

Full Paper

Occupational cancer in Britain
Nasopharynx and sinonasal cancers

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OVERVIEW OF NASOPHARYNGEAL AND
SINONASAL CANCERS

Pharyngeal cancer

Pharyngeal cancer includes cancer of the oropharynx, nasopharynx, pyriform sinus and hypopharynx, and may also include unspecified cancers of the oral cavity/pharynx and tonsil. Because of different aetiologies, nasopharyngeal cancer (NPC) will be considered separately from other pharyngeal cancers.

More than 90% of pharyngeal cancers are papillary and squamous cell carcinomas (Daley and Darling, 2003). Worldwide, levels of pharyngeal cancers are generally higher in developed countries including Central and Eastern Europe, and have been linked to tobacco smoking, alcohol consumption, oral human papillomavirus infection, diet, oral hygiene, genetic predisposition and exposure to dusts/chemicals (Mayne *et al*, 2006). Incidence of and mortality caused by pharyngeal cancers in the United Kingdom have generally been stable (Quinn *et al*, 2001), with ~400 cases diagnosed each year and fewer than 150 people dying from the condition annually (HSE, 2012a). NPC has a very distinctive geographic distribution, with high age-standardised incidence rates recorded for populations living in or originating from Southern China and Asia, the Arctic region, North Africa and parts of the Middle East (Yu and Yuan, 2002). Causal factors that have been reported are Epstein–Barr virus infection, consumption of preserved food such as salt-preserved fish, family history of NPC, respiratory tract infections and environmental/occupational exposure to various dusts and chemicals (Yu and Yuan, 2002). Five-year survival during the period 1971–1990 increased for most pharyngeal cancers from 29 to 38% (Quinn *et al*, 2001; Mayne *et al*, 2006).

Sinonasal cancer

Worldwide patterns of incidence and mortality from cancers of the nasal cavity and paranasal sinuses are similar to NPC, with higher

risks in certain ethnic groups. About 70% of SNCs are squamous cell carcinomas, and adenocarcinomas are the next most common histology type accounting for 10–20% (Cancer Research UK, 2012). The 5-year relative survival rate is about 50% (Roush, 1996). This cancer has few non-occupational causes with high relative risks (RRs) for specific chemical exposures and occupational settings, such as nickel refining and woodworking. For these reasons, SNC has been designated a ‘sentinel cancer’ that may permit the identification of environmental cancer risk factors (Rutstein *et al*, 1984). Although environmental and occupational risk factors dominate for SNC, inconsistent associations have been reported with smoking, alcohol consumption, diet and human papillomavirus/Epstein–Barr virus infections (Roush, 1996).

METHODS

Occupational risk factors

Group 1 and 2A human carcinogens The agents that the International Agency for Research on Cancer (IARC) has classified as either definite (Group 1) or probable (Group 2A) human carcinogens for SNC and pharyngeal cancer, for which estimation has been carried out, are summarised in Table 1. Employment in isopropanol manufacture industry was not considered for the SNC-attributable fraction (AF) calculation, as no data were available on which to base estimates. Other exposures and industries/occupations that appear to be associated with an increased risk of SNC but not classified by IARC as a group 1 or 2A carcinogen include polycyclic aromatic hydrocarbons and the textile manufacturing industry.

Choice of studies providing risk estimates for
pharyngeal, nasopharyngeal and sinonasal cancers

A detailed review of occupational risk factor studies identified for pharyngeal cancers (including NPC) and SNC is provided in the relevant Health and Safety Executive technical reports (HSE, 2012a, b).

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See Appendix for the members of the British Occupational Cancer Burden Study Group.

