Reviewer's report

Title: ANGPTL4 variants E40K and T266M are associated with lower fasting triglyceride levels in Non-Hispanic White Americans from the Look AHEAD Clinical Trial

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Reviewer: Anke Tonjes

Reviewer's report:

Smart-Halajko et al. investigated the effects of the two ANGPTL4 E40K and T266M on fasting triglyceride levels in the Look AHEAD study.

The manuscript is in general well written. And especially the potential interaction with treatment interventions is of interest.

However, several issues should be considered:

1) A power calculation should be added.

2) The authors should more appropriate differentiate between effects in patients on specific lipid lowering drugs or different antidiabetic medication.

3) Is the association also detectable in subjects without lipid-lowering medication?

4) Fasting glucose levels differ between the genotype groups. Even this difference is not significant analyses should be adjusted by plasma glucose since the strong interaction with triglyceride levels are known.

5) The regression model used should be tested for overfitting since 13 covariates are included. Have the authors performed a stepwise inclusion? Furthermore, a stratified analysis for subjects with and without lipid lowering medication should be performed.

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'