Review of: "Why Non-HDL Cholesterol is Preferred over Apolipoprotein B-100 (Apo B)"

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Potential competing interests: No potential competing interests to declare.

This report addresses an important issue, which is the need beyond traditional cholesterol testing, and to consider particle size and composition. The authors suggest that Apo B may provide a more sensitive bioindicator of risk for ASCVD.

Given that the study focused just on men with the age range of 40-70 yr, it seems that at a minimum, they should more clearly acknowledge that the absence of women is a limitation at this point. Perhaps they could at least speculate whether they believe the conclusions would apply to women.

They indicated that one of their exclusion criteria was CKD. It would be helpful if they provide the eGFR cutoff that was used, so that the reader can know they defined that as Stage 4, or if reduced renal clearance indicative of Stage 3 was also a reason for exclusion.

They also state that they excluded for type 2 diabetes. Again, the issue is what diagnostic test were used and what cutoff. Was it based on HA1c or HOMA-IR?

The relevance of T2D is how common it now is, and whether it would alter conclusions about the sensitivity and specificity of Apo B?

It was surprising to not see any descriptive summaries about racial/ethnic makeup of the patients. It should be provided in a brief way in Methods, and probably included as a table in supplemental materials.

They also indicate that they excluded for lipid-lowering medications. There are two aspects of this exclusion that warrant a some more explanation. First, why were these men not taking lipid-lowering and anti-hypertensive medication if they

were unhealthy? The second aspect is whether they would speculate on the likely influence of these medications on Apo B given that it would certainly be an issue if switching to Apo B testing in a typical practice and community setting.

Finally, are there any other constituents of cholesterol that could be employed in the same way as they suggest for Apo B? There is a lot of interest in how inflammatory and oxidative factors influence the structure and function of cholesterol, even reversing the usual beneficial actions of HDL.