discovery rate procedures,⁸ or more Bayesian approaches like false positive report probability (FPRP), in which the prior probability of a true association of the gene (exposure) with a disease is specified a priori.⁹ Although the number of comparisons in occupational studies is very much lower than in genetics, it is our opinion that such approaches should start to find their way into case-control studies that focus on multiple occupational exposures. At a minimum, authors should make clear how many exposures were considered at that time, justifying their inclusion in the study hypotheses. Furthermore, presenting initial observations together in one paper, and applying state-of-the-art statistical analyses accounting for multiple exposures (e.g. hierarchical regression) would be extremely helpful for the readership and would better reflect the complexity in which occupational exposures occur.

Occup Environ Med 2007;**64**:4–5.
doi: 10.1136/oem.2006.027920

Authors' affiliations

H Kromhout, R Vermeulen, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, Netherlands

Correspondence to: Professor H Kromhout, Institute for Risk Assessment Sciences, Utrecht University, PO Box 80176, 3508 TD Utrecht, Netherlands; H.Kromhout@iras.uu.nl

Competing interests: None.

REFERENCES

- 1 Karipidis K, Benke G, Sim M, et al. Occupational exposure to power frequency magnetic fields and risk of non-Hodgkin lymphoma. *Occup Environ Med* 2007;**1**:25–9.
- 2 Villeneuve PJ, Agnew DA, Miller AB, et al. Non-Hodgkin's lymphoma among electric utility workers in Ontario: the evaluation of alternate indices of exposure to 60 Hz electric and magnetic fields. *Occup Environ Med* 2000;**57**:249–57.
- 3 Fabbro-Peray P, Daures JP, Rossi JF. Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France. *Cancer Causes Control* 2001;**12**:201–12.
- 4 Hughes AM, Armstrong BK, Vajdic CM, et al. Sun exposure may protect against non-Hodgkin lymphoma: a case-control study. *Int J Cancer* 2004;**112**:865–71.
- 5 Fritschi L, Benke G, Hughes AM, et al. Occupational exposure to pesticides and risk of non-Hodgkin's lymphoma. *Am J Epidemiol* 2005;**162**:847–57.
- 6 Fritschi L, Benke G, Hughes AM, et al. Risk of non-Hodgkin lymphoma associated with occupational exposure to solvents, metals, organic dusts and PCBs (Australia). *Cancer Causes Control* 2005;**16**:599–607.
- 7 De Roos AJ, Poole C, Teschke K, et al. An application of hierarchical regression in the investigation of multiple paternal occupational exposures and neuroblastoma in offspring. *Am J Ind Med* 2001;**39**:477–86.
- 8 Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B* 1995;**57**:289–300.
- 9 Wacholder S, Chanock S, Garcia-Closas, et al. Assessing the probability that a positive report is false: an approach for molecular epidemiology studies. *J Natl Cancer Inst* 2004;**96**:434–42.

COMMENTARY

Cancer risk in the semiconductor industry: responding to the call for action

K A Mundt

Commentary on the paper by Bender *et al* (see page 30)

In a 2002 editorial, an international group of occupational physicians and health scientists issued a “call for action”, specifically raising concerns about cancer risk in the semiconductor industry.¹ Citing the small number of published papers available at that time,^{2,3} and some unpublished and anecdotal reports, the authors of the editorial highlighted ways in which “some real elevation in the cancer risks” might remain unascertained. They noted, “Though the [earlier] findings are not conclusive, it is clear that more detailed studies are urgently needed to determine whether or not there is a workplace risk, and if so to determine its specific nature and size”.¹ Subsequent epidemiological investigations of cancer risk in the semiconductor industry have been limited to two cohorts of about 1800 and 4900 employees in the semiconductor industry in the UK.^{4–6} These studies identified increased risks

for a few cancer sites; however, the numbers of cases were small and it could not be determined whether occupational exposures played any part.

In this issue of *Occupational and Environmental Medicine*, Bender *et al*⁷ respond to the “call for action” with a large, detailed cohort study of cancer risk in nearly 90 000 semiconductor workers in the semiconductor and storage device sectors employed at two IBM facilities between 1965 and 1999. Although the median follow-up was modest—16 years for semiconductor manufacturers and 11 years for storage device manufacturers—more than 17 000 cohort members were first employed before 1974. Results of thorough, systematic analyses of site-specific cancer risks are reported by industry sector, years of employment and potential for exposure to non-office workplaces (but not specific chemicals), as well as for specific job activities.

Observed incidence rates for all cancers combined were 81% and 87% of the local state rates for workers in semiconductor and storage device sectors, respectively. Nearly all cancer-specific relative risk estimates were near or below unity, some (including colorectal and lung cancers) indicating significant deficits. Even when cancers related to smoking and other lifestyle factors were excluded from the analyses, no excess risks were seen. Cancers of the prostate and the female breast were observed in excess, with prostate cancer being the only significant excess. Such patterns of cancers detected through screening are not unusual in employed populations that are generally healthy and medically well served.⁸

Analyses stratified by work group generated a handful of increased relative risk estimates. However, most of these estimates were based on small numbers of cases, and only soft tissue sarcomas (based on six cases) generated a relative risk estimate >2.5.

Although reporting a few excesses of specific cancers, some of which may be expected owing to random error, the study offers some reassurance that at this stage of follow-up no noteworthy increases in cancer risk are seen among employees in the semiconductor production and storage device sectors. Results may differ for those employed in the earliest years or outside Europe or North America because of differences in workplace conditions or cancer screening and

registration. Also, cancer risks among the cohorts reported here may change over time, and additional follow-up should be considered.

