

Re: “The hidden impact of a healthy-worker effect on the results of the Diesel Exhaust in Miners Study”

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We thank the Journal for providing us the opportunity to respond to Dr. Mohner’s letter regarding the analyses of data from both the cohort [1] and case-control [2] components of the Diesel Exhaust in Miners Study (DEMS).

In his letter, Dr. Mohner contends that the DEMS analyses suffer from a healthy-worker effect (HWE), which presumably led to biased estimates of the lung cancer risk associated with diesel exhaust exposure. Dr. Mohner argues that workers who started employment at the surface of the study mine and moved to underground jobs were healthier than those who remained in jobs at the surface. Workers move to underground jobs for a variety of reasons

including preferences regarding type of work and work environment. We know of no evidence to suggest that workers who moved to underground jobs were healthier than those who did not move underground. Importantly, the movement patterns were similar in cases and controls. Of those in the case-control study who were first employed in surface jobs, 10 % of cases and 13 % of controls made permanent moves from above ground to underground jobs. A more likely scenario is that unhealthy underground workers would have moved to surface jobs. Again, the percent of workers who moved to surface jobs and never returned to underground jobs was similar in cases and controls (14 and 17 %, respectively). The similarity in movement patterns in the cases and controls provides evidence against a HWE that would have biased estimates of lung cancer risk in DEMS.

In addition, it appears that the observed higher lung cancer risks among surface-only workers compared with those among ever-underground workers in the cohort [1] have led to misinterpretation of our findings by Dr. Mohner. In DEMS, it is critical to take worker location into account in estimating the diesel exhaust exposure–response relationship. In fact, to simply estimate risk by exposure with adjustment for smoking, as is done conventionally, without adjustment for worker location, would have led to erroneous results. The smoking effect among surface-only workers shown in Table 2 [2] is similar to that observed in previous cohort studies of smoking and lung cancer [3], whereas the smoking effect among underground workers who smoke at least 1 pack per day is attenuated. As shown in Table 2 [2], *after adjustment for diesel exposure*, the risk among underground nonsmoking workers is virtually identical to that among surface-only nonsmoking workers (OR for 15-year lagged cumulative REC = 0.90), providing evidence that the observed difference in risk between

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surface only and underground workers is explained by smoking and diesel exposure, not by other factors such as dust exposure as Dr. Mohner suggests. It is noteworthy that, with adjustment for worker location, results for the overall DEMS cohort [1] are consistent with those of the overall case-control study [2], as well as with DEMS findings for ever-underground workers in both the cohort and case-control studies.

The effect of smoking in this study cannot be understood by simply comparing smoking prevalences among surface versus underground workers, as proposed by Dr. Mohner. Rather, it is the relationship between smoking status/intensity and quantitative levels of diesel exhaust that is important. Although surface-only workers have a lower prevalence of smoking than underground workers, smoking is inversely related to diesel exhaust exposure among underground workers, resulting in negative confounding by smoking. Failure to take this negative confounding into account will lead to underestimation of the estimates of lung cancer risk associated with diesel exhaust.

Dr. Mohner contends that findings from the DEMS cohort are null, which he argues is consistent with the German potash miners study [4]. However, findings from DEMS are positive and are highly consistent with two other studies that quantified diesel exposure and estimated lung cancer risk [5]. Reasons for the null findings in the German potash miners study have been examined in detail elsewhere [5]. They include the absence of a none/low-exposed referent group as the referent in the potash miners study had an extremely high mean cumulative respirable elemental carbon level of $624 \mu\text{g}/\text{m}^3$, which is higher than nearly all of the exposure categories in the other studies including DEMS (referent in DEMS case-control study is 0 to $<19 \mu\text{g}/\text{m}^3$). Other methodological shortcomings include the lack of smoking data on 53 % of cases and 45 % of controls, and potential confounding from previous employment as a uranium miner. The latter was addressed by attempting to control for prior work in uranium mines [4], which did indeed diminish the effect of diesel exhaust on lung cancer risk in the German potash miners study.

However, the adjustment was based on linkage with another data set of uranium miners, and thus was highly dependent on the accuracy of this linkage, which was based on small numbers (e.g., only 7 of 68 lung cancer cases were linked to the uranium miners roster).

Lastly, Dr. Mohner calls for a “complete reanalysis of the DEMS data”, despite the fact that several independent investigators, including an expert panel commissioned by the Health Effects Institute [6], have reanalyzed the DEMS data and replicated both the cohort [1] and case-control [2] published findings. At this juncture, a more valuable use of resources would be to establish exposure limits that would protect workers’ health and to conduct research to identify the constituents of diesel exhaust that are carcinogenic to the lung.

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