be more predictive for hip fractures than BMD at the femoral neck. One could argue that there is inconsistent outcome regarding fracture risk association and ultrasound velocity measurements at the tibia.

The article is important in its field. The work is informative but major editing needs to be performed before publication is considered.

**Specific comments:**

**Title**

**Major Compulsory Revisions:**

Since the bone measurements were performed in 2006, the term of 'prediction of fractures' seems to overestimate the results of the study and should be replaced by association.

**Introduction**

**Major Compulsory Revisions:**

The first paragraph is not leading to the meaning of bone measurement on fracture risk evaluation. The context of fracture risk assessment including DXA measurement as diagnostic criterion and clinical risk factors (FRAX® etc.) is missing. Ref 1 is inappropriate (review). Without knowing the authors’ previous
article in BMC msd, the rationale for the specified combination of ultrasound measurements and clinical risk factors is missing as well and deserves explanation.

Please edit/correct the following sentences:
- 'The most common osteoporotic fractures occur at wrist, lumbar spine, and hip.'
- 'Quantitative ultrasound (QUS) has raised interest as an alternative method for measuring bone strength.' Alternative to what?

Subjects and methods
The subtitle 'Subjects' should be Subjects and clinical assessment.'

Major Compulsory Revisions: A consort chart would be very helpful.
The reviewer does not understand the reference 10 in this context: 'The standardized coefficient of variation (SCV) [10] of the method was 6.6%. Due to the lack of established reference population data, we used the present study population to define the range in SCV calculation.'

Statistics
What is the exact hypothesis?

Minor Essential Revisions
DXA criterion for osteoporosis (Ref 11) was stated in 1993, not 2003.

Results
The statement 'Femoral neck BMD did not reach statistical significance when included in the regression analyses.' does not fit 100% into the data from table 5. Please revise.

Conclusions
Major Compulsory Revisions:
Essence is not properly supported by the provided data: The statement 'In conclusion, despite the limited measurement precision low-frequency ultrasound velocity was shown to be a promising tool for assessing the risk of hip fracture.'

Level of interest: An article of importance in its field

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests