

The Occupation of Firefighting and Cancer Risk: Assessment of the Literature A Response to Reviewer Comments

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by:

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On June 15 2004, Cancer Care Ontario submitted a report to the Workers' Compensation Board of British Columbia on The Occupation of Firefighting and Cancer Risk. The Workers' Compensation Board of British Columbia commissioned Drs. Pierre Band and David Parker to provide independent reviews of our report.

The reviewers have raised a number of helpful and thoughtful points. It is interesting to note that the conclusions reached by the reviewers regarding firefighters and cancer are for the most part consistent with ours. This is despite the facts that they included different studies and used different methods for combining results. In the following sections we respond to the reviewers' comments.

2.0 Objectives

The reviewers note a discrepancy between the cancers we listed in the objectives and those we presented in the results. The objectives included those cancers that were specifically of interest to WCB. Although urethral cancer is among them, we found only one study which reported results for this cancer (4 cases were reported). As well, there were no studies which reported results for lung cancer specific to non-smoking firefighters, or which stratified results by smoking status, so we included all studies reporting lung cancer outcomes. Lastly, although rectal cancer was not a cancer of particular interest to WCB, there is a potential for misclassification between colon and rectal cancers, especially on death certificates; as a result, rectal cancers were included to perform a combined analysis of colon and rectal cancers. We note these points in the methods section of the report.

While we agree with the reviewers that an analysis by subtypes of leukemia would have been useful, there were too few studies that reported these outcomes to allow a meaningful analysis.

3.0 Methods

Systematic literature search and inclusion of studies (3.1,3.2)

The reviewers raise a few questions with respect the inclusion of studies. In our review we include all studies which assessed the risk of cancer among firefighters and which provided risk estimates in comparison to a non-firefighter population. Any exclusions were noted in the methods. For each cancer site, results from all studies (whether included in our quantitative analysis or not) may be found in tables accompanying the text, as well as in the appendices.

We did not include proportional mortality studies in the quantitative component since estimates using a proportional mortality ratio (PMR) are sensitive to the number of non-cancer deaths. Because PMR analyses are comparing the distribution of causes of death in two populations, a finding of an increased risk of cancer among firefighters in this type of study may reflect a decreased risk of death from other non-cancer causes in firefighters relative to the reference population. Although occupational surveillance (cross-sectional) studies were not included in the quantitative analysis, they did contribute other information to our review, and findings from these studies were brought into the discussion of specific cancer sites. (For further discussion of the limitations of these studies, see section titled “Analysis (3.5)” below.)

We performed a search of Toxline, as suggested by the reviewers, and found no additional studies assessing cancer outcomes among firefighters. We identified fewer than 5 non-English language studies as part of our literature search.

A glossary has been provided to clarify some of the technical terms used in the report.

Quality assessment (3.4)

The process of assessing the quality of studies contains subjective elements. Although tools for standardizing quality assessment have been proposed in the literature, at present there is a lack of consensus about applying these to observational studies. As indicated by the reviewers, there are discrepancies between themselves with respect to inclusion and exclusion of studies. As is common practice in systematic reviews, we randomly assigned each study to be independently assessed by two of our four reviewers; any discrepancies were discussed and resolved through consensus among all four reviewers.

Analysis (3.5)

We elected to use a random effects model in our meta-analysis (Fleiss, 1993). This approach takes into account that participants included in the analysis were selected from different populations. Although we acknowledge that there is no consensus regarding the best modeling approach, we believe that the random effects model is appropriate in this case. Since the reviewers use a fixed effects method, one would expect to see some difference between our results and theirs.

The healthy worker effect, often a factor in occupational studies, generally has less impact on deaths due to cancer as compared to other causes. As well, the effect tends to lessen with increasing years since first employment (Checkoway et al., 2004). The follow-up period for cohort studies, where reported, was typically in the order of decades. Case-control studies did not report information on years of service. Cross-sectional and PMR studies, which are more likely to be affected by the healthy worker effect, were not included in our quantitative analysis. Therefore, the healthy worker effect is not likely to be a strong factor in the results.

Criteria for Conclusions (3.6)

In reaching our conclusion for each type of cancer, we took into account a number of factors, including consistency of the association, strength of the association (as reflected in the summary risk estimate), the likelihood that results could be due to other known risk factors, and evidence of carcinogenicity of work-related exposures. Below we describe how our criteria relate to those of Bradford Hill.

