Reviewer's report

Title: Recent findings on the health effects of omega-3 fatty acids and statins, and their interactions. Do statins inhibit omega-3?

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Reviewer: Merritt Raitt

Reviewer's report:

The authors have written a review examining the effects of n-3 PUFA and statins and their interactions when used for the prevention of cardiovascular disease. The paper includes 4 major interesting and sometimes controversial observations. 1) statins appear to inhibit the benefits of n-3 PUFA, 2) The benefit of n-3 PUFA supplementation is minimized in patients with greater baseline n-3 PUFA consumption, 3) The beneficial effects of statins have not been evident in recent trials and the clinical enthusiasm for the use of statins is not justified given their true efficacy and side effects, 4) Early studies showing the beneficial effects of statins may have been significantly influenced by investigator bias.

The first 2 points are well supported by the presented evidence and are important observations supported by original synthesis of the existing data.

The third assertion is controversial and in my opinion is not as well supported as it should be. It is unclear in what clinical situations the author is objecting to the data for the beneficial effects of statins: primary prevention, secondary prevention, or both. Since the use of fish oil in the context of this paper is in patients with established heart disease then the relevant indication to question would be secondary prevention. The cited studies are primary prevention. In fact I think the argument regarding recent studies being negative is in large part because recent studies were not secondary prevention studies. Furthermore, though the author reverences one of his own papers on the topic there is no mention of the Jupiter study which was published in the New England Journal of Medicine in 2008 and was a strongly positive primary prevention trial with more patients than the negative studies reviewed in the paper and was published around the same time.

It is an interesting, important, and highly controversial assertion that statin study results have been affected by biased investigators. Given the implications of such an assertion I believe it should be rigorously supported in the text. Pointing out the possible appearance of conflict of interest is important but not an adequate support for such a sweeping assertion. The authors does go into more detail in other papers they have written and referenced in this paper. In my mind such a reference is not adequate to support the assertion. In fact, when I read the referenced critique of the Jupiter trial I was not convinced by the authors arguments. Others may agree with them but I think if one is going to make such strong iconoclastic assertions the details supporting it should be in this paper.
Finally, I am not sure why the authors devote a large section of the paper to the efficacy and adverse effects of statins. I presume it is because they feel statins inhibit the benefits of n-3 PUFA and therefore clinicians should choose one or the other and that the authors think that n-3 PUFA is the better choice. I think it would be a no less important paper if the authors focused on the question of an interaction between the two “medications”. I do not think this point is proven. First the recent data for n-3 PUFA is not great even if one takes into account the potential confounder of statins and second even in light of the authors concerns about the statin data, the data for statins in secondary prevention of CAD is much stronger than that for n-3 PUFA. I suggest that this section be removed as I do not think there is room in the paper to support the assertions about the statin data and I do not think that the authors will have the data to effectively argue that statins are not effective in secondary prevention which is the main subject of the n-3 PUFA review in the paper. It might be reasonable to suggest that in situations where the utility of statins is less clear and that of n-3 PUFA is more apparent that statins should not be used but this will be a somewhat unusual situation.

Major Compulsory Revisions

1) Since the presented data for n-3 PUFA is for secondary prevention please limit the review of statin efficacy to secondary prevention.

2) If the authors decide to continue to include the discussion of potential bias and ethical misconduct in statin studies they will need to present more original specific examples of studies in which there is reason to believe there is bias and explain why.

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests