Letter to the Editor

Leukemia Risk and Relevant Benzene Exposure Period—Re: Follow-up Time on Risk Estimates, Am J Ind Med 42:481–489, 2002

To the Editor:

In Silver et al. [2002], ''Effect of follow-up time on risk estimates: A longitudinal examination of the relative risks of leukemia and multiple myeloma in a rubber hydrochloride cohort,'' the authors point out that time since exposure to benzene has an effect on risk of leukemia. It has been suggested that benzene exposure which took place more than 15–20 years in the past may no longer be a strong risk factor for leukemia [Finkelstein, 2000; Rinsky et al., 2002]. Evidence from our case-control study of leukemia and benzene exposure supports this suggestion.

This study was nested in a prospective cohort study (Health Watch) of employees who had worked for more than 5 years in the Australian petroleum industry. Thirty-three men with leukemia have been identified in the Health Watch cohort. Five age-matched male controls for each case were selected from the cohort, giving a total of 198 subjects [Glass et al., 2003]. We calculated the likely extent of exposure to benzene on an individual subject basis, using the job history and site- and period-specific information in an algorithm based on measured exposure data from the Australian industry [Glass et al., 2000]. This model is similar to that used in other petroleum industry studies [Armstrong et al., 1996; Lewis et al., 1997]. The case-control study demonstrated a strong exposure–effect relationship between leukemia and cumulative occupational benzene exposure expressed in parts per million-years (ppm-years) [Glass et al., 2003].

We divided each subject's benzene exposure into two periods, that which occurred within 15 years of the date of diagnosis of the matched case and that occurring more than 15 years prior to diagnosis. We analyzed matched sets for the risk of leukemia using conditional logistic regression, with the statistical analysis package StataTM to calculate the odds ratios and 95% confidence intervals.

We found that leukemia was most strongly associated with benzene exposures in the period 15 years prior to diagnosis, and exposures more than 15 years before diagnosis made little contribution to the risk. The increased risk observed for the high exposure group (exposed more than 15 years before diagnosis) may reflect the probability that these individuals are also more likely to have been highly exposed recently (Fig. 1).

The exposure assessment was very complete after 1975 but there was greater uncertainty about exposure pre-1975 because the available exposure data post-dated this period and there were changes that took place at that time in technology and working practices [Glass et al., 2000]. However, the earliest case in this study was diagnosed in 1981 so exposures after 1965 were within 15 years of this diagnosis and likely to have been important for this case. Half of the cases were diagnosed after 1990 so that only exposures after 1975 were within 15 years of the diagnosis and therefore likely to have been relevant for these cases.

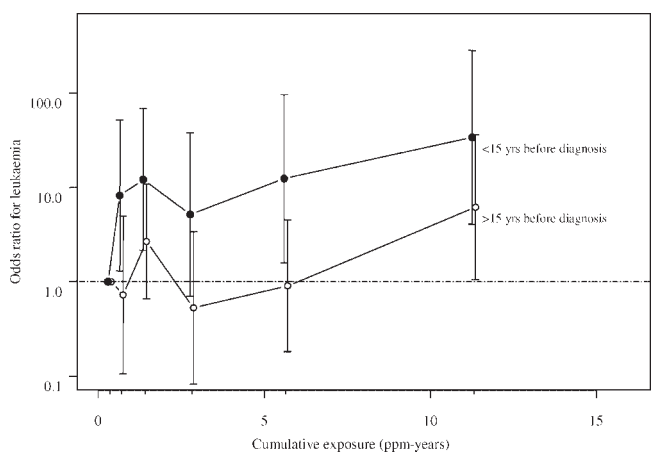

FIGURE 1. Cancer type, odds ratios, and 95% confidence intervals by lag period.

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One implication of our findings is that exposure estimation to investigate the risk of benzene-induced leukemia can be restricted to the period up to 15 years prior to diagnosis. This should help to reduce any misclassification introduced by the uncertainty of exposure assessments carried out for jobs held in the distant past.

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