Table 1 Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1–97 (IARC, 1972–2008), into Groups 1 and 2A, which have the pharynx, nasopharynx, nasal cavity and paranasal sinuses as target and for which burden has been estimated

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Source of data for estimation of numbers ever exposed over the REP	Comments
Group 1: Carcinogenic to humans				
Agents, groups of agents				
Formaldehyde	Production; pathologists; medical laboratory technicians; plastics; textile industry	Nasopharynx <i>sufficient</i> Other pharynx; nasal cavity; paranasal sinuses <i>limited</i>	CAREX	
Wood dust	Logging and sawmill workers; pulp and paper, and paperboard industry; woodworking trades (e.g. furniture industries, cabinet making, carpentry and construction); used as a filler in plastic and linoleum production	Nasal cavity; paranasal sinuses <i>sufficient</i> Nasopharynx <i>suggestive</i> Other pharynx <i>limited</i>	CAREX	
Chromium VI	Chromate production plants dyes and pigments; plating and engraving; chromium ferro-alloy production; stainless-steel welding; in wood preservatives; leather tanning; water treatment; inks; photography; lithography; drilling muds; synthetic perfumes; pyrotechnics; corrosion resistance	Nasal cavity; paranasal sinuses <i>sufficient</i>	CAREX	Processes changed in the United Kingdom in 1958–1960, so included for pre 1960 exposures only
Nickel compounds	Nickel refining and smelting; welding	Nasal cavity; paranasal sinuses <i>sufficient</i>	Sorahan and Williams (2005)	812 Workers first employed in the period 1953–1992 with at least 5 years of employment at Clydach
Mineral oils	Production; used as lubricant by metal workers, machinists, engineers, printing industry (ink formulation); used in cosmetics, medicinal and pharmaceutical preparations	Nasal cavity; paranasal sinuses <i>sufficient</i>	LFS	
Exposure circumstances				
Boot and shoe manufacture and repair (leather dust)	Leather dust; benzene and other solvents	Nasal cavity; paranasal sinuses <i>sufficient</i>	CoE	
Furniture and cabinet making	Wood dust	Nasal cavity; paranasal sinuses <i>sufficient</i>		Considered with wood dust

Abbreviations: CAREX = CARcinogen EXposure database; CoE = Census of Employment; IARC = International Agency for Research on Cancer; LFS = Labour Force Survey; REP = risk exposure period.

Occupational exposures common to nasopharyngeal and sinonasal cancers

Wood dust Occupational exposure to fine particulate wood dust is an established cause of NPC and SNC. No consistent associations have been found between wood dust and other pharyngeal cancers. The highest exposures to wood dust have generally been reported for occupations in the furniture-making industry, although carpenters, machine operators, workers in the construction industry and in logging/forestry operations also experience exposure to wood dust (Demers *et al*, 1995). In the United Kingdom, despite a decline in exposures to wood dust at levels in excess of the maximum exposure limit between 1990 and 2000, exposures to high levels of wood dust remain in some wood-working activities (Dilworth, 2000). Associations appear to be strongest for exposure to hardwood dust and fine particulate dust, with a dose–response relationship reported for both wood dust levels and duration of exposure (IARC, 1995).

Risk estimates for occupational exposure to wood dust and SNC and NPC The risk estimates used for the calculation of the

AF for both SNC and NPC have been taken from a pooled reanalysis of data from five cohort studies (British furniture workers, members of the union representing furniture workers in the United States, plywood workers and wood model makers; Demers *et al*, 1995). A significantly high excess of nasal cancer was observed (standardised mortality ratio (SMR) = 3.1, 95% CI = 1.6–5.6), particularly among furniture workers (SMR = 4.3, 95% CI = 2.2–7.8) and among those with definite wood dust exposure (SMR = 8.4, 95% CI = 3.9–16.0). The overall risk estimate for SNC (SMR = 3.1, 95% CI = 1.6–5.6) is based solely on cases from a British furniture worker cohort and has been used for the AF calculation for the high-exposure group. As no dose–response data are available, a RR of 2.0 (95% CI = 0.3–5.2), based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project for which data were available, has been estimated for the low-exposure level category.

Demers *et al* (1995) also report a statistically significant increase in mortality for NPC in woodworkers (specifically furniture and plywood workers: SMR = 2.4, 95% CI = 1.1–4.5), and this has been used to determine the AF for NPC for woodworkers in all relevant

high-exposure industries. Although a dose-response relationship was identified for definite exposures (SMR = 5.3, 95% CI = 1.7–12.4), this risk estimate is considerably higher than that reported in other studies. As low-exposure risks are not easily converted from the qualitative grading provided in the paper by Demers *et al* (1995), the risk estimate for low-exposed groups has been set to 1.

