

## SHORT REPORT

# Persisting risk of nickel related lung cancer and nasal cancer among Clydach refiners

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*Occup Environ Med* 2006;**63**:365–366. doi: 10.1136/oem.2005.026336

**Objective:** To evaluate the risk of lung cancer and nasal cancer among workers employed at the Clydach nickel refinery, South Wales since 1930 by combining data from the two most recently published papers on this cohort.

**Methods:** Observed and expected numbers of cancer deaths were extracted for workers who had a minimum of five years service and were employed for the first time between 1902 and 1992. Standardised mortality ratios (SMR) were calculated for subgroups according to year of employment, time since first employment, and process work.

**Results:** A persisting excess of respiratory cancer was found for workers employed in the period 1930–92, with a lung cancer SMR of 133 (95% CI 103 to 172) and a SMR for nasal cancer of 870 (95% CI 105 to 3141). The lung cancer excess was most clearly seen 20 years or more after first employment and seemed to be confined to process workers. There was no indication of a further reduction in risk since 1930.

**Conclusion:** The extreme nickel related cancer hazard at the refinery before 1920 was greatly reduced during subsequent years. Some of the carcinogenic exposures seem to have remained after 1930, producing an elevated risk of nasal cancer and a 30% excess of lung cancer in the workforce. There was evidence of a persisting risk among process workers first employed since 1953.

The excess of respiratory cancer in workers employed at the nickel refinery in Clydach, South Wales during the first two decades of operation (1902–23) was so high that the existence of an occupational hazard was beyond doubt, long before any specific cause had been recognised.<sup>1,2</sup> The mortality of the refiners has been the subject of extensive research in an attempt to identify the specific compounds and processes that caused the risk.<sup>3–9</sup> The recent contribution by Sorahan and Williams<sup>10</sup> to this classic series of studies adds another 15 years of follow up to the youngest part of the workforce.

Sorahan and Williams<sup>10</sup> studied workers with at least five years' service first employed in 1953 or later, in whom no elevated risk had been seen before.<sup>8,9</sup> There was an overall standardised mortality ratio (SMR) for lung cancer of 139 (95% CI 92 to 201), and a single nasal cancer death. These apparently non-significant findings are important in the light of earlier studies.

The basic principles of the refinery process have been maintained for more than a century, and the relevant carcinogens might cause some risk even at low concentrations. It is therefore interesting to see whether workers hired from 1930 onwards still suffered a detectable hazard, and if so whether exposures had become negligible by 1950, as suggested by previous studies.<sup>8,9</sup>

In 1990, Sir Richard Doll and colleagues attempted to identify the compounds responsible for the cancer risks in nickel workers by combining worldwide data.<sup>8</sup> Their conclusion was that both soluble and insoluble nickel compounds probably contributed to the risk, but no formal dose-response analysis was carried out because many historical exposure estimates were so unreliable. A moderate risk in more recent employees whose exposures may have been better monitored and closer to current working conditions could provide much needed evidence on the safety of the modern nickel producing industry. Whether some cancer risk persisted in the 1950s is therefore important.

Table 1 displays the risk of lung cancer and nasal cancer by period of first employment, based on data from the two most recent articles.<sup>9,10</sup> The data suggest a small excess of lung cancer among workers employed in all periods since 1930. The group as a whole had 62 lung cancer deaths against 46.5 expected, and two nasal cancer deaths against 0.23 expected ( $p = 0.017$  and  $p = 0.023$  for lung cancer and nasal cancer, respectively, one sided tests).

Studies among refiners with a recognised nickel related risk, suggest that an excess of lung cancer would be most clearly seen 15 years or more after first employment.<sup>8,11</sup> Among workers employed since 1953, observed from the 21st year after joining the refinery, Sorahan and Williams<sup>10</sup> reported 26 deaths against 15.8 expected, giving an SMR of 165 (95% CI 108 to 243;  $p = 0.011$ , one sided test).

In the late 1930s, Hill<sup>3</sup> noted that the cancer hazard at the refinery seemed to be confined to process workers, and 20 years later, Doll<sup>4</sup> found a doubling of the lung cancer risk in process workers compared to non-process workers. A similar gradient appears to be present even in the 2005 study.<sup>10</sup> The long term non-process workers in engineering or site-wide activities, representing 42% of the cohort, had no lung cancer excess (SMR of 90),<sup>10</sup> while in the remainder of the cohort, the SMR was 169 (95% CI 105 to 259;  $p = 0.016$ , one sided test).

