Reviewer’s report

Title: Arachidonic acid and cancer risk: a systematic review of observational studies

Version: 1 Date: 21 June 2012

Reviewer: Shu-Chun Chuang

Reviewer’s report:

This is a systemic review on arachidonic acid (ARA, from diet and markers from blood or tissue) and cancer risks (colorectum, skin, breast, and prostate). A meta-analyses was not conducted because of the number of studies and the methodically issues. Nevertheless, the authors concluded that ARA is not associated with cancers reviewed in the present manuscript.

Major compulsory revisions –

Background:
It is not clear in this section that why a meta-analyses or a review is necessary in this topic. The authors have cited some studies with inconsistent results, but have not discussed why the results were inconsistent and how a meta-analyses or a review will improve the current knowledge on this topic.

Methods:
As the authors stated and commented in their articles that they only searched for ‘specific words that stands for “arachidonic acid”’ and additional articles could be identified by other terms such as “fatty” or “fatty acid”. There is strong concern that the review may not be completed.

In the “quality assessment and data extraction section”,
1. It is not clear how the authors scored the data quality. For example, how much score did a publication obtain if it is a cohort study vs. a case-control study?
2. What is the theoretical range of the quality score?
3. How did the author define high/medium/low quality studies?
4. How did the author score the “methods for controlling confounders”? The publication got a score as long as it adjusted for a confounder or the publication got scores when it adequately adjusted for a set of confounders? If the later, what are the minimal sets of confounders for each cancer site?

Results:
The authors mentioned “the temporal relationship is not clear” in several places. The authors should have it in mind that the ability to assess temporal relationship depends on the study design. Only trials could provide information on temporal relations, but trials were not reviewed in the current study; other observational epidemiological studies, including cohort studies, have limitations on cause-effect
inferences. Case-control, cross-sectional, and surveys are not suitable to evaluate the temporal relationship.

Discussion:

1. What are the associations between diet, blood, and tissue ARA? If the correlations are low, which one would be the best indicator for ARA status? How is the association between this marker and cancer risks?

2. Line 286, discussion on selection bias: there is selection bias in case-control studies, how about the results from cohort studies?

3. How the authors assessed the publication bias? How publication bias affected your review results on breast and prostate cancers? The conclusion was that “ARA exposure is not associated with increased breast and prostate cancer risk”.

4. Line 262: Nevertheless, how big the studies were? Was there adequate power to detect a statistical significance? Would a meta-analyses be helpful to address the question?

5. Is there any difference by publication year? Is there any change in ARA definition over years, e.g. calculation from the FFQ or the assay to measure the concentrations in blood or tissue? Would the changes influence the observed results?

6. Is there any difference by population, e.g. western or Asian populations?

Tables:

1. What are the statistical analyses for each study?

2. For case-control studies, were the cases and controls matched? What are the matching criteria? How the authors treated the matching variables in their analyses?

Discretionary revisions –

Methods:

Line 108: How many studies were excluded for each exclusion criteria?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**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