Other studies have also found similar increased risks for SNC in relation to wood dust exposure in several countries. These include the following: an increased risk of SNC for men exposed to wood and wood dust in British Columbia, Canada (RR = 2.3, $P = 0.02$), which remained significant after adjusting for smoking and ethnicity (RR = 2.5, $P < 0.03$; Elwood, 1981); very high excesses of SNC in men working in furniture factories in Buckinghamshire, UK (Rang and Acheson, 1981); and high risks in people working in the wood and paper industry, in furniture and cabinet making and in carpentry work, in a case-control study in the Netherlands (Hayes *et al*, 1986). Two population-based case-control studies in Washington State also found that nasal cancer was strongly associated with employment in wood-related occupations (odds ratio (OR) = 2.4, 95% CI = 0.8–6.7) increasing to an OR of 3.1 (95% CI = 1.0–9.0) after a 15-year induction period was considered (Vaughan and Davis, 1991). The authors suggest that exposure to softwood dust increases the risk of sinonasal squamous cell cancer.

Other studies also support the association between wood dust exposure and NPC, although there is potential coexposure to formaldehyde reported in some of these studies (Armstrong *et al*, 2000; Vaughan *et al*, 2000).

Formaldehyde Formaldehyde is used mainly in the production of phenolics, urea, melamine and polyacetal resins, and as an intermediary in industrial chemical manufacture. These have wide uses as adhesives and binders for wood products, pulp and paper manufacture; in synthetic vitreous fibre industries, for the production of plastics and coatings; and in textile finishing. High formaldehyde exposure occupations include textile operations and wood product manufacture/processing (with coexposure to wood dust); short-term high-exposure episodes have been reported for embalmers, pathologists and paper industry workers.

Risk estimates for occupational exposure to formaldehyde and NPC The risk estimate for the calculation of the AF for NPC in association with exposure to formaldehyde has been taken from a study of workers in formaldehyde industries in the US (Hauptmann *et al*, 2004), which was cited as key defining evidence by IARC in support of the NPC and formaldehyde link (IARC, 2006). The SMR value of 2.10 (95% CI = 1.78–9.13) from this study has been used for the high-level-exposure industries, including embalmers and funeral directors. There is, however, some uncertainty about the risk of NPC at low-level exposure to formaldehyde, and the RR for low or background exposures to formaldehyde has thus been set to 1 for AF estimation.

In addition to the study by Hauptmann *et al* (2004), there are a large number of studies of different groups of workers investigating the association between exposure to formaldehyde and NPC with some positive and negative risk estimates (HSE, 2012a). Marsh *et al* (2007) reanalysed the cohort mortality data for >25,000 workers in 10 US plants (manufacturing formaldehyde or using it in the manufacture of other products) reported by Hauptmann *et al* (2004), and suggested that the SMR calculated in Hauptmann's paper (2.1, 95% CI = 1.05–4.21) may be biased because of unusual findings at one of the 10 factories included in the NCI cohort study. A study by Coggon *et al* (2003) of a cohort of ~14,000 workers from UK chemical facilities employed between 1937 and 1965, reported fewer observed deaths from NPC than were expected (SMR 0.5, 95% CI = 0.01–2.79). Pinkerton *et al* (2004) and Dell and Teta (1995) did not

observe any cases of NPC in retrospective cohort studies of mortality in workers (garment and plastic manufacturing respectively) exposed to formaldehyde. Case-control studies such as those by Vaughan *et al* (2000) (OR = 1.3, 95% CI = 0.80–2.10) and Hildesheim *et al* (2001) (OR = 1.4, 95% CI = 0.93–2.2) generally reveal higher RRs than cohort studies. In addition, higher risks for NPC have been reported in studies of embalmers and funeral directors, for example, SMR = 2.10 (95% CI = 0.6–5.4; Hayes *et al*, 1990).

