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

Version: 0 Date: 05 May 2017

Reviewer: Mieke Van Hemelrijck

Reviewer's report:

Background

First sentence: association - please specify the direction of the associations for all markers. The authors only describe how LDL is positively associated with CVD risk.

Line 43: What about women??

Overall the introduction would benefit from some further structuring. It includes a vague description in the context of CVD, a description of the lipid components, and a description in the cancer setting. All sections are rather vague and would benefit from adding some quantifications (i.e. provide some example studies).

Methods

Study design: It would be helpful to see a justification for their choice of a case-cohort design (as opposed to the standard cohort design that EPIC has).

Results

It would benefit the reader to have Table 1 in the actual table as this information forms the basis for the study.

It would be informative to see medical cut-offs as low HDL and low apo-A are in general bad, whereas for all the other markers high levels are bad. It now seems that this study found trends in the opposite direction? However, for the CVD outcomes the trends seem as expected - an inverse association for HDL and apoA and a positive association for all the others.

The entire results section is very long and detailed. It would help the reader if this was shortened to the important findings as the tables provide all the other details.
Discussion

The use of the term "directly" associated is confusing. The markers are either positively or negatively/inversely associated. A direct association can be in either direction if it remains after adjusting for all relevant confounders. It would be helpful if the authors also discussed the clinical relevance of the findings. They could write something along the lines of: as expected HDL and apoA were inversely associated with CVD outcomes and other lipid components (i.e. XXX) were positively affecting the risk for CVD outcomes. However, for cancer we observed …

Can the authors explain why they are not looking into LDL? Since they have HDL and TC, it should be possible to calculate LDL - they could then investigate whether the findings for apoB and LDL are similar (as is the case for HDL and apoA).

It would benefit the discussion if the entire section of plausibility was moved to the beginning of the discussion as it then provides context to the results. Moreover, a smaller version of this rationale could already be included in the introduction.

Are the authors convinced that two years is sufficient to assess reverse causation? Wouldn't it be worth doing further sensitivity analyses excluding more years to see whether the results weaken - given the rather long lag time for some of these cancers?

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

No

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.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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