

The correspondence section is a public forum and, as such, is not peer-reviewed. EHP is not responsible for the accuracy, currency, or reliability of personal opinion expressed herein; it is the sole responsibility of the authors. EHP neither endorses nor disputes their published commentary.

Occupational Benzene Exposure and Lymphoma Risks

<http://dx.doi.org/10.1289/ehp.1104167>

In their recent meta-analysis, Vlaanderen et al. (2011) claimed to show evidence for associations between occupational benzene exposure and risks of multiple myeloma, acute lymphocytic leukemia, and chronic lymphocytic leukemia. However, one of the larger available studies, including 5,514 benzene-exposed UK workers (Sorahan et al. 2005), was excluded from this meta-analysis, apparently because the study had an elevated standardized mortality ratio (SMR) for secondary and unspecified cancers. On the basis of national mortality rates, we would have expected 7% of all cancer deaths in the UK study to have been in the unspecified category (e.g., carcinomatosis, mesothelioma with site unspecified); however, 9% of deaths were unspecified. Given the size of the study (2,430 deaths from all causes), this difference was statistically significant (Sorahan et al. 2005). Is it reasonable to conclude that a study with 93% of cancer deaths with site of cancer specified is informative but one with only 91% specified is not? I do not believe that it is. Vlaanderen et al. (2011) are of course free to come to a different conclusion, but any conclusion they reach must be implemented in an even-handed way. Some obvious questions then arise: *a*) How elevated did the SMR for unspecified cancers have to be for a study to be excluded from their meta-analysis? *b*) Were all the other studies assessed against this criterion? *c*) How many studies did not provide enough information for this criterion to be assessed? *d*) Why was this number not supplied by Vlaanderen et al. (2011)?

The author received a research award from the UK Energy Institute in 2009 to enable the university to carry out an analysis of cancer risks in oil refinery petroleum-distribution workers.

Tom Sorahan

Institute of Occupational and Environmental Medicine
University of Birmingham
Edgbaston, Birmingham, UK
E-mail: T.M.Sorahan@bham.ac.uk

REFERENCES

Sorahan T, Kinlen LJ, Doll R. 2005. Cancer risks in a historical UK cohort of benzene exposed workers. *Occup Environ Med* 62:231–236.
Vlaanderen J, Lan Q, Kromhout H, Rothman N, Vermeulen R. 2011. Occupational benzene exposures and the risk of lymphoma subtypes: a meta-analysis of cohort studies incorporating three study quality dimensions. *Environ Health Perspect* 119:159–167.

Occupational Benzene Exposure and Lymphoma Risks: Vlaanderen et al. Respond

<http://dx.doi.org/10.1289/ehp.1104167R>

We appreciate Sorahan’s interest in our study (Vlaanderen et al. 2011). We first evaluated the article by Sorahan et al. (2005) for inclusion in our meta-analysis based on its analysis of cancer incidence, which is consistent with our stated preference for using incidence rather than mortality data when both were available (Vlaanderen et al. 2011). Because the authors themselves had expressed serious concerns with regard to the underascertainment

of cancer registrations (incidence) (Sorahan et al. 2005), we decided not to include these data and instead considered their mortality analysis, which was included in the same article (Sorahan et al. 2005). We then decided to exclude their mortality data as well because of their “inability to identify the type of cancer for a number of cancer deaths” (Vlaanderen et al. 2011). A total of 9% of all cancer deaths were not identified by type by Sorahan et al. (2005), compared to 2–6% from the publications we considered for inclusion that provided such data (9 of 40 cohorts reviewed). We did not make this decision based on the SMR for this category, as Sorahan claimed in his letter. Inclusion of the mortality data from Sorahan et al. (2005) has a negligible impact on our results [Table 1 compared with Supplemental Material, Table 1 of our paper (<http://dx.doi.org/10.1289/ehp.1002318>)]

