Reviewer’s report

Title: Differential Effects of the Changes of LDL Cholesterol and Systolic Blood Pressure on the Risk of Carotid Artery Atherosclerosis

Version: 4 Date: 10 February 2012

Reviewer: Eric Yang

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Previous studies have established a strong link between low-density lipoprotein cholesterol (LDL-C), systolic blood pressure, and carotid intima-media thickness (CIMT) measurements each with cardiovascular outcomes. As the authors have reported in their study, results from other investigations have yielded considerable heterogeneity on the reported link for CIMT measures with lipid parameters and blood pressures. Thus, Chien et al. have presented interesting results from the Chin-Shan Community Cardiovascular Cohort Study (CCCC) to better define this link.

On review, there were several points that should be addressed before publishing the manuscript.

Major Compulsory Revisions

1) The use of a novel statistical technique, the latent growth curve modeling, was the most interesting draw for the study. The technique would be of interest primarily to biostatisticians and epidemiologists. Even though the authors justified its use, most clinicians would still find the statistical methods and results difficult to interpret in a clinically useful context (e.g., the Figure and the non-linear increases in LDL-C and systolic blood pressures).

Inclusion of the clinical implications of the study would strengthen the Discussion considerably.

2) In the Methods (page 10), 3602 participants (1703 men, 1899 women) were initially recruited in 1990. In the Results (page 4), 2572 were reported to have 3 complete exams and much of the analyses centered on this set of individuals. However, on page 11, only 2244 participants were reported to have completed carotid ultrasonography.

Please account for the exclusion of 1030 participants and then the inclusion of 328 individuals without carotid ultrasonography for the primary analysis. A figure similar to the ones endorsed by the CONSORT Group for clinical trials might be helpful.

3) The underlying premise for the study was to examine the components of metabolic syndrome in relation to CIMT. The premise was raised in the Introduction (page 3, 1st paragraph) and again in the Discussion (page 6, 2nd paragraph). The authors did acknowledge lack of data on lipid lowering and
antihypertensive therapy use as a limitation. However, the Methods clearly indicated that high-density lipoprotein cholesterol (HDL-C) levels were assayed in the cohort. Moreover, a quick search of the literature revealed that the authors possess data on smoking status and fasting glucose levels.

Please include the HDL-C and fasting glucose levels, important components of metabolic syndrome, and smoking status in at least the baseline data. Please also examine these as covariates in the models. Otherwise, please justify their exclusion.

4) Traditional multiple linear regression models should not be considered a suitable comparison with latent growth curve models for longitudinal analyses.

Was there a reason for not examining longitudinal modeling with traditional multilevel approaches?

Minor Essential Revisions

5) On page 5, the authors refer to a “one unit increase of baseline LDL and blood pressure.” Does the unit increase refer to mg/dL and mm Hg, respectively, or to a unit standard deviation increase?

6) I would urge caution in interpreting the use of certain antihypertensives as simply increasing / decreasing CIMT in the Discussion (page 8, 2nd paragraph). In theory, the CIMT could change for other reasons then atherosclerotic progression or regression. For example, the overall arterial volume changes (e.g., net arterial volume expansion appearing as a decrease in CIMT).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.