Reviewer's report

Title: Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study

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Reviewer: Peter Lee

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“Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED study”

by M Guasch-Ferré et al

Comments on the paper submitted to BMC Medicine

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The authors describe analyses of results from a prospective study in which baseline total olive oil consumption proved to be a significant predictor of reduced cardiovascular disease and mortality. This advantage seemed mainly due to extra-virgin olive oil consumption rather than to common olive oil consumption.

While the study is an important one, the paper suffers from a number of limitations discussed below.

A. Major compulsory revisions

1 The abstract gives too much space to methods and background, and not enough to results. The reader should be told that there were no significant associations with cancer or all-cause mortality, and that the associations with CV disease and CV mortality were limited to those in the two Mediterranean Diet groups.

2 The methods paragraph on page 8 should be rewritten. In particular I failed to understand why (lines 8-10) total olive oil = olive oil + extra virgin olive oil + common olive oil. From the results in Tables 2 to 4, total olive oil is only the sum of the last two. What is the difference between “total olive oil” and “olive oil”? Also it is completely incomprehensible to me how the scores were defined. Perhaps the details might be described more clearly in a supplementary file, and summarized in the text of the methods section.

3 In Table 1 it is stated that means and SEs are given for the qualitative variables. However the numbers given after the ± are clearly not SEs as these
would imply SDs larger by about 50 times (square root of group size which is about 2400), giving for example an SD of almost 200 for BMI, which is impossible. I imagine these numbers are actually SDs. Also the text of the first paragraph of the results section draws conclusions from Table 1. Without statistical testing of the differences between the tertiles, this seems inappropriate. P values for these differences should be included in Table 1.

4 HRs are estimated separately for the three intervention groups, but no formal test of homogeneity of the three HRs is presented. It should be, as it is not readily apparent whether the three HRs actually do differ significantly. Thus I note that the 95% CIs for the HRs of 0.43, 0.45 and 1.09 all include 0.65, the overall estimate.

5 Analyses of prospective studies make the implicit assumption that characteristics measured at baseline have changed little during follow-up. Here this is clearly not the case as the subjects were subsequently given treatments in order to affect olive oil consumption. In these circumstances it is essential to present information showing how olive oil consumption varied by year after baseline, within the baseline tertiles of total olive oil consumption, not only for all subjects, but also by intervention group.

6 In the second paragraph on page 18, reference is made to the generalizability of the results. Another major factor affecting generalizability, which should be mentioned, is that the results relate to people who following baseline suddenly changed their olive oil consumption, which is hardly the general situation. Indeed there might be more extensive discussion of the problems of interpretation related to this unusual feature of the study.

B. Discretionary revisions

1 Given that actual olive oil consumption would have varied by baseline, it would be interesting to know if there was any evidence that the advantage of olive oil consumption on CV events varied by time.

2 The authors should consider the use of supplementary files to provide more detail of their methods and analyses, rather than presenting results for which data are “not shown”.

3 The English is not that bad, but could still be improved. It may be worth getting a science writer who is a native English speaker to improve the text.

C. Minor essential revisions

1 The first paragraph of the background describes virgin olive oil, but does not use the term extra-virgin olive oil. If they are different, the difference should be explained. If not, use the same term throughout.

2 The second paragraph of the background would be clearer if the results were separated by study. Thus the EPIC-Spain study is mentioned in relation to reference 6, without noting that reference 4 also describes results from the same
study. Also, in that paragraph, there is a statement that “most studies made no
distinction among the different varieties of olive oil”, without saying which studies
did make a distinction and what their results were.

3 It should be made clear in the methods that “baseline” refers to the time before
the allocated treatments were given, and also how long the interventions were
applied for.

4 The last sentence of the paragraph “Ascertainment of cardiovascular disease
and mortality” on page 9 raises two points. Firstly, did the Committee also
adjudicate on whether or not a CV disease had occurred? Also “lately” seemed
the wrong word; perhaps “finally” or just omit “finally”.

5 In the first line of page 17 one should replace “future studies” by “future larger
studies” or “future larger studies or meta-analyses”.

6 In the first paragraph, large sample size is mentioned as a strength of the
study. While the number of CV major events is reasonably large, the numbers of
CV deaths and cancer deaths are not, and allow little precision in the HR
estimates.

Minor issues not for publication

1 In various places, including the abstract, statements are made about
“cardiovascular disease and mortality” and it is not always clear to the reader
whether total mortality or cardiovascular mortality is meant. This should be made
completely clear.

2 Six abbreviations are referred to on page 19. These omit some of those used
(e.g. LDL, FFQ). Also it is usual to define an abbreviation once the first time it is
used in the main paper, and then not to use the full word subsequently.
Particularly for CVD, there are numerous exceptions to this.

3 In the background, para 1, line 5 “refined one” should be “refined oil”.

4 In the same paragraph, and in other places, there is a tendency, which should
be avoided, to use semi-colons rather than full stops, to separate what are
separate sentences. See also the first sentence on page 8 which covers six lines
and would be better as three sentences.

5 In the first paragraph on page 10, the order of the second and third sentences
should be reversed as the analysis as a continuous variable has been carried out
for all three oil variables. Also in these sentences and elsewhere, it would be
better to say total olive oil rather than simply olive oil. Indeed one could define
abbreviations for total olive oil and common olive oil, as well as for extra-virgin
olive oil, and virtually always refer to these.

6 In the text of the results section some results are presented as percent
decreases and some as hazard ratios. To avoid confusing the reader it would be
better to be consistent. Perhaps give all as percent decreases, clarifying the first
time results are quoted that the two methods of quantification are equivalent.
7 On page 18, in line 5 of para 2, the word “though” is missing after “even”.

8 In Table 1 the value of 21.4 for tertile 1 for extra-virgin olive oil seems wrong, being the same as for total olive oil. I imagine it should be about 9.

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests