

Review of “Impact of phenol-based cleaners at Royal Perth Hospital” and the subsequent independent, expert perspective.

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This review was initiated to provide an external review of the Department of Health Report and also to examine the conclusions of the final summary report, from someone who had not been previously involved with any aspect of the investigation.

Main report

Epidemiological studies like this are carried out to examine possible human health effects because no direct experimentation can be done. Analyses are carried out with various assumptions and careful attention is made to the possible, but unknown, effect of biases that could have arisen because of the observational nature of the data. The work in this report has been carried out with thorough and careful methods, including sensitivity analyses of various assumptions, and the conclusions seem appropriate.

There were some minor errors in Tables within the report, which might just be due to transcription errors, or possibly arising from issues with the software used for calculating SMRs. When expected cases are estimated, they are based on age, sex, and period specific rates for the outcome in question in the comparison population. Therefore, in whichever ways the data are then split or subdivided, the total expected cases should remain the same, apart from minor differences caused by date rounding changes at the various time, age, etc., boundaries. It seems to me that, while the differences in expected numbers in Table 5 (around 10 or less) might possibly be caused by date rounding issues, the differences in total expected cases between

groupings in Table 9, 11, and 13, with up to 40 or more expected cases difference, are too large to be caused by rounding, especially considering the exact correspondence between the sums of the expected cases in Tables 11 and 13 and the expected cases in Table 9. Such large differences could possibly (but probably not) make some difference to SMRs and hence to conclusions, depending on where the mistakes have occurred. Table 10 also has an error in the number of deaths column.

A second, also probably minor issue with the analysis, was the lack of an upper age cut-off in the calculation of person-time. It is usual in cohort studies like this, that rely mainly on passive follow-up, to censor follow-up at an upper age (usually 85), to avoid problems caused by missed deaths or other outcomes (see e.g. Sorahan et al, 2005). Without the cut-off, there may be an increase in person-years at higher ages and hence increased expected numbers and decreased SMRs/SIRs in the highest age group and in the longest category of time from first employment.

I also wondered why no attempt had been made to examine and compare hospital admission rates for at least some illnesses, especially respiratory diseases, given that the cohort was linked to the WA HMDS, and that ill health other than cancer was one of the major outcomes of interest. Separate analyses could have been done, as in the main report, for both the whole cohort and for survey responders, and may have clarified some of the issues about the health of these workers, and differences between responders and non-responders.

The independent expert perspective

The conclusions reached by Prof Armstrong's review of the report are clear and sensible and summarise the main findings in more detail than the Executive Summary in the main report, in particular in the interpretation of the findings related to duration of employment and time since start of employment. Interpretation of these temporal effects has been a longstanding difficulty in occupational epidemiological studies and were initially outlined clearly in Enterline's paper (1976). One of the main points being that people who are more sensitive to a particular harmful agent will succumb to its effects sooner, leading to apparent lower risks with greater exposure. However here, there were increases in risks of cancers, cancer deaths, and non-cancer deaths,

with increasing duration of exposure, and after adjustment for age, sex and duration, the peak risks were in the 9-18 year time from first employment, which is compatible with many carcinogenic agents. The conclusions on page 4 of the perspective seem appropriate, especially in light of the differences in patterns of risk between incident cancers and cancer deaths.

It is clear also that the male workers are generally sicker than a matched Perth population and that this is unlikely to be due to exposure to phenol-based cleaners, especially given the male-female differences and the consistency over different outcomes. I endorse the recommendations for possible interventions with staff on page 7.

I am not sure, however, that further study in this group of the unknown primary cancers via a nested case-control study (Perspective – bottom of page 6) would reveal a lot more, unless there were more information available about the pathology of the cancers, especially as 3 of the 12 cases were second cancers. Also, some could well have been missed prostate cancers given the significantly low rate there (see Table 7). If the total exposures could be assessed quickly, easily, and accurately, however, then such a study would definitely be worthwhile.

I agree with Prof Armstrong about the issues with the lack of representativeness of survey, but the findings, as he and the Report suggest, are convincing. It might also possibly be of value to maintain follow-up the cross-sectional survey participants as a cohort to examine longer term within group differences and as a precursor to any of the workplace interventions suggested.

On a final note, I hope the Epidemiology Branch are able to have these findings published (probably requiring 2-3 separate papers) in an established journal to ensure the their carefully collected and analysed data can reach a wide audience and also inform reviews and meta-analyses that will be looking at similar questions.

References

Enterline PE. Pitfalls in epidemiological research. *J Occup Med* 1976;18:150-156.

Sorahan T, Kinlen LJ, Doll R. Cancer risks in a historical UK cohort of benzene exposed workers. *Occup Environ Med* 2005;62:231-236.