Reviewer's report

Title: Beneficial association of serum ghrelin and peptide YY with bone mineral density in the Newfoundland population

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Reviewer: PJD Delhanty

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The study by Amini et al. examines the relationship of the gut-derived peptides ghrelin and PYY with bone mineral density (BMD) in a relatively large population of 2257 adult subjects. BMD was measured using dual-energy X-ray absorptiometry (DEXA), at a number of different sites. Ghrelin and PYY were measured by ELISA. No significant association was discovered between PYY and BMD at any of the sites measured, whereas ghrelin was positively associated with BMD and BMD Z-score in lumbar spine and femoral neck, interestingly only in women.

This is an interesting study that appears to have been performed well, although there are some issues that need to be addressed in the paper, as follows:

Major Compulsory Revisions/Comments

1. There was a significantly greater number of women in the study than men. It is unclear if the reason for the sex-dependent association between ghrelin and BMD is biased in any way by this imbalance in numbers. Additionally, there is no difference in levels of ghrelin between men (with no bone phenotype) and women (with altered bone phenotype) in the study. Could the authors comment.

2. Acylated ghrelin is extremely sensitive to de-acylation. Lack of correct stabilization could cause abnormally low measured levels. The authors must include a sentence or two describing the method they used to stabilize the acylated ghrelin in the blood samples before assaying the plasma.

3. Page 13. A recent study by van der Velde et al. (2012 Endocrinology 153:3593-602) shows that Ghsr KO mice have altered bone microarchitecture (particularly a reduction in BV/TV) at 6 months of age. This could fit with the authors’ observations in middle-aged humans, although only male mice were examined.

Minor Essential Revisions

1. The sentence beginning “A few studies were done...” on page 5 makes no sense.

2. Page 6, para. 3 change to “...performed with participants....hospital gowns.”

3. Page 7, para. 2 “According to...”. The English must be corrected.

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.