Author's response to reviews

Title: A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis. Results from a randomized controlled trial

Authors:

Dirk W Droste (droste.dirk@chl.lu)
Catalina Iliescu (iliescu.Catalina@ghicl.net)
Michel Vaillant (michel.vaillant@crp-sante.lu)
Manon Gantenbein (manon.gantenbein@crp-sante.lu)
Nancy De Bremaeker (nancy.debremaeker@crp-sante.lu)
Charlotte Lieunard (charlotte.lieunard@crp-sante.lu)
Telma Velez (telma.velez@crp-sante.lu)
Michele Meyer (MischMeyer@web.de)
Tessy Guth (tessy.guth@crp-sante.lu)
Andrea Kuemmerle (andrea.kuemmerle@crp-sante.lu)
Georges Gilson (georges.gilson@chl.lu)
Anna Chioti (anna.chioti@crp-sante.lu)

Version: 2 Date: 3 October 2013

Author's response to reviews: see over
Dear Sir,

We are very grateful for the reviewer’s comments and the opportunity to respond to their suggestions. Please find below the corrections. We hope the paper is now suitable for publication.

Sincerely yours

D. W. Droste

Reviewer's 1 report
Title: A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis. Results from a randomized controlled trial
Version: 1 Date: 10 August 2013
Reviewer: Ramon Estruch
Reviewer's report:
In this trial, the authors analyzed the effects of some lifestyle changes in order to upgrade the quality of the diet towards the traditional Mediterranean diet and to increase physical activity, as well as the moderate intake of wine in blood lipids. Although the effects of red wine on blood lipids are well known (see for instance Estruch R et al, Nutr Med Cardiovas Dis 2011;21:46-53), the additional effects of a moderate intake in a healthy diet (i.e. Mediterranean diet) are not so known. However, the authors should take into account the following in order to increase the quality of the manuscript:

Major points:
1. The authors should treat to determine the additional effect of red wine consumption on blood lipids in group of lifestyle changes. This impact should be remarked in the abstract and commented in the Discussion section.
   We added in table 3 the values for each of the 4 groups separately to give an idea of the individual effect. The statistical model already takes into account the independent and additional effect of red wine on lipids. We added in the abstract and in the discussion the sentence: The effect on LDL/HDL ratio after 20 weeks was, however, more pronounced in the non-LC group. In the discussion, we added the sentence: “This is probably due to a ceiling effect”.

2. The "atherosclerotic burden" of the population analyzed should be specified in order to better characterize the patients studied.
   We added the following section in the methods: We used the Mannheim definition for plaques: It is defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness >1.5 mm as measured from the media-adventitia interface to the intima-lumen interface (Touboul et al 2012). NASCET criteria were used to define high-grade stenosis (Arning et al 2010, von Reutern et al 2013).
3. The characteristics of red wine administered should be included in the Material and Methods section.

We added the following section in the methods: The sort of red wine was at the participants’ discretion.

4. The PP analysis may be omitted. The results do not differ substantially from those obtained in the ITT analysis.

We omitted the PP analysis from figure 2 and the results, and added in the results “results obtained on the PP population were similar.”.

5. The Methods section should be re-written and divided into different parts: Population analyzed, Intervention administered, analyses performed and statistical analysis.

We re-wrote and divided the method section as suggested.

Minor points
1. Abstract: Include the period of study and the duration of the intervention in "Methods". Omit the reference to ITT analysis in the "Results".

We added in the method section of the abstract: from 2009 to 2011 and for 20 weeks as suggested.

2. The reference no. 28 should be updated. In this study the aim was to analyse the effects of a Mediterranean intervention on a composite end-point that included myocardial infarction, stroke and cardiovascular death. Not only stroke.

We added more recent literature than reference 28.

3. The "definition of plaque" in the carotid ultrasonography should be included. The number and characteristics of the plaques detected should also be included in order to know the "atherosclerotic burden" of the population studied.

We included the definition of plaques (see above). In the ultrasound reports of our laboratory, we report only the presence of plaques, not their number.

4. The number of subjects "eligible", the number of subjects finally included in the study and the drop-outs should be specified.

The number of eligible patients is difficult to assess, as we included only patients who seemed to be intellectually and physically capable and willing to follow such a study based on a subjective impression. We specified the dropouts in figure 2.

5. At the end of the discussion, the strengths of the study should be remarked, not only the limitations.

We added at the end of the conclusions: The strength of the study is the demonstration of an additional beneficial effect of red wine on top of otherwise healthy lifestyle on blood lipids.

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: No conflict of interest related to this study.
Reviewer's 2 report
Title: A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis. Results from a randomized controlled trial
Version: 1 Date: 15 September 2013
Reviewer: Armin Imhof
Reviewer's report:
General comments:
Droste and co-workers present a randomized interventional study in predominantly male patients (mean age ~63.5 years) with known carotid artery sclerosis including 2 interventions:
1. Life style change program with recommending physical activity and diet but not controlling for it.
2. Additionally daily alcohol consumption (males 200ml/d of red wine, females 100ml/d)
The question whether such interventions showed any (beneficial) effect on the patients atherosclerotic risk profile (here lipids) is old but still of general interest and a matter of debate.

Major comments:
Overall the study design is complex and appropriate for the question raised. The manuscript is well written but data presentation might be clearer. However, there are several major points to be addressed:
1. There is one most important methodological flaw with respect to the effects of alcohol consumption. As the authors themselves address in their discussion carry-over effects of previous alcohol consumption till time of study inclusion potentially affect the results and can not be estimated in this study.

We discussed that carry-over effects of previous alcohol consumption till time of study inclusion potentially affect the results and can not be estimated in this study. This is however the situation we are faced with in medicine, cerebrovascular patients drink not or drink alcohol, and if yes the quantities they tell us are often not correct. Our study tested advice on red wine consumption, not the actual amount of alcohol consumed (which is probably not very reliable from questionnaires).

2. Data presentation allows not to differentiate between effects of LC or alcohol or their combination in a "dose dependent" manner. I.g. Results should be presented for the four groups at least additionally (No LC+No Alc/LC+No-Alc/No-LC+Alc/LC+Alc)

We presented the results for the four groups additionally in table 3 as suggested.

3. How did the author ensure adherence to the study protocol over 20 weeks? At least according to the alcohol intervention this is of essential importance.

We cannot ensure adherence to the study protocol over 20 weeks, we hope that due to selection of “reliable” patients, their compliance was more or less correct. As already stated, we tested dietary and lifestyle counselling, not their implementation.

Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests.