Author's response to reviews

Title: Update on the NCEP ATP-III Emerging Cardiometabolic Risk Factors

Authors:

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Author's response to reviews: see over
May 5, 2014

RE: MS#2120362812449199 – Update on the NCEP ATP-III Emerging Cariometabolic Risk Factors

Ursula D’Souza, PhD
Senior Editor
BMC Medicine

Dear Dr. D’Souza,

We would like to thank you for considering and reviewing our manuscript titled “Update on the NCEP ATP-III Emerging Cariometabolic Risk Factors”. We appreciate the reviewers’ comments and suggestions. We have revised the manuscript with the following changes:

Reviewer 1:
This is a timely update on the relevant background of emerging cardiometabolic risk factors that may be included in future recommendations on cardiovascular risk stratification and management. The authors are well positioned in this regard and the manuscript reads well. I have the following minor essential suggestions/revisions.

Thank you.

It is suggested to include a comment on how the literature was perused. Which search engine(s) and key words were employed, and how were articles selected?

We have reviewed a large sampling of reviews published in BMC Medicine and in none could we find a description of the methods used for reviewing the relevant literature. We have also reviewed the instructions to authors and have again found that methods are not expected to be included. As this is not a meta-analysis or intended to be an extensive review of the literature we do not feel that a methods statement or section is indicated. We do appreciate the reviewer’s comments, though, and have added a brief statement in the “Author Contribution” section about this.

In the first paragraph on apolipoprotein B, I would consider including a comparison with total cholesterol/HDL cholesterol.

We have now added a sentence at the terminus of the 1st paragraph of the apolipoprotein B section comparing apolipoprotein B to total cholesterol/HDL cholesterol in CVD outcome trials.
In the last paragraph on apolipoprotein B, line 5 and 6 of the respective page, ‘hypertriglyceridemic’ should be replaced by ‘hypertriglyceridemia’ (3 times). In the last paragraph on lipoprotein (a), first sentence, please include the reference.

Corrected as suggested, thank you.

In the section on pro-inflammatory factors, it may help to include that methotrexate as antiinflammatory therapy is associated with reduced cardiovascular risk in rheumatoid arthritis even when this is a high grade inflammatory disease.

We have added a sentence in this section that there is evidence that methotrexate is associated with reduced CVD risk in patients treated for RA.

In the first paragraph on subclinical ASCVD, first sentence, please include a reference.

Thank you. The sentence has been modified and referenced.

Regarding several of the references, the journals are cited using only small case rather than capital letters.

Thank you. These have been corrected.

Reviewer 2:
This qualitative review deals with an important clinical topic – the evidence base and current clinical utility of “emerging cardiometabolic risk factors.” My comments are all "qualitative." Each falls under a single common theme; each requires a response.

Generally, the manuscript deals rather informally with the relevant literatures. By that I mean the text comments upon supporting and non-supporting research with no apparent method for prioritizing research or determining the kinds of studies most needed to establish the clinical utility of each considered risk factor. For example, mention of measurement reliability is made just once, and cost and general clinical availability are not considered. For example, ABI is a simple, very widely available and inexpensive test whereas CIMT has many varied and specialized methodological issues. This review leaves ABI out entirely and does not consider many of limitations to CIMT as a clinical measure.

We are sorry for these omissions but the length limitations precluded coverage of every aspect of emerging cardiometabolic risk including comparative analysis of clinical utility and cost. Nevertheless ABI is now included and a sentence regarding the limitations of CIMT has been added.

The key evidence of the utility of a new risk factor is its ability to improve prediction above and beyond current multivariate prediction. So, studies like that of Yeboah (ref 74) where the improvement in ROC characteristics of most of the current “emerging risk factors” are compared should be emphasized over most other epidemiologic studies. In this regard, I refer the authors to 3 important papers not part of their review – Lloyd-Jones Circ 2010;121:1768, Tzoulaki et al JAMA 2009;302:2345, van den Oord et al Atherosclerosis 2013;228:1-11.

Thank you for this important point. The text around reference #74 has been modified to reflect the importance of this improvement in ROC. The references you have provided helped to support this point, thank you again.
It is worth pointing out that the need here is for improved prediction in primary prevention among patients considered to be at intermediate risk. High risk patients likely warrant statin and ASA, and low risk do not. But separating the millions of intermediate risk patients into those destined to get premature ASCVD and those not would be a tremendous aide to clinicians and avoid the huge costs of prescribing lifelong statins and ASA to all intermediate risk patients.

*The purpose of this manuscript was to review the current data on these risk markers but not to make specific recommendations. Nevertheless, we agree with the comment as noted in our concluding remarks.*

Were this review to be more thoughtful and methodical, it will still need to distinguish how it adds the very thorough review of many of these issues within the new US cholesterol guidelines. I will concede that the 2013 guideline report does not feature its systematic review of these biomarkers and that their conclusions and recommendations tend to get lost in the very long document. Therefore, clinicians could use a more accessible digest of the 2013 systematic review.

*We agree that the 2013 ACC/AHA guidelines do not feature a review of these markers and thus we feel that this update on the NCEP/ATP-III guidelines is important at this time and does add to the current literature.*

Thank you again for reconsidering this manuscript. If you have any questions please do not hesitate to contact me at (303) 724-3923 or at robert.eckel@ucdenver.edu.

Sincerely,

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