Table 1. Pooled risk estimates (and 95% confidence intervals) for AML and five lymphoma subtypes stratified by start of follow-up and AML significance level and including data from Sorahan et al. (2005).

| Lymphoma subtype/ AML significance level ^a | No. of studies | No. of cases | Meta relative risk (all studies) | No. of studies | No. of cases | Meta risk ratio (start follow-up before 1970) | No. of studies | No. of cases | Meta risk ratio (start follow-up 1970 and later) |
|--|----------------|--------------|----------------------------------|----------------|--------------|---|----------------|----------------|--|
| AML | | | | | | | | | |
| A–E (all studies) | 22 | 229 | 1.69 (1.38–2.08)* | 13 | 131 | 1.47 (1.12–1.92)* | 9 | 98 | 2.08 (1.59–2.72) |
| A–D | 22 | 229 | 1.69 (1.38–2.08)* | 13 | 131 | 1.47 (1.12–1.92)* | 9 | 98 | 2.08 (1.59–2.72) |
| A–C | 17 | 204 | 1.87 (1.57–2.22) | 9 | 112 | 1.72 (1.38–2.15) | 8 | 92 | 2.11 (1.61–2.77) |
| A–B | 12 | 144 | 2.15 (1.76–2.63) | 6 | 76 | 1.99 (1.51–2.60) | 6 | 68 | 2.41 (1.77–3.29) |
| A | 10 | 120 | 2.38 (1.89–2.99) | 5 | 63 | 2.13 (1.57–2.89) | 5 | 57 | 2.88 (1.95–3.99) |
| HL | | | | | | | | | |
| A–E (all studies) | 28 | 149 | 1.00 (0.84–1.18) | 20 | 126 | 1.01 (0.84–1.23) | 8 | 23 | 0.91 (0.59–1.40) |
| A–D | 13 | 72 | 0.99 (0.78–1.27) | 9 | 61 | 1.03 (0.79–1.35) | 4 | 11 | 0.83 (0.47–1.48) |
| A–C | 10 | 42 | 0.84 (0.61–1.16) | 6 | 31 | 0.84 (0.57–1.24) | 4 | 11 | 0.83 (0.47–1.48) |
| A–B | 6 | 10 | 0.57 (0.30–1.10) | 3 | 9 | 0.65 (0.31–1.38) | 3 | 1 ^b | 0.40 (0.11–1.44) |
| A | 5 | 10 | 0.61 (0.31–2.19) | 3 | 9 | 0.65 (0.31–1.38) | 2 | 1 ^c | 0.46 (0.10–2.09) |
| NHL^d | | | | | | | | | |
| A–E (all studies) | 34 | 662 | 1.00 (0.89–1.12)* | 23 | 467 | 0.93 (0.82–1.05) | 11 | 195 | 1.21 (0.94–1.55)* |
| A–D | 16 | 398 | 0.96 (0.81–1.14) | 9 | 223 | 0.83 (0.68–1.01) | 7 | 175 | 1.18 (0.91–1.53)* |
| A–C | 14 | 359 | 0.98 (0.81–1.18) | 7 | 184 | 0.83 (0.65–1.05) | 7 | 175 | 1.18 (0.91–1.53)* |
| A–B | 8 | 145 | 1.16 (0.85–1.57) | 3 | 55 | 0.89 (0.62–1.27) | 5 | 90 | 1.38 (0.92–2.06)* |
| A | 7 | 116 | 1.10 (0.78–1.55) | 3 | 55 | 0.89 (0.62–1.27) | 4 | 61 | 1.40 (0.79–2.51)* |
| MM | | | | | | | | | |
| A–E (all studies) | 27 | 290 | 1.11 (0.97–1.26) | 17 | 210 | 1.06 (0.92–1.22) | 10 | 80 | 1.26 (0.92–1.71) |
| A–D | 15 | 166 | 1.13 (0.93–1.37) | 8 | 111 | 1.06 (0.87–1.30) | 7 | 55 | 1.27 (0.81–2.00)* |
| A–C | 13 | 143 | 1.15 (0.91–1.44) | 6 | 88 | 1.08 (0.86–1.34) | 7 | 55 | 1.27 (0.81–2.00)* |
| A–B | 8 | 75 | 1.40 (1.02–1.90) | 3 | 35 | 1.20 (0.73–2.00) | 5 | 40 | 1.58 (1.03–2.44) |
| A | 7 | 62 | 1.42 (0.97–2.08) | 3 | 35 | 1.20 (0.73–2.00) | 4 | 27 | 1.75 (0.94–3.26) |
| ALL | | | | | | | | | |
| A–E (all studies) | 18 | 47 | 1.41 (1.02–1.97) | 11 | 30 | 1.27 (0.86–1.87) | 7 | 17 | 1.92 (1.00–3.67) |
| A–D | 18 | 47 | 1.41 (1.02–1.97) | 11 | 30 | 1.27 (0.86–1.87) | 7 | 17 | 1.92 (1.00–3.67) |
| A–C | 12 | 29 | 1.36 (0.88–2.10) | 6 | 15 | 1.04 (0.60–1.81) | 6 | 14 | 2.10 (1.04–4.25) |
| A–B | 8 | 16 | 1.59 (0.85–2.99) | 3 | 5 | 0.98 (0.38–2.58) | 5 | 11 | 2.28 (0.99–5.26) |
| A | 6 | 12 | 1.52 (0.71–3.26) | 2 | 3 | 0.88 (0.27–2.81) | 4 | 9 | 2.30 (0.84–6.29) |
| CLL | | | | | | | | | |
| A–E (all studies) | 19 | 116 | 1.16 (0.81–1.65)* | 12 | 74 | 0.91 (0.56–1.48)* | 7 | 42 | 1.63 (1.09–2.44) |
| A–D | 19 | 116 | 1.16 (0.81–1.65)* | 12 | 74 | 0.91 (0.56–1.48)* | 7 | 42 | 1.63 (1.09–2.44) |
| A–C | 14 | 98 | 1.20 (0.78–1.84)* | 8 | 60 | 0.91 (0.47–1.75) | 6 | 38 | 1.61 (1.00–2.59) |
| A–B | 9 | 62 | 1.37 (0.80–2.35)* | 5 | 43 | 1.13 (0.43–2.97) | 4 | 19 | 1.84 (1.12–3.02) |
| A | 7 | 50 | 1.36 (0.74–2.51) | 4 | 41 | 1.40 (0.49–4.01) | 3 | 9 | 1.33 (0.64–2.76) |

