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EDITORIAL

When Are Risk Analyses on Job Titles Informative?

In the January issue of the *Annals of Occupational Hygiene*, we published a paper by Garabrant *et al.* (2016a), 'Mesothelioma among Motor Vehicle Mechanics: An updated review and Meta-analyses'. The paper described an update from a 2004 meta-analyses performed largely by the same authors. The updated meta-analyses included 10 case–control studies, 1 cohort study, and 5 proportional mortality ratio/standardized mortality odds ratio (OR) studies. The results of the meta-analyses indicated that the summary risk estimates were generally <1 and that no statistically significant increases in mesothelioma were observed. The authors therefore concluded that 'this meta-analysis of the epidemiologic studies provides evidence that motor vehicle mechanics, including workers who were engaged in brake repair, are not at an increased risk of mesothelioma' (Garabrant *et al.*, 2016a). This conclusion is similar to the conclusion of the 2004 paper that concluded, based on seven studies of which six studies were also included in the current meta-analyses, that 'employment as a motor vehicle mechanic does not increase the risk of developing mesothelioma' (Goodman *et al.*, 2004). Although there were some methodological differences between the two meta-analyses in how the quality of the studies was scored the two ranking systems showed overall good correspondence and resulted in a similar classification in quality categories. Analyses by quality of the studies did not show an association between study quality and the log OR and of the 10 studies only 2 studies had an OR > 1. All together, the conclusion of the papers seemed therefore scientifically justified.

However, there is a question in how one should interpret this result. As Teschke (2016) pointed out in her letter to the editor, the issue of interest is whether chrysotile asbestos exposure among mechanics causes mesothelioma. Mechanics perform a variety of tasks and not all mechanics will be involved in break repair. The ones that do in turn may only do so for part of the time. Using broad categories of job titles (e.g. garage workers, auto repair and related services, and auto engineers) are therefore likely poor proxies of chrysotile asbestos exposure. As such although the conclusion of the paper is correct in that no elevated risks are found among motor vehicle mechanics as a whole this cannot be equated to mean that there is no risk of mesothelioma among mechanics that were involved in break repair and that had potential chrysotile exposure. In their answer to the letter to the editor, Garabrant *et al.* (2016b) indicated that the results may indicate that motor vehicle mechanics and brake workers are perhaps not at increased risk of mesothelioma as they may not have sufficient exposure to observe an increased risk. Again, this statement is correct at the job-title level but may not hold for specific subgroups and/or individuals that may have been higher exposed. As such, the question can and perhaps should be raised in how far job-title-based analyses are informative and when. A similar debate arose during the International Agency of Research of Cancer (IARC) on the evaluation of the carcinogenic risk among firefighters. Firefighters are exposed to numerous known carcinogens among which benzene, diesel exhaust, formaldehyde, and polycyclic aromatic hydrocarbons (IARC, 2010). However, epidemiological studies based on having a job as a firefighter have rendered heterogeneous results with some indications of elevated risks of testicular and prostate cancer and non-Hodgkin lymphoma. Based

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on the available epidemiological evidence, the IARC expert group concluded that there is limited evidence in humans for the carcinogenicity of occupational exposure as a firefighter. Again, the scientific evidence supports this statement, but similar as to the case of motor vehicle mechanics, the epidemiological results may well have been severely attenuated due to exposure misclassification. It could be argued that a job in which known carcinogenic agents are present should by definition be defined as an exposure circumstance that entails carcinogenic risk. An evaluation of disease risk within such job titles is in essence not a hazard evaluation but an indirect quantitative risk assessment question, as it will depend on the level and prevalence of exposure and the associated risk if a risk at the job-title level can be observed statistically.

So how should we view these analyses on job titles with known carcinogenic exposures? Clearly, such analyses cannot be used to inform on the carcinogenicity of known carcinogenic exposures. In other words, we would not, based on the absence of an association between working as a motor vehicle mechanic and mesothelioma, conclude that there is no association between chrysotile exposure and mesothelioma. As evidenced in a recent meta-regression analyses on chrysotile exposure and mesothelioma risk, there is a monotonic association between occupational chrysotile exposure and mesothelioma risk with no evidence of a threshold (van der Bij *et al.*, 2013) These analyses would suggest that motor vehicle mechanics who are exposed to chrysotile would be at increased risk for mesothelioma. Therefore, analyses on job titles that constitute known carcinogenic exposures are only useful as to investigate the overall risk as to judge the likelihood and level of exposures within the broad job-category. However, this is a rather insensitive tool, as it depends strongly on the validity and power of the epidemiological study. Using industrial hygiene observations and historical measurements may be a more direct and valid way to determine this. The latter also applies to the argument made by Garabrant *et al.* (2016b) that the absence of an effect may be due to the fact that, besides low exposures and potency, fibers are short in friction materials and that they maybe degraded by temperature and physical force into even shorter fibers and forsterite. Again, this may be true but hard to prove based on epidemiological studies by the absence of an effect. Again here, detailed studies of the asbestos fibers in this industry have to be examined carefully, and if identifiable as asbestos, have to be assumed to carry cancer risk even in the absence of epidemiologic evidence.

In the case of job titles with no known carcinogenic exposures, analyses on job-title levels may be informative and may provide clues to work circumstances and exposures that are detrimental to health. A good example of such an analysis is rubber workers where there is consistent epidemiological evidence of increased risks of leukemia, lymphoma, and cancers of the urinary bladder (also after the ban on beta-napthylamine), lung, and stomach (IARC, 2012). In this case, analyses on the job-title level resulted in the identification of increased cancer risks in the rubber manufacturing industry that in turn let to more detailed research on trying to identify the specific agents responsible for the observed risk. Although this has not necessarily led to a clearer picture on what is causing cancer in the rubber industry, it is an example of how analyses on job titles can be used to generate new hypotheses. Such hypotheses would then need to be followed up with more specific (quantitative) studies on potential harmful agents.

In a more sophisticated way, one could combine information on job title and quantitative exposure in a hierarchical regression model (Corbin *et al.*, 2012). Such an analysis would decrease the possibility that an occupation entailing exposure to known occupational carcinogens is rejected, while occupations not entailing exposure to known occupational carcinogens would be highlighted. Such job titles should be further investigated and are more likely to provide information on the role of new or suspected occupational carcinogens. To date, few studies have however implemented such hierarchical methods.

So when are risk analyses on job titles informative? Analyses on job titles can be informative in the situation where job titles entail unknown carcinogens or a mix of known and unknown carcinogens. In these situations, job-title-based analyses can provide information on the role of new or suspected occupational carcinogens. However, as exposures vary considerably within job titles depending on their job activities, they can at best be regarded as crude measures of exposure. As such, positive results may provide new information; however, null results cannot be used to exclude that there is no effect of a known carcinogen within that occupation.

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DECLARATION

The author declares no conflict of interest relating to the material presented in this editorial.

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