Reviewer's report

Title: Differential effects of the changes of LDL cholesterol and systolic blood pressure on the risk of carotid artery atherosclerosis

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Reviewer: Fruhling V Rijsdijk

Reviewer's report:

In terms of the statistics (regression analyse and explanation of the Latent Growth Curve model, novel to clinicians), the authors have made quite some changes to address the reviewers concerns, but perhaps they have done the wrong things. From a statistical point of view I would suggest the following changes (listed under Major Points) in presenting the results.

Major points:

Statistical Analysis and Report

(1)
I would strongly suggest deleting Figure 1 and to not report the two separate nonlinear LGC models of LDL cholesterol and IMT and for SBP and IMT. The authors claim to have added these to make it clearer for a clinical (non-stats) audience. I don't see how this will help. It makes things more complicated and the effect sizes are exactly the same and there is more statistical power to detect the effects in the bivariate model, so this is an unnecessary repetition of the results (Table 3). The authors can easily use the added explanation of the models (page 13) to explain the final (bivariate) LGC model as presented in Figure 2. Please change txt to match this.

(2)
My second objection (not totally unrelated to point 1) is the report of the results of the LGC model in Table 3. 75% of Table 3 is useless as it contains rows with the fixed path loadings of the observed variables on the latent Intercept and Slope factors (which we can see in the Figure). My suggestion is to delete the Table completely and report the results (4 causal effects and 2 path loading) in the bivariate model Figure, including a significance indicator of some sort, 95%CI or p-value and the error variances on the observed variables of SBP and LDL). It would also be good to report the means and variances of the latent I and S factors (+ SE or 95%CI) as estimated by MPLUS.

(3)
The fit statistics at the bottom of Table 3 are again not very helpful for a clinical audience. Please just indicate in the text that the final model fits well, chi-square (DF=15) of 21.2, p-value =.13, which essentially means that the predictions of the model are consistent with (non-sig different from) the observed data. In addition this is supported with other fit indices like CFI, RMSEA and SRMR. You
have done this on Page 5, this should suffice.

Reporting the results in a nice (inclusive) path diagram will make it a much better story to follow.

(4) Were the covariates (Table 2) accounted for in the MPLUS LGC modeling? This is not clear. Rather than regressing out gender, given the big sample size, could you not have fitted the model on males and females separately or is there no theoretical reason to assume that there might be a different relationship across gender?

(5)
Meaning of the results. It’s not clear to me if the effects reported in Table 3 for the bivariate model are standardized? It would be helpful to report the mean and variance of IMT and mention how much of the variance of IMT is actually explained by the significant effects of Intercept LDL, Intercept SBP and Change SBP. Or perhaps find another way to indicate if the significant effects (big sample size) are really important and helpful from a clinical point of view in predicting IMT?

Minor Comments:

(1)
ABSTRACT (Results): Greater baseline LDL and blood pressure were associated with an increase in IMT (0.005±0.002mm per 1 mmHg [p=0.006] and 0.041±0.004mm per 1 mg/dL [p<0.0001], respectively).

Should be:
Greater baseline LDL and blood pressure were associated with an increase in IMT (0.005±0.002mm per 1 mg/dL [p=0.006] and 0.041±0.004mm mmHg [p<0.0001], respectively).

(2)
Table2: Units for 1st HDL cholesterol and 1st fasting glucose should be in +1 mg/dL not mmHg.

(3)
Statistics. Check the description of the LGC model figure carefully. In the txt (pg 13) you refer to paths 'b1-b3' and 'a1-a3' which are not indicated in the Figure aa such. Please delete, or add in Figure.

Level of interest: An article of outstanding merit and interest 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