The possible contribution of social class differences in smoking to the elevated lung cancer risk among workers employed after 1953 cannot be assessed. Smoking habits were unknown for half the cohort, and the lower than expected all cause mortality among smokers suggests that the data were not collected prospectively.<sup>10</sup>

Sorahan and Williams<sup>10</sup> concluded that the non-significant overall excess of lung cancer, together with a nasal cancer death, might well be a chance finding. This seems a slightly optimistic interpretation. The primary aim of the study was "to provide information on any lung cancer risks in relation to exposure to four nickel species: metallic, oxide, soluble compounds, and subsulphide".<sup>10</sup> A statistically significant excess of lung cancer has emerged in men first employed since 1930 ( $p = 0.017$ , one sided test), together with two nasal cancers ( $p = 0.023$ , one sided test), and there is no evidence of a reduction in risk since that year. In men employed since 1953, the overall excess risk is statistically

**Table 1** Observed (Obs) and expected (Exp) numbers of lung cancer and nasal cancer among Welsh nickel refinery workers according to period of first employment (data from Easton *et al*, 1992<sup>9</sup> and Sorahan and Williams, 2005<sup>10</sup>)

Reference	Year of first employment	Follow up	Lung cancer				Nasal cancer			
			Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Easton <i>et al</i> , 1992	1902–1919	1930–1985	83	13.46	617	494–769	55	0.15	37647	28461–49318
Easton <i>et al</i> , 1992	1920–1929	1930–1985	88	28.04	314	253–390	12	0.17	7255	3751–12696
Easton <i>et al</i> , 1992	1930–1939	1935–1985	20	14.45	138	84–213	1	0.07	1434	36–7987
Easton <i>et al</i> , 1992	1940–1949	1945–1985	14	11.88	118	64–198	0	0.06	–	–
Sorahan and Williams, 2005	1953–1992	1958–2000	28	20.17	139	92–201	1	0.10	995	25–5542
Combined	1930–1992	1930–2000*	62	46.50	133	103–172	2	0.23	870	105–3141

SMR, standardised mortality ratio; CI, confidence interval.

Data from Easton *et al* (1992)<sup>9</sup> on men employed between 1950 and 1964 and followed through 1985 are not shown, as most of them are included in Sorahan and Williams (2005).<sup>10</sup>

\*Workers who started before 1950 were only followed through 1985.

significant 20 or more years after first exposure, and appears to be higher among process workers. The nickel related excess risks of lung cancer and nasal cancer among Clydach refinery workers thus seem to have persisted, although at about one twentieth of the level suffered by men employed before 1920.

A prudent conclusion is that current exposure levels in the refinery should be substantially lower than they were in the 1950s, when the hazard may still have been causing lung cancer in a few percent of long term employees. Easton *et al*<sup>9</sup> tested a dose-response model based on pre-1930 workers by comparing observed numbers in later workers against model predictions. A similar prediction of the effects of current working conditions based on mortality rates and estimated exposures of men employed since the 1950s is needed to indicate whether the working conditions throughout the nickel industry are likely to be acceptably safe. The data from this refinery are too sparse to estimate the hazard precisely or to inculpate particular nickel compounds. Formal pooling of updated results on more recent employees from this and other studies might now provide the dose specific risk estimates that Sir Richard Doll and his colleagues were unable to derive from earlier data on heavily exposed workers.

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Competing interests: none

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#### REFERENCES

- 1 **Bridge JC**. Annual report of the chief inspector of factories and workshops for the year 1932. London: His Majesty's Stationery Office, 1933:103–9.
- 2 **Hill AB**. Principles of medical statistics, 8th edn. London: The Lancet, 1966:308–9.
- 3 **Hill AB**. Unpublished report to the nickel company, 1939, cited in: Morgan JG. Some observations on the incidence of respiratory cancer in nickel workers. *Br J Ind Med* 1958;**15**:224–34.
- 4 **Doll R**. Cancer of the lung and nose in nickel workers. *Br J Ind Med* 1958;**15**:217–23.
- 5 **Doll R**, Mathews JD, Morgan LG. Cancers of the lung and nasal sinuses in nickel workers: a reassessment of the period of risk. *Br J Ind Med* 1977;**34**:102–5.
- 6 **Peto J**, Cuckle H, Doll R, *et al*. Respiratory cancer mortality of Welsh nickel refinery workers. In: Sunderman FW Jr, ed. *Nickel in the human environment, proceedings of a joint symposium held at IARC, Lyon, France, 8–11 March 1983*. IARC Scientific Publication No. 53. Lyon: IARC, 1984:37–46.
- 7 **Kaldor J**, Peto J, Easton D, *et al*. Models for respiratory cancer in nickel refinery workers. *J Natl Cancer Inst* 1986;**77**:841–8.
- 8 **Doll R**, Andersen A, Cooper WC, *et al*. Report of the International Committee on Nickel Carcinogenesis in Man. *Scand J Work Environ Health* 1990;**16**(1, special issue):1–82.
- 9 **Easton DF**, Peto J, Morgan LG, *et al*. Respiratory cancer mortality in Welsh nickel refiners: which nickel compounds are responsible? In: Niebor E, Nrigau JO, eds. *Nickel and human health: current perspectives. Advances in environmental sciences and technology*. New York: Wiley & Sons, 1992:603–19.
- 10 **Sorahan T**, Williams SP. Mortality of workers at a nickel carbonyl refinery, 1958–2000. *Occup Environ Med* 2005;**62**:80–5.
- 11 **Grimsrud TK**, Berge SR, Martinsen JI, *et al*. Lung cancer incidence among Norwegian nickel-refinery workers 1953–2000. *J Environ Monit* 2003;**5**:190–7.