

# Cancer of the nose and paranasal sinuses in the metal industry: a case-control study

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## Abstract

**The association between nasal cancer and work in the metal industry was investigated in a case-control study located in the province of Brescia, north eastern Italy. Thirty five cases of malignant epithelial neoplasms of the nasal cavity and paranasal sinuses who were resident in the province of Brescia and diagnosed or treated by the ear, nose, and throat department and the radiotherapy unit (Centro Alte Energie) of the Brescia Hospital in the years 1980-9 were included in the study. Controls (102) were patients affected by benign and malignant neoplasms of the head and neck who were resident in the Brescia Province and matched the cases by age and sex. All the subjects were interviewed by telephone. Metal workers showed an increased risk of nasal cancer (odds ratio (OR) 3.1; 90% confidence interval (90% CI) 0.48-20); a higher risk was associated with work in foundries (OR 5.9; 90 CI 0.77-46). Work in wood, leather, and textile industries was also associated with increased risk of nasal cancer.**

The first reported case of occupationally induced cancer of the paranasal sinuses occurred in a chromate pigment manufacturer who developed the neoplasm several years after suffering from a chromate induced perforation of the septum.<sup>1</sup> Early reports also appeared about nasal cancer in the nickel

refinery workers of the Mond factory in Wales.<sup>2,3</sup> Subsequent epidemiological investigations on nasal cancer in the metal industry have confirmed an occupational cancer risk from chromium<sup>4-6</sup> and nickel compounds.<sup>7-11</sup> Besides chromium and nickel workers, foundry workers,<sup>12,13</sup> welders,<sup>14</sup> and toolmakers<sup>15</sup> appeared to have increased risk of nasal cancer.

In a case-control study carried out at the National Cancer Institute in Milan, an odds ratio (OR) of 4.5 (95% confidence interval (95% CI) 1.4-14.2) was associated with metal work; the job titles at high risk were those of smelter, smith, and mechanic.<sup>16</sup>

Investigations into the risk of nasal cancer in the metal industry are of interest for two main reasons: firstly, the association of nasal cancer with specific job titles in the metal industry might help to identify the aetiologically relevant exposures. Secondly the detection of an increased risk of nasal cancer, which is a rare disease, can be predictive of the presence of a carcinogenic hazard in general and for the respiratory tract in particular.

The purpose of the present study was to investigate the occurrence of nasal cancer, especially in relation to exposures in the metal industry. The study was located in the province of Brescia in northern Italy, east of Milan, where the metal industry has a longstanding tradition. According to the 1981 national census, 31% of the active male population worked in this industrial sector. Average annual mortalities for nasal cancer in the province of Brescia in the years 1983-7 were 5.32 and 0.77 per million person-years in men and women respectively. In the same quinquennium the corresponding rates in Italy were 2.33 and 1.36 cases per million person-years.

## Materials and methods

The study concerned a population of about a million inhabitants, and included cases of malignant epithelial neoplasms of the nasal cavity and paranasal sinuses diagnosed and treated by the ear, nose, and throat (ENT) department and the "Centro Alte Energie" (radiotherapy unit) of the Brescia Hospital from 1980 to the end of 1989. Cases diagnosed in

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Brescia but resident in other provinces were excluded. Controls were selected from the files of the ear, nose, and throat (ENT) department and the radiotherapy unit and included patients affected by benign and malignant neoplastic diseases of head and neck, excluding epidermoid carcinomas of the tongue, oral cavity, oro- and hypopharynx, and larynx. These tumours are known to be associated with intake of alcohol, and a different distribution of alcohol consumption among cases and controls could have resulted in an unbalanced distribution of social class, ultimately leading to spurious associations between the disease of interest and various occupations. Four controls resident in the Brescia province were matched to each case taking into account age (five year classes) and sex. When it was not possible to find four controls complying with the admissibility criteria, fewer were recruited. Altogether, 35 cases and 102 controls were enrolled in the study. One case and four controls refused to be interviewed; the four controls were substituted.

Cases and controls, or the next of kin if the subject had died, were contacted over the telephone by a trained interviewer who filled in a questionnaire without knowing whether the subject was a case or a control. The information collected included a detailed occupational history plus a number of specific items, especially concerning work in the metal industry but also work in leather and wood industries, which was regarded as a potential confounder.

The material was analysed by means of the biomedical data program (BMDP) statistical package. A stratified analysis was performed using the Mantel and Haenszel procedure<sup>17</sup> and 90% confidence intervals (90% CIs) were estimated according to the approximate method of Miettinen.<sup>18</sup> Logistic regression analyses were performed according to the BMDP program.

## Results

Table 1 shows the age and sex distribution of cases and controls. Among men, 82.6% of cases and 65.7% of controls were smokers resulting in an odds ratio (OR) of 2.5 (90% CI 0.93–6.6). Among women, the corresponding proportions of smokers were 27% and 13% respectively, with OR 2.6 (90% CI 0.65–10.3).

