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Authors' reply: Comment to "Vinyl chloride exposure and cirrhosis: A systematic review and meta-analysis"

Dear Editor,

We wish to reply to the comments by Mastrangelo et al. [1] about our recently published meta-analysis [2]. The authors wrote that we "examined only mortality cohort studies concluding for absence of increased cirrhosis risk in workers exposed to VC"; however in our description of our literature search strategy and our discussion we did consider other types of studies, including animal research, even when they were at odds with our conclusions.

In our meta-analysis of cohort studies, which included over 40,000 workers exposed to vinyl chloride (VC) in North America and Europe resulting in 203 deaths from cirrhosis, the risk of cirrhosis-related death was about 25% less in VC workers than in the corresponding reference populations. Mastrangelo et al. commented that we failed to include a study that reanalyzed subgroups within an exposed cohort and that found a 2.8-fold increased relative risk in the highest exposed group [4]. However, that estimate did not reach significance. Moreover, subgroup analyses may be affected by selection, information and reporting bias. In addition, in the presence of an overall decreased risk (as shown by our meta-analysis), this would imply that the risk in unexposed and weakly exposed workers was very low (half or less than the risk in the reference population), an implausible hypothesis.

Mastrangelo et al. stated that we did not consider the case-control study they published in 2004 [3]. However, we considered it in our discussion, mentioning that their "reported association of VC with cirrhosis [was] at variance with the overall results of [a] partially overlapping cohort study". In fact, the results of their case-control study contrast with those of the cohort study [5] in which the case-control was nested (and which we did include in our meta-analysis). Their selection of controls remains open to discussion, and consequently their results need confirmation.

Mastrangelo et al. also claimed that cirrhosis is underrepresented in mortality statistics because, when cancer is also indicated

in the death certificate, other medical conditions are ignored. This statement represents their personal opinion and differs from the consolidated international rules for the coding of causes of death from death certificates [6].

Lastly, Mastrangelo et al. observed that we did not consider a cross-sectional study on liver fibrosis in polyvinyl chloride workers [7]. We would point out that the study in question reports an association between VC exposure and liver fibrosis, not cirrhosis [7].

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