Reviewer's report

Title: Systematic review with meta-analysis of the epidemiological evidence in the 1900s relating smoking to lung cancer

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Reviewer: Geoffrey C Kabat

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This is a prodigious piece of work, which synthesizes the results of studies of the association of smoking with risk of lung cancer during the twentieth century. The authors have done a meticulous job of selecting studies (and avoiding double-counting from multiple reports), extracting the available information, and conducting meta-analyses on all major aspects of smoking, as well as examining heterogeneity among studies. The findings are both important and, in some cases, surprising. They provide an extremely valuable summation of what is known from epidemiologic studies of smoking and lung cancer, and they raise certain questions for future study.

Just to mention several of the major findings that struck me: the heterogeneity of the association of smoking with lung cancer by geographic location, the fact that the association does not differ significantly between Blacks and Whites, and that there was no evidence of heterogeneity between those with occupational exposures and those without such exposures. Other valuable points are that pack-years is not a valid measure of exposure and that the lower risk of lung cancer among smokers of filter cigarettes compared to smokers of non-filter cigarettes cannot be explained by accounting for compensation due to switching from a higher to a lower tar cigarette, as argued in NCI Monograph #13.

I have only relatively minor comments, below.

Specific comments

p. 14. The authors might explain for the general reader the objective of meta-regression – i.e., to examine the influence of 6 different factors on the results.

p. 15. Para starting with “First..” needs to refer to Table 5 – in order to orient the reader.

p. 23. Last line. “This results” Should be “This result” -- need a comma after “counter-intuitive”

p. 50, line 14. Should be “smoke fewer cigarettes”

I found the years preceding the refs used in the figures confusing. For example, the main ref for CARPEN is 120. In Fig. 23 CARPEN is preceded by 1991. But if one looks up ref. #120, which is London et al., it was published in 1995. So there is something confusing about this numbering scheme.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No competing interests