Risk estimates for occupational exposure to formaldehyde and SNC The risk estimate used in the calculation of the AF for SNC in relation to exposure to formaldehyde was taken from a pooled analysis of European case-control studies, including use and production of formaldehyde (Mannetje *et al*, 1999). No excess of SNC associated with formaldehyde was observed for female workers (OR = 0.83, 95% CI = 0.41–1.69); there was a significantly increased risk found in men (OR = 1.66, 95% CI = 1.27–2.17), adjusted for other concurrent exposures including wood dust. This has been used for the high-exposed industries. The RR for low and background exposures and exposures of female workers to formaldehyde has been set to 1 for AF estimation.

Results from epidemiological studies of SNC and formaldehyde are inconsistent, with a number of studies showing an increased risk and others showing no excess risks, and often different findings for NPC and SNC (HSE, 2012b). For example, Hauptmann *et al* (2004) found too few deaths from SNC to confirm an association with formaldehyde exposure. Coggon *et al* (2003) also reported a lack of association for SNC (SMR = 0.87, 95% CI = 0.11–3.14) as for NPC. In contrast, Hansen and Olsen (1995) found, in a mortality study of 265 companies in Denmark where exposure to formaldehyde occurred, a significantly elevated risk for SNC cancer overall (standardised proportionate incidence ratio (SPIR) = 2.3, 95% CI = 1.3–4.0) plus elevated risks for workers exposed to both wood dust and formaldehyde (SPIR = 5.0, 95% CI = 0.5–13.4) and among workers moderately exposed to formaldehyde but with no probable exposure to wood dust (SPIR = 3.0, 95% CI = 1.4–5.7).

Other occupational exposures considered for NPC

Mustard gas (sulphur mustard/bis(2-chloroethyl)sulphide) Mustard gas was used as a vesicant in chemical warfare during the First World War, but its use was prohibited thereafter by the Geneva Convention of 1925. Currently, this chemical is only produced for use in military research and is a recognised carcinogen in humans (IARC, 1987). A few studies have reported excesses of pharyngeal and/or laryngeal cancer in workers at mustard gas factories employed up to 1945 (Blair and Kazerouni, 1997), but the manufacture of mustard gas ceased in the United Kingdom in the 1940s. Given the low numbers likely to be exposed during the relevant exposure period, an attributable risk has not been calculated.

Other occupational exposures considered for sinonasal cancer

Risk estimate for work in boot and shoe manufacture and repair The risk estimate used in the calculation of the AF for SNC in relation to boot and shoe manufacture and repair has been taken from a mortality study of men employed in the boot and shoe manufacturing industry in Great Britain (Fu *et al*, 1996). An increased overall risk of nasal cancer was found and has been used for the AF calculation (SMR = 7.41, 95% CI = 3.83–12.94). The risk in the English cohort appeared to be associated with exposure to leather dust (probable: SMR = 11.70, 95% CI = 5.34–22.20, based on nine cases; high: SMR = 25.00, 95% CI = 0.63–139.00, based on one case).

In the same paper, Fu *et al* (1996) also investigated an Italian cohort and found an excess risk of 9.09 (95% CI = 0.23–50.65, based on one case) for nasal cancer. The results support earlier studies where RRs for SNC well in excess of 10-fold have been reported, with workers in the dustiest operations at greatest risk (Pippard and Acheson, 1985; Merler *et al*, 1986). However, not all epidemiological studies have reported an excess of nasal cancer (HSE, 2012b).

Nickel Nickel is used in the production of stainless steel, copper–nickel alloys and other corrosion-resistant alloys, as well as in electroplating, as a chemical catalyst, and in the manufacture of alkaline batteries, coins, welding products, magnets, electrical contacts and electrodes, spark plugs, machinery parts and surgical and dental prostheses. Exposure to nickel occurs by inhalation, ingestion and skin contact of airborne fumes, dusts and mists in nickel and nickel alloy production plants, as well as in welding, electroplating, grinding and cutting operations.

