Reviewer's report

Title: Associations of GC and NADSYN1 polymorphisms with vitamin D and metabolic profile in healthy adults

Version: 1 Date: 12 July 2013

Reviewer: Tamuno Alfred

Reviewer's report:

Discretionary Revisions

- Consider constructing a VitD-raising (of insufficiency risk) allelic score based on counts of the number of vitD-raising alleles each individual has and performing additional analysis

- Is it appropriate to refer to these participants as 'healthy' given the high proportions of hypertension, dyslipidemia, etc?

- In the Results section reference has been made to sex differences, and this data can easily be included in Table 1 by presenting additional columns for males and females. Consider presenting other analyses stratified by sex as supplementary tables.

- In Table 1, present, numbers as well as percentages

Minor Essential Revisions

- State the age range of participants and location of health centre in the abstract

- Phrases such as 'had overweight' do not read well. Replace with 'had an overweight status' or 'were overweight'. Consider having the paper read by a native English speaker.

- In abstract, references such as 'TG genotype' do not make the associations clear. Please clarify by referring to the specific alleles, (e.g. the T allele was associated with increased risk) or referring to the specific genotypic comparison (e.g. TT vs GG)

- It would be clearer for the reader if for all SNPs the alleles were coded for the analysis in the same direction in terms of effect on VitD, i.e. use appropriate reference alleles that leads to all vitD ORs being >1 (or all <1).

- Authors should provide analysis to show whether the genotypes have an impact on dyslipidemia and an overweight status independent of vitD or whether the effects are only through their effects of vitD, or at least state their belief. In addition, authors should consult two recent papers Vimaleswaran KS, et al. PLoS Med. 2013;10(2):e1001383 and Skaaby T et al. PLoS One. 2013;8(2):e57647

- Please state the linkage disequilibrium of the two GC SNPs in your study or from
published data from a similar population

-First sentence of the Statistical analyses section should be removed and instead an appropriate replacement should go into table footnotes

-The second sentence of the Statistical analyses section seems to refer to the analysis in Table 2, but these results appear to be unadjusted and do not come from a multivariable regression model, therefore reference to adjustment should be removed. Make reference to the genotypes.

-why has 25 (OH)D been excluded from Table 1?

-What is the heading for the first P column of Table 2? Additive?

-Only one comparison can be done for the analysis of rs2282679 in Table 2, therefore the p-values should not be repeated.

-Reference to the low sample size is limited. Include references to power calculations and the possibility of this leading to false positives.

**Level of interest:** An article of limited interest

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

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

**Declaration of competing interests:**

I declare that I have no competing interests