Nevertheless, by most indicators, the Bender *et al* study of the IBM semiconductor and storage device workers seems to be negative. Assuming that these findings are robust, some interesting questions may be posed. For example, have the limits of observational epidemiological methods been reached for detecting human cancer risks that might at most be seen as a few excess cases of a particular cancer out of a cohort of nearly 90 000? How long should such a population be followed up before exposure-related risks may be identified, especially in light of improved production processes and better employee protection that may reduce or eliminate exposure? Detecting small cancer risks and risks due to exposures at or near background levels as early as possible are not new challenges, but they require creative solutions. Biomarkers of exposure and early biological response are attractive, but are costly and rarely implemented

as comprehensively as might be useful epidemiologically.⁹

Bender *et al*'s study, by indicating no clear cancer risks at this time, provides valuable information on cancer risk. It also sets a high standard for occupational epidemiological studies of cancer, drawing on cancer incidence rather than on cancer mortality, which lacks the sensitivity to detect risks of cancers that are treatable or have a low death rate. As workplace conditions and production processes improve, hazardous exposures will be reduced, and any associated risks should also decline. The search for small risks, whether in the semiconductor industry or other modern industrial sectors, will necessitate even more sensitive occupational health research methods and tools.

Occup Environ Med 2007;**64**:5–6.
doi: 10.1136/oem.2006.029504

Correspondence to: K A Mundt, ENVIRON International Corporation, PO Box 2424, Amherst, MA 01004-2424, USA; kmundt@environcorp.com

Competing interests: None.

REFERENCES

- 1 Bailer JC III, Greenberg M, Harrison R, *et al*. Cancer risk in the semiconductor industry: a call for action. *Int J Occup Environ Health* 2002;**8**:163–8.
- 2 Vagero D, Olin R. Incidence of cancer in the electronics industry: using the new Swedish Cancer Environment Registry as a screening instrument. *Br J Ind Med* 1983;**40**:188–92.
- 3 Beall C, Delzell E, Cole P, *et al*. Brain tumors among electronics industry workers. *Epidemiology* 1996;**7**:125–30.
- 4 Nichols L, Sorahan T. Cancer incidence and cancer mortality in a cohort of UK semiconductor workers, 1970–2002. *Occup Med (Lond)* 2005;**55**:625–30.
- 5 McElvenny DM, Darnton AJ, Hodgson JT, *et al*. Investigation of cancer incidence and mortality at a Scottish semiconductor manufacturing facility. *Occup Med (Lond)* 2003;**53**:419–30.
- 6 Sorahan T, Pope DJ, McKiernan MJ. Cancer incidence and cancer mortality in a cohort of semiconductor workers: an update. *Br J Ind Med* 1992;**49**:215–6.
- 7 Bender TJ, Beall C, Cheng H, *et al*. Cancer incidence among semiconductor and electronic storage device workers. *Occup Environ Med* 2007;**1**:30–6.
- 8 Arrighi HM, Hertz-Picciotto I. The evolving concept of the healthy worker survivor effect. *Epidemiology* 1994;**5**:189–96.
- 9 Schulte PA. The use of biomarkers in surveillance, medical screening, and intervention. *Mutat Res* 2005;**592**:155–63.

The chlorine hypothesis: fact or fiction?

M J Nieuwenhuijsen

Commentary on the paper by Nickmilder and Bernard (*see page 37*)

In this issue, Nickmilder and Bernard¹ report on the relationship between the number of indoor chlorination swimming pools and prevalence of wheeze, asthma, hay fever, rhinitis and atopic eczema in European study centres of the International Study of Asthma and Allergies in Childhood (ISAAC) using an ecological study design with adjustment for several indicators such as social economic and lifestyle factors. They found statistically significant positive relationships for all outcomes for the whole of Europe, but fewer when examining specific regions of Europe. They found no statistically significant relationships within countries, but the number of

study centres within a specific country was generally small. The relationship was stronger for 13–14-year-olds than for 6–7-year-olds.

Does this ecological study help to move the field forward? We are all aware of the strength and particularly the limitations of an ecological study design, and the interpretation of the results is generally far from straight forward. Over the recent years several analytical studies have been published that provide some support for a relationship between swimming or attending chlorinated swimming pools and respiratory disease, primarily asthma. Bernard *et al*² found that regular attendance at chlorinated pools by young

children was associated with an increase in lung epithelium permeability and an increase in the risk of developing asthma. Pool attendance was the most consistent predictor of lung epithelium permeability, which was already considerably increased after 1 h at the poolside without swimming. They also found a marked association between cumulated pool attendance and the prevalence of asthma in children. Lagerkvist *et al*³ studied children before and after exercise for 2 h, and found that those who visited chlorinated indoor swimming pools had significantly ($p < 0.002$) lower CC16 levels in serum than did non-swimming children both before and after exercise. Bernard *et al*⁴ reported that cumulative pool attendance was an important predictor for raised exhaled nitrogen oxide levels (eNO; odds ratio (OR) 1.30, 95% confidence interval (CI) 1.10 to 1.43) and asthma in the presence of high immunoglobulin E (IgE) levels (OR 1.79, 95% CI 1.07 to 2.72) in children. Swimming as a baby was the only significant predictor for serum CC16 levels ($p = 0.01$).⁵ Nystad *et al*⁶ found that the prevalence of recurrent respiratory tract infections was higher (12.3%) among children who took part in baby