Reviewer’s report

Title: The longitudinal association of common susceptibility variants for type 2 diabetes and obesity with fasting glucose level and BMI

Version: 2 Date: 29 April 2010

Reviewer: Anke Tonjes

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Webster et al. analyzed effects of selected T2D risk variants on fasting glucose and of the FTO SNP rs9939609 on BMI using a cross-sectional as well as a longitudinal approach in about 4500 subjects included in the Busselton Health Study.

The manuscript is in general well written, provides an appropriate methods section including a power calculation and discussion of study limitations.

However, several minor issues could be considered:

1) At present more than 20 T2D risk loci have been identified. How have the genes been selected for the current analysis? Do these variants show any association with T2D in the BHS (even power is low due to only 271 diabetic subjects)? The authors should include in the discussion for which variants any effects on fasting glucose and/or indices of beta cell function have been reported.

2) The authors report that there was no significant association of the FTO variant on BMI in the subsample of about 2800 unrelated subjects. Based on the previously reported effect size in the British cohort the detection of an association would be expected. Are the allele frequencies the BHS similar to European samples? It would be helpful to include this in the discussion. Furthermore, based on the fact of missing association in the cross sectional analyses it is not clear if any effects would be expected in the longitudinal analyses? This issue should be shortly discussed.

3) The authors report that the whole cohort of 4554 subjects was included in cross-sectional analyses. Please clarify that T2D subjects (6% based on table 1) or subjects with lipid-lowering drugs (2.5% based on table 1) were excluded while assessing glucose and insulin levels or lipids respectively.

4) In the legend for ESM Table 2 it is not completely clear what age and BMI 2 or 3 refer to. It would make understanding easier if the authors would clarify these terms.

5) Please include a reference for the last sentence on page 3.

Level of interest: An article of importance in its field
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.