Reviewer's report

**Title:** A genetic variant of the atrial natriuretic peptide gene is associated with left ventricular hypertrophy in a non-diabetic population - The Malmo Preventive Project Study

**Version:** 4 **Date:** 1 March 2013

**Reviewer:** Carolina Medina-Gomez

**Reviewer's report:**

**Major Compulsory Revision**

1. The numbers in table 2 are not explained in the document and is surprised the elevated sample size. As far as I understand the reported analysis of association is based in are based in 968 individuals, so it is not clear what reference population the authors are using which has a frequency of 16,931 subjects. I think it is important the comparison of subjects with diabetes and non diabetes, although I think it is more interesting if the analyzed sample (n=968) is divided based on the outcome of interest. Moreover, how can the total sample represents only 92.8%?. Why the total numbers are not the sum of diabetic and non diabetic individuals?

2. Based on the discussion of the authors perhaps LVH indexed for height should be used as “gold standard” although under that model the effect of the SNP is even less significant, this is never discussed by the authors.

**Minor Essential Revisions**

1. In tables 7 and 8 do not need to report the “Full equation” line. Nonetheless the information of the explained variance is important and should be discussed both in results and discussion sctions. In these tables what do the authors refer as B and what as Beta it should be clearly stated for the readers to follow

2. The table regarding multicollinearity is based on the model LVM Indexed for Height and not in the LVM, I do not think results are different is just strange to me since it seems for the authors the main interest is in this model.

3. In page 8, regarding the p-value you can report less significant figures for the p-value.

4. In page 9 what do the authors mean by “Our sample size was relatively small and despite significant associations, the results warrant replication in a larger cohort”. The success of the replication is uncertain until the replication of the findings is done. This lack of replication is by far the weakest point in this article.

5. In the conclusion “However, our findings suggest that rs5068 or genetic variant in linkage disequilibrium might affect susceptibility for LVH and support the possible protective role of NP.” The word variant should be changed to variants.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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