Reviewer's report

Title: Coffee consumption and risk of cancers: a meta-analysis of cohort studies

Version: 2 Date: 5 January 2011

Reviewer: Teresa Norat

Reviewer's report:

The authors have conducted an extensive work of literature search and data analysis. The question posed by the authors is well defined. The methods seem appropriate but not clearly explained and the reporting of results requires improvement. The conclusions are not adequately supported by the data. The manuscript requires compulsory revisions before a decision on publication can be reached. Main issues are the lack of clarity on how the statistical analyses were conducted, specifically how study-specific relative risk estimates were derived and what studies were included in each analysis, and second, the inconsistency between the main conclusions of the authors and the results of the dose-response meta-analyses on specific cancer sites.

-The authors combined results from 40 cohort studies that reported association with coffee drinking and cancer risk for different cancer sites. The overall relative risk estimate is presented in Figure 2 under the title “Summary RRs of cancer for coffee drinkers versus non/lowest drinkers”. Pooling together results from different cancer sites may be misleading. More weight may be given to cancer sites for which there is the suspicion of an association with coffee intake. The reviewer recommends to do the analyses separately by cancer site. The studies that reported results on “all cancers combined or several cancer sites” could eventually be pooled together.

-It is unclear how the authors derived the study specific RR’s shown in Figure 3 (RRs of low to moderate versus non/lowest drinkers) and Figure 4 (RRs for high coffee drinkers versus non/lowest drinkers). For example, the RR in Figure 4 for the study of Michaud et al, 2001 on pancreatic cancer, reference 55 is 0.90 (0.82-0.98) but in Table 1 the RR for >=3 cups/day versus no coffee consumption was 0.62 (0.27-1.43). (High consumption of coffee was >=3 cups/day according to footnote of Table 2). The same happens for other studies. There are statistical methods for combining RRs from different categories when the referent category is the same, but these methods are not cited in the manuscript under review. This requires clarification.

-In Table 2 (Results by cancer site), the authors should add the number of cohort studies included in each analysis. For instance, the reviewer identified only one study on leukemia in Table 1 (Characteristics of included studies). However, a summary RR for leukemia is presented in Table 2. Since the RRs estimates are different in both tables, the reviewer presumes that other studies were used to obtain the summary estimate but it is not clear which and how many were used to derive the summary relative risk for leukemia. The same is valid for other
cancer sites.

-The interpretation of results seems to be based in the categorical analyses but not in dose-response analyses. The authors don’t explain why they have decided to ignore the dose-response analyses. For example, it is concluded that coffee consumption is inversely associated with the risk of bladder cancer (but RR for an increase of 1 cup for day was 1.03 (0.99-1.06) in Table 2), and colorectum (but RR for an increase of 1 cup for day was 0.99 (0.97-1.01) in Table 2). The authors concluded that coffee intake is not a risk factor for cancer. However, the summary RR of stomach cancer for an increase of 1 cup/day was 1.13(1.03-1.24). Similar inconsistencies are observed in the conclusions for other cancer sites. This needs to be addressed.

The heterogeneity of results within each cancer site investigated was not explored by the authors.

Other minor revisions:

The Discussion is very long and should rely more on the findings and limitations of the study under review instead of being mostly a description of results of other studies.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I am working in a project funded by the World Cancer Research Fund to do systematic reviews on the association between diet and cancer.