Reviewer's report

Title: Maternal and offspring fasting glucose and type 2 diabetes-associated genetic variants and cognitive function at age 8: a Mendelian randomization study in the Avon Longitudinal Study of Parents and Children

Version: 2 Date: 19 July 2012

Reviewer: Mikko Mikko Lehtovirta

Reviewer's report:

Dear Sir,

The manuscript has been improved and I find the answers by the authors quite sufficient. However, I still would like them to reconsider and reformulate, what they really are after, and categorize my comment as a Discretionary Revision.

The problem I find is that, at present there is no knowledge about which of the following schemes is contributing, and to what extent, to the measured childhood intelligence (g), L1 and L2 being latent factors (i.e. not fasting glucose) mediating the influence of glycaemia and T2D risk genes:

A. glucose-SNP:s -> fasting glucose -> g
B. T2D-SNP:s ->fasting glucose -> g
C. glucose-SNP:s -> L1 -> g
D. T2D-SNP:s -> L2 -> g

As the vast majority of the variance of fasting glucose is due to influences other than the SNP:s included in the study, an approach where only alternatives A. and B. are considered, seems unjustified.

Why not explore the pooled influence of all available SNP:s on g, and then discuss how much of this seems to be mediated via fasting glycaemia.

Level of interest: An article of importance in its field

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.