Consistency – We considered whether or not the association was consistent across studies, whether it pointed in the same direction for both incidence and mortality studies, and whether it was qualitatively altered in the sensitivity analyses (criterion 2 in our report). The requirement of a minimum of three studies (criterion 1 in our report), although somewhat arbitrary, took into account whether the association was reported by different investigators for different study populations, thus allowing an evaluation of consistency.

Strength – We considered the size and significance of the pooled risk estimate (criterion 3 in our report).

Temporal relationship – Although not explicitly included, we addressed this requirement through exclusion of cross-sectional studies.

Specificity – This criteria was addressed in part by requiring that there be evidence of carcinogenicity for the cancer under consideration of at least one agent to which firefighters are potentially exposed. As well, greater weight was placed on the results of incidence than mortality studies. In incidence studies, the outcome is more likely to be identified if it has occurred (i.e., many more people are diagnosed with cancer than die of it) and is less subject to misclassification (i.e., cancer diagnoses are more accurate than cancer causes of death).

Dose-response – We considered evidence for dose-response relationship (criterion 6 in our report). The classification of ‘limited evidence’ was used where other criteria were met but a dose-response relationship could not be demonstrated.

Biological plausibility – We considered whether there was good evidence that at least one documented work-related substance was carcinogenic to the specific cancer site (criterion 4 in our report). Firefighter exposures could occur through a number of routes (inhalation,

ingestion, or skin contact). Protective equipment has been introduced over the past two decades, however, there have been situations in which equipment is removed for short or extended periods of time or situations in which equipment was not sufficient to prevent certain exposures (NIOSH, 2004).

Experimental evidence – Not applicable.

Given the small body of evidence, the small numbers of cases for many cancers, and the available exposure measures, we found it necessary to be flexible in our application of the Bradford Hill criteria.

4.0 Findings

Brain and Nervous System Cancers

The reviewers agreed with us that there was evidence of an association between firefighting and cancers of the brain and nervous system. However, the reviewers also suggested that a stronger conclusion may be appropriate. We concluded that there is “limited evidence” rather than “sufficient evidence” because of the lack of data (partially due to small numbers of cases) with which to assess a dose-response relationship. We agree that there is evidence in the literature to suggest that agents to which firefighters may be exposed (e.g., vinyl chloride) are associated with risk of brain cancer and we have discussed this in the report.

Bladder Cancer

While one reviewer (PB) was in agreement with the conclusion of insufficient evidence, the other favoured a stronger conclusion. Our conclusion of “insufficient evidence” was based on the limited number of incidence studies, as well as inconsistency in results across mortality studies.

Colorectal Cancer

While one reviewer (DP) was in agreement with our conclusion, the other (PB) would have favoured separate analyses for colon and rectal cancers. Given the high chance of misclassification between these two cancers (particularly as reported on death certificates) we believe a combined analysis is appropriate. There is evidence in the literature for an association between work-related exposures and colon cancer. As the reviewers note, there is less information in the literature on the association between exposures and rectal cancer.

Kidney Cancer

We concluded that there was no evidence for an increased risk of kidney cancer based on estimates from available studies, while one of the reviewers (PB) concluded there was insufficient evidence. These distinctions are fine and due to application of different criteria as discussed.

Conclusion

Given the currently available data on cancer outcomes among firefighters, we concluded that there is limited evidence of an association between the occupation of firefighting and cancers of the brain and nervous system, and colorectal cancers. Although the reviewers raise a number of good points, and suggest an alternate analysis for colon and rectal cancers, the conclusions appear to be compatible. The main difference between our conclusions and those of the reviewers is qualitative and lies in the strength of the concluding statements. In the end this would suggest that our conclusions for these cancers are defensible.

Following consideration of points raised by the reviewers and given the current state of evidence, we remain satisfied that the conclusions presented in our report are sound and supported.

References

Checkoway, H, Pearce N, Kriebel D. Research Methods in Occupational Epidemiology. New York: Oxford University Press Inc., 2004.

Centers for Disease Control and Prevention. A Summary of Health Hazard Evaluations: Issue Related to Occupational Exposure to Fire Fighters, 1990-2001. U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health, January 2004. Publication No. 2004-115.

Fleiss JL. The statistical basis of meta-analysis. Stat.Methods Med.Res. 1993;2:121-45.