Abbreviations: ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CLL, chronic lymphocytic leukemia; HL, Hodgkin lymphoma; MM, multiple myeloma; NHL, non-Hodgkin lymphoma. Data presented here correspond to Supplemental Material, Table 1 from Vlaanderen et al. (2011); <http://dx.doi.org/10.1289/ehp.1002318>. Sorahan et al. (2005) was categorized as follow-up starting before 1970; AML significance level A [relative risk > 1 ($p < 0.1$)]; exposure assessment quality D (qualitative indication that benzene exposure had occurred). No observed cases were reported for ALL by Sorahan et al. We therefore calculated continuity-corrected relative risks (observed and expected number of cases + 1) and estimated associated 95% confidence intervals with mid-P exact. Values that are different from those in the original analyses are in italic type. ^aAML significance level categories: A, AML risk estimate > 1 ($p < 0.1$); B, AML risk estimate > 1 ($p < 0.2$); C, AML risk estimate > 1 ($p > 0.2$); D, AML risk estimate reported; E, AML risk estimate not reported. ^bTwo of three studies reported null cases (continuity correction was applied in the meta-analysis). ^cOne of two studies reported null cases (continuity correction was applied in the meta-analysis). ^dNHL or lymphosarcoma/reticulosarcoma (preferred NHL if the study reported both). * $p < 0.1$ for between-study heterogeneity.