Risk estimates for occupational exposure to nickel and SNC Early studies of industrial cohorts suggested that the risk of SNC associated with nickel exposure arose in the course of the nickel refining process, probably through exposure to nickel oxides or a mixture of oxides and sulphides of nickel (Roush *et al*, 1980). Most of the observations of elevated risk appear to be in workers exposed to high levels of soluble nickel compounds through processes that have not been used in Britain for many years. The risk estimate used in the calculation of the AF for SNC in relation to nickel exposure has been taken from a study by Grimsrud and Peto (2006) of workers employed at the largest nickel carbonyl refinery in Europe, located in Clydach, Swansea, Wales (SMR = 8.70, 95% CI = 1.05–31.41, based on only two cases).

Chromium VI Similar to nickel, chromium VI (Cr VI) is resistant to corrosion and is widely used in chromium alloys and chrome plating, as well as in steel production. Exposures to chromium and particularly Cr VI occur during a range of mining, refining and production activities including chromate production, welding, chrome pigment manufacture, chrome plating and spray painting.

Risk estimates for occupational exposure to Cr VI and SNC The risk estimate used in the calculation of the AF for SNC in relation to Cr VI exposure has been taken from a cohort of chromium smelter workers at four plants in New Jersey, USA, employed between 1937 and 1971 (Rosenman and Stanbury, 1996). After adjustments for age and time period, a significantly elevated risk for SNC was found in white male employees (proportionate cancer mortality ratio = 5.18, 95% CI = 2.37–11.30). This risk estimate has been used for the high-exposure group, offering a more cautionary estimate than risk estimates from other, smaller studies (HSE, 2012b). Positive associations were found for duration of employment, as well as time from first employment to last known employment, and deaths were distributed across all four plants. Because of the absence of sufficient dose–response data specific to chromium and sinonasal cancer (SNC), a risk estimate of 3.34 (95% CI = 0.4–10.5) was estimated for the low-exposure-level category based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project for which data were available.

Mineral oils Mineral oils are primarily used as a lubricant base to produce further refined oil products, including engine oils, machine oils and metalworking oils for a variety of industries.

Risk estimates for occupational exposure to mineral oils and SNC Few studies have evaluated the association between occupational exposure to mineral oils and SNC. However, Roush

et al (1980) reported a case–control study that identified a positive association between employment involving exposure to cutting oils and SNC (OR = 2.8, 95% CI = 1.4–5.7), although exposure to individual substances was not evaluated. This estimate has been used for the high-exposure group. A risk estimate of 1.8 (95% CI = 0.2–5.3) has been estimated for the low-exposure-level category based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project for which data were available. An RR of 1 was used for background-level exposure.

Estimation of numbers ever exposed

The data sources, major industry sectors and jobs for estimation of numbers ever exposed over the risk exposure period (REP) defined as the period during which exposure occurred that was relevant to the development of the cancer in the target year 2005, are given in Table 1.

Wood dust exposure was categorised as high in the construction, furniture-making, wood product manufacture and forestry/logging industries where exposure to fine particulate dust was common. High exposures to formaldehyde were assumed for textile and glass manufacture, education, research, health, household and personal services. In the boot and shoe manufacturing and repair industry, only individuals exposed to vegetable-tanned leather dust are believed to be at risk (Coggon, personal communication).

Estimation for nickel was restricted to men employed since 1953 at the only British refining plant at Clydach, South Wales. For exposure to mineral oils, work involving exposure to metalworking fluids as a fine mist spray was assumed to have high exposure; this included metal workers such as machine operators, tool setters and fitters.

RESULTS

Because of assumptions made about cancer latency and working age range, only cancers in patients aged 25 years and above in 2005/2004 could be attributable to occupation. In the present study, a latency period of at least 10 years and up to 50 years has been assumed for NPC and SNC, which corresponds well with the mean latency period of 43 years reported for SNC (Roush, 1996). Attributable fractions for NPC and SNC have been calculated for formaldehyde and wood dusts (for both cancers) and in addition for SNC, leather dust, nickel, Cr VI and mineral oils. Table 2 provides a summary of the attributable deaths and registrations in Britain for 2005 and 2004 and shows the separate estimates for men and women, respectively.

