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
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Dear Dr. Edmunds,

We are glad once again to reviewers for their helpful and encouraging comments. It has been delightful to have the opportunity to enrich a work like this. This investigation had no official fund and it was freely conducted in the framework of a civil action. These conditions partially explain the difficulties in obtaining additional data and performing additional analyses. Said that, we agree with the comments by dr. Mundt about the importance of confounding by smoking habits in occupational epidemiology studies, especially when lung cancer is one of the target diseases. Anyway, it was observed that smoking can be considered a relevant confounder only when relative risks (RRs) are between 0.5 and 1.5 (Axelson O. Aspects on confounding in occupational health epidemiology. Letter to the editor. Scand J Work Environ Health, 1978; 4: 85-89 / Axelson O, Steenland K. Indirect Methods of Assessing the Effects of Tobacco Use in Occupational Studies. In: National Cancer Institute and National Institute for Occupational Health and Safety, Conference on obtaining and using information on smoking in occupational epidemiologic studies. Program and Manuscripts. Bethesda, Maryland, 15-16 Dicembre 1986). Besides, the use of an internal reference group can be considered as a procedure of “good epidemiological practice”, as RRs obtained using an internal reference are more reliable than both national and local reference and it was observed that “internal analyses of "dose-response" in cohort studies are unlikely to be seriously confounded by smoking habits” (Siemiatycki J, Wacholder S, Dewar R, Wald L, Bégin D, Richardson L, Rosenman K, Gérin M. Smoking and degree of occupational exposure: are internal analyses in cohort studies likely to be
confounded by smoking status? Am J Ind Med. 1988; 13: 59-69). According to socio-economical status, in Italy there is not such a great difference between white and blue collar workers and differences in cancer risk are mainly attributable to exposures at workplace and not to social behaviours during leisure time. Finally, as suggested by dr. Mundt, we performed an analysis on non-malignant respiratory diseases, finding no cases in the referent group, but also no case among autoclave workers, and SMRs for each job category was lower than the external reference. We also agree on the opportunity of a new update of follow-up, but the lack of fund prevented this opportunity; on the other hand, a previous study based on results of a follow-up updated to 1995 leaded to similar conclusion and we are confident that a new follow-up won’t disagree with those already performed. By the way, 90% CI were not introduced to “desperately” produce statistically significant results, but just to yield “an enhanced insight into the importance of some increases of borderline significance at 95% observed in some job categories”, as declared in the text, or, in other words, to support the observation that those increased risks were real.

The few modifications suggested by the other reviewers have been taken in consideration and included in this final version, as appropriate.

Do not hesitate to ask for any further information, if something sounds not good to you. We hope that our paper could be finally accepted for publication in your Journal.

Yours sincerely,

Dr. Fabio Montanaro
(on the behalf of all coauthors)