Author's response to reviews

Title: Reanalysis of updated mortality among vinyl and polyvinyl chloride workers: confirmation of historical evidence and new findings

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Author's response to reviews: see over
Dear Dr. Edmunds,

thank you for the deep review of our manuscript. We are pleased to answer to the criticism moved by the reviewer no. 2 to as follows.

The major criticism concerned the reference group. Technicians and clerks (T&C) were chosen as the internal reference group for many reasons: a) it was the best, homogeneous and large internal unexposed group of workers available; b) they were found, according to previous studies conducted by other authors, to be workers with less (or null) exposure to carcinogenic and toxic agents (especially to VC and PVC dusts) [see reference n. 10] and for this reason we already included them in our first paper [see reference n. 6]. We tried to clarify this point in the “Subjects and methods” section (page 4, line 23) and then discussed at page 13, line 24-26 and following.

On the other hand, other blue collar workers was a heterogeneous group of workers whose various occupational tasks were scattered over 24 small areas (including maintenance staff, cleaning operators, etc.), implying different type and level of exposure according to area of work. As they handled or were exposed to practically all the toxic substances listed in the table 1, including VC and PVC, this group was too heterogeneous and it could not reasonably be used as a reference group, as suggested by Dr. Mundt. Moreover, we have to bear in mind that a closed-cycle production system had not been implemented in the chemical plant at that time, thereby allowing conditions for the possible diffusion of chemical pollutants outside the specific production areas. Finally, the condition of exposed workers experienced by “other blue collar workers” is demonstrated by the increased relative risks, whilst not statistically significant. We added a comment also on this point at page 14, line 1-3.

The second point was about smoking habits. Although we do not have specific data to sustain the claim, we believe it is reasonable to hypothesize that T&C smoked not less than blue collar workers, given that they were not subject to the strict smoking restrictions imposed on these latter for safety reasons (e.g., no smoking areas in the plant where flammable substances were handled). Anyway, as suggested, we applied the Axelson adjustment for smoking confounding and it came out that the increased RRs we found could not likely be due to the effect of smoke (page 14, line 21-23). In the occasion, we better clarified that a case-control study conducted within the same cohort obtained results
consistent with ours, and case-control studies by definition takes into account of smoking and other confounding factors (page 15-18). What's more, we had the opportunity to update the analysis about the dose-response relationship among PVC baggers, confirming a clear trend by length of employment, unequivocally not affected by smoking confounding (page 14, lines 18-24).

We agreed with the point about 90% CIs and excluded this items. Anyway, we'd like to point out that very high RR s with a one-tailed 95% significant increase in occupational epidemiology can be considered as statistically significant, as a carcinogen can not have a protective effect. The modification of this point caused changes in many sections of the manuscript: page 6, lines 19-21; page 9, lines 3-8; page 11, line 1; page 11, lines 9-10; page 11, lines 25-26.

Finally, we agreed to leave the political perspectives out of the scientific context. Then, conclusions are slightly changed, as references 26-30 of the former draft of the paper and related comments have been dropped and the comment about the paper by Parodi et al. [actual reference no. 24] moved to page 14, lines 3-8.

Thank you for your kind attention.

Your sincerely,

Fabio Montanaro (on the behalf of all authors)