Reviewer’s report

Title: Blood lipids and lipoproteins in relation to incidence and mortality risks for CVD and cancer in the prospective EPIC-Heidelberg cohort

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Reviewer: Paulette Chandler

Reviewer's report:

The paper is well written and reports interesting findings including the positive association of higher HDL-C with breast cancer higher Lp(a) with prostate cancer. The reported cancer risk pattern differs from the CVD risk pattern. A gender subgroup analysis should be done for colorectal cancer and lung cancer to identify if reported findings for these site-specific cancers are associated with gender.

1. Line 66-67 "Prospective studies on the association of HDL-c-- are few , where as those on apob-100 are entirely lacking". A prospective lipids and incident cancer and mortality paper in AJCN 2016 "Lipid biomarkers and long-term risk of cancer in the Women's Health", Chandler et al. reported a significant inverse association between HDL and Apo A1 and total cancer mortality (Supplemental Table 8 and Figure 2). Total cholesterol, LDL and apo-B 100 were not associated with cancer mortality.

2. Line 189 " High HDL-C and apob-100 levels were no longer associated with lung cancer risk after .." It would be helpful to look at the association between lipid biomarkers and lung cancer in nondrinkers of alcohol versus drinkers since alcohol is associated with higher HDL and apo-A1.

3. Models adjust for HRT use and lipid lowering medication use, but a sensitivity analysis that excludes individuals that used lipid lowering medications and HRT would be helpful to remove any residual confounding by HRT and lipid lowering medications.

4. For breast cancer, an age-stratified analysis (age<55 and age>=55) should be done to investigate if the association of higher HDL with increased risk of breast cancer is associated with menopause status. In the AJCN lipid and cancer paper, we observed that high LDL was associated with decreased risk of breast cancer in women age <55 years (HR 0.88(0.80-0.97) and LDL was not associated with decreased risk of breast cancer in women age 55 years or older. Interestingly, we found that high HDL was associated with a reduced risk of breast cancer in women age less than 55 years (HR 0.89(0.81-0.98)) but this association was absent for women older than 55 years.

5. Supplemental Table 1. Is postmenopausal HRT use reported as current HRT use?
6. A limitation of the paper is that MI and strokes were only defined by ICD-10 codes.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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