Reviewer’s report

Title: Association between metabolic syndrome and bone fractures: a meta-analysis of observational studies

Version: 5
Date: 16 January 2014
Reviewer: Peter Ebeling

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In this well written paper, Sun et al. have conducted a meta-analysis of observational studies to determine the association between metabolic syndrome and fractures. They included eight epidemiological studies involving 39,938 participants. In the overall analysis, metabolic syndrome was not associated with either prevalent fractures (OR 0.93, 95% CI 0.84 - 1.03) in cross-sectional studies or incident fractures (RR 0.88, 95% CI 0.37 - 2.12) in prospective cohort studies. A substantial heterogeneity was detected in cohort studies, but there was no indication of significant publication bias. Estimates of total effects were substantially consistent in the sensitivity and stratification analyses. The authors conclude this meta-analysis of observational studies suggests that metabolic syndrome may not increase the risk of bone fractures.

This reviewer has the following comments/questions:

Major Compulsory Revisions
1. The conclusion of the abstract is vague as currently written. Is there no effect on bone fractures or not? Please amend accordingly.
2. Perhaps a lack of effect is surprising as some recent papers have shown that both obesity and type 2 diabetes have been associated with an increased risk of fractures? As metabolic syndrome may include obesity and is a risk factor for T2DM one might well expect an increase in fracture risk. These newer papers should be critically discussed in the discussion. Nielson CM et al., JBMR 27:1-10, 2012; Compston J Curr Osteop Rep 11:305, 3013; Hamman C et al., Nat Rev Endocrinol 8:297-305, 2012; Hofbauer LC et al. JBMR 22:1312-28, 2007.
3. The article by Gagnon C et al. Osteoporos Int. 21:2067-74 2010 showed incident fractures were reduced in individuals with elevated 2-h PG levels and pre-diabetes independently of BMI and fasting insulin levels. This paper should also be cited.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests