Reviewer’s report

**Title:** The association between ambient fine particulate matter and incident adenocarcinoma subtype of lung cancer.

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**Reviewer:** Enrica migliore

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This is an interesting article examining the effect of environmental exposure (PM2.5) on adenocarcinoma (AC) in a wide cohort of non-smokers. The authors report an increased risk of 31% for AC for each 10 µg/m3 increment in ambient PM2.5 concentrations, which becomes statistically significant when the analysis is restricted to subjects who spent more than 1 h/day outdoors.

These results are interesting because they supplement the results reported by the same authors in a previous papers on lung cancer and air pollution (Gharibvand L. et al, Environ Health Perspect 2016) focusing on a specific subtype of lung cancer. Moreover, similar results were recently reported in the literature, showing that the effect of air pollution is particularly evident in AC.

However my biggest concern related to the results of this study regards the effect modification of PM2.5 when results are stratified for presence/absence of non-melanoma skin cancer (NMSC, on which instead the authors point their attention (also including this in the title). In particular, the apparently protective effect of PM2.5 on AC among NMSC cases is quite worrying.

I think that this association, also based on small numbers (22 exposed to NMSC between cases), it is very difficult to explain, and that the discussion supported by the authors is not acceptable. They report in the discussion section (rows 283-290) "The increased HR of incident lung AC among persons without prevalent NMSC and the very low HR of incident lung AC among subjects with prevalent NMSC could potentially be explained by misclassification of air pollution estimates among subjects with prevalent NMSC. Since it is well known that sun exposure is a strong risk factor for NMSC, it may be reasonable to think that there is an element of reverse causation and that subjects who have been diagnosed with NMSC spend less time outdoors, at least during clear days, and thus are exposed to lower concentrations of the ambient air pollution at their place of residence than the recorded ambient levels". Reverse causation is not relevant here, because they NMSC is another exposure and not the outcome (the study outcome is always the AC), but in reality the result found could be explained by a variety of scenarios with completely different explanations (including collider bias, different patterns of interactions, etc) and it is therefore very difficult to explain. Moreover, the authors should try to justify their choice of analysing NMSC (by the way: are these identified at baseline or ascertained during follow-up?) as an effect modifier a priori.
Their interpretations about the use of vitamin D or the avoidance of spending time outdoor because of a previous NMSC remain unconvincing and the proposed title is therefore inappropriate. The focus of the paper on this single debatable result should be avoided.

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