Table 2 shows the ORs and the corresponding 90% CIs associated with different occupations for men. Although it was not intended to study the wood and leather industries, a 10-fold increase in risk was associated with this kind of work and a still higher risk was associated with work in the textile and garment industry. Three out of four cases who had worked in this area had presumably been exposed to cotton dust, two of them being sock manufacturers, and one being a cotton garment worker. No corresponding risk was seen, however, for women in this

industry. Metal workers showed a threefold increase in risk, which did not reach statistical significance; if foundry workers alone were considered, the OR was 5.9 (90% CI 0.77–46). To further investigate the association between work in the metal industry and nasal cancer, the potential confounding role of cigarette smoking was assessed by means of logistic regression analysis. The ORs adjusted for smoking were 2.8 (90% CI 0.4–19) for metal workers and 10 (90% CI 0.9–110) for foundry workers. If the analysis was restricted to patients with adenocarcinoma, two cases appeared to be foundry workers, whereas no case was unexposed. One of the two adenocarcinoma cases had been a leather worker as well as a foundry worker. Some extra risk was associated with farming, breeding, and other occupations entailing exposure to dusts and fumes (table 2).

Among women a non-significant increase in risk was associated with farming (table 3).

## Discussion

The present study was especially aimed at studying the risk of nasal cancer for metal workers and a threefold increase in risk was found for this occupation. Foundry workers and smelters had an OR of 5.9, but the few cases found resulted in a wide 90% CI that included unity.

Nevertheless, these findings confirm previous observations by us and by other authors.

A study on the incidence of nasal cancer in England and Wales detected a significant risk associated with work in furnaces, foundries, forges, and rolling mills, the standardised incidence ratio being 250.<sup>12</sup> In a case control study performed in Denmark, Olsen<sup>13</sup> showed significantly increased standardised proportionate incidence ratios (SPIRs) associated with work in the basic metal industry (SPIR = 351), manufacture of metal packaging (SPIR = 571) and bodywork (SPIR = 600). A hospital based programme of surveillance of nasal cancer in Italy detected 17 cases of nasal cancer among metal workers<sup>19</sup>; a subsequent case-control study carried out at the National Cancer

Table 1 Age and sex distribution of cases and controls

	Cases	Controls	Total
Men:			
< 60	10	31	41
61–70	3	14	17
≥ 70	10	25	35
Total	23	70	93
Women:			
< 60	3	8	11
61–70	1	7	8
≥ 70	7	17	24
Total	11	32	43

Age range 28–88.

Table 2 Odds ratios for men associated with various occupations

	No of cases	OR (crude)	OR (log) (90% CI)
Woodworkers*	3	13.5	11 (0.85-139)
Leather workers	1	9.0	—
Metal workers†	9	2.9	3.1 (0.48-20)
foundry workers	5	6.4	5.9 (0.77-46)
Textile and garment workers†	4	18	17 (1.9-162)
Miners and construction workers†	5	3.8	1.2 (0.11-13)
Farmer†	4	1.6	1.9 (0.25-14)
Breeders†	2	3.0	2.0 (0.09-43)
Other occupations entailing exposure to dusts and fumes†	4	1.8	1.5 (0.18-12)
All occupational exposures	22	3.3	(0.59-18)
Reference	1	1.0	1.0

\*Adjusted for age.

†Adjusted for age and exposure to wood and leather dusts.

Institute in Milan showed an OR of 4.5 (95% CI 1.4-14.2).<sup>16</sup>

Although the epidemiological investigations carried out so far have not clearly indicated the nature of the causative agent for nasal cancer in the metal industry, relatively large particles coated with polycyclic aromatic hydrocarbons might play an aetiological part. This hypothesis is consistent with the finding of an increased risk of nasal cancer among gas workers.<sup>20,21</sup> Foundry workers can be exposed not only to aromatic polycyclic hydrocarbons, but also to metal dusts and to mineral oil mists; furthermore, urethane and other plastic products are found in the casting forms.

The high risk of nasal cancer in wood workers and textile workers is consistent with earlier findings. For wood workers it is generally agreed that the high incidence of nasal cancer is causally related to the inhalation of wood dust.<sup>22-24</sup>

Also the finding for textile workers appears to be consistent with data from various countries that suggest an aetiological role for textile dusts. Exposure to cotton dust has been shown to be associated with nasal cancer.<sup>25</sup> This was subsequently confirmed by Brinton *et al.*,<sup>26,27</sup> who found an increased risk of nasal cancer among textile workers employed in dusty occupations. The occurrence of nasal cancer in the textile industry has been further described in Sweden,<sup>28</sup> Hong Kong,<sup>29</sup> Denmark,<sup>13</sup> and Italy.<sup>16</sup>

For the province of Brescia major improvements in

the work environment in the textile industry occurred in the 1980s with regard to the air concentration of dusts and mineral oils.

Our present study suffered from low statistical power because of the low incidence of the disease. An indication of a sixfold increase in risk, however, was still obtained for foundry workers. Any major bias is unlikely to affect this investigation; the selection of cases and controls did not imply recruitment of subjects conditionally on their exposure patterns, the collection of information was performed blindly with respect to case and control state, and the effect of established risk factors for nasal cancer (inhalation of wood dust and leather dust) was taken into account by means of logistic regression. Cigarette smoking, a suspected aetiological agent of nasal cancer<sup>26,30,31</sup> was also taken into account by means of modelling.

The excess risk of nasal cancer among foundry workers and textile workers appears to reflect a causal phenomenon and it seems appropriate to recommend the adoption of remedial action, essentially by abating ambient dust concentrations.

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Table 3 Odds ratios for women associated with various occupations

	No of cases	OR (90% CI) (crude)
Textile and garment workers	3	0.82 (0.20-3.3)
Farmers	4	2.0 (0.51-7.9)
Other occupations entailing exposure to dusts and fumes	1	1.5 (0.16-14)
Reference	5	1.0

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