For all exposure scenarios combined, the overall AFs and attributable deaths and registrations for NPC and SNC were 8.03% (95% CI = 1.78–34.33%) and 32.67% (95% CI = 21.53–55.01%), respectively, giving in total 8 (95% CI = 2–33) deaths and 15 (95% CI = 3–65) registrations for NPC, and 38 (95% CI = 25–63) deaths and 126 (95% CI = 83–212) registrations for SNC.

Exposures affecting nasopharyngeal cancer and SNC

In total, there were an estimated 342 048 men and 182 153 women exposed to formaldehyde across the various industries and professions over the REP. For NPC, the overall AF from exposure to formaldehyde was 0.44% (95% CI = 0.00–2.18%), with 0 (95% CI = 0–2) attributable deaths and 1 (95% CI = 0–4) attributable registration. The overall AF for SNC from exposure to formaldehyde was 0.17% (95% CI = 0.10–0.45%), with 0 (95% CI = 0–1) attributable deaths and 1 (95% CI = 0–2) attributable registration.

There were an estimated 1 744 690 men and 404 352 women in total exposed to wood dusts across the various wood industries

Table 2 Nasopharyngeal and sinonasal cancer burden estimation results

Agent	Number of men ever exposed	Number of women ever exposed	Proportion of men ever exposed	Proportion of women ever exposed	AF men (95% CI)	AF women (95% CI)	Attributable deaths (men) (95% CI)	Attributable deaths (women) (95% CI)	Attributable registrations (men) (95% CI)	Attributable registrations (women) (95% CI)
Nasopharyngeal cancer										
Formaldehyde	342,048	182,153	0.0176	0.0087	0.0051 (0.0000–0.0256)	0.0029 (0.0000–0.0141)	0 (0–2)	0	1 (0–3)	0 (0–1)
Wood dust	1,744,690	404,352	0.0899	0.0193	0.1035 (0.0148–0.2410)	0.0209 (0.0028–0.0554)	7 (1–16)	1 (0–2)	13 (2–31)	1 (0–3)
Totals ^a					0.1081 (0.0234–0.4787)	0.0237 (0.0064–0.0684)	7 (2–31)	1 (0–2)	14 (3–61)	1 (0–4)
Sinonasal cancer										
Chromium VI	446,917	244,475	0.0230	0.0116	0.0723 (0.0275–0.1938)	0.0380 (0.0143–0.1073)	5 (2–12)	2 (1–6)	16 (6–42)	6 (2–17)
Formaldehyde	342,048	182,153	0.0176	0.0087	0.0031 (0.0019–0.0081)	0 (0)	0 (0–1)	0	1 (0–2)	0
Leather dust	216,814	384,133	0.0112	0.0183	0.0668 (0.0328–0.1231)	0.1049 (0.0526–0.1874)	4 (2–8)	5 (3–10)	15 (7–27)	17 (8–30)
Mineral oils	442,658	466,252	0.2282	0.0222	0.2240 (0.0167–0.6253)	0.0347 (0.0100–0.1043)	14 (1–39)	2 (1–5)	49 (4–137)	6 (2–17)
Nickel	164	0	0.0000	0.0000	0.0001 (0.0000–0.0004)	0 (0)	0	0	0 (0–1)	0
Wood dust	1,744,690	404,352	0.0899	0.0193	0.1533 (0.0594–0.2912)	0.0349 (0.0129–0.0789)	10 (4–18)	2 (1–4)	34 (13–64)	6 (2–13)
Totals ^a					0.4330 (0.2732–0.7404)	0.1979 (0.1444–0.3160)	27 (17–47)	10 (8–16)	95 (60–162)	31 (23–50)

Abbreviation: AF = attributable fraction. ^aTotals are the product sums and are not therefore equal to the sums of the separate estimates of AF, deaths and registrations for each agent. The difference is especially notable where the constituent AFs are large.

over the REP (1956–1996). For NPC, the overall AF from exposure to wood dust was 7.62% (95% CI=1.08–17.98%), with 7 (95% CI=1–17) attributable deaths and 14 (95% CI=2–34) attributable registrations. The overall AF for SNC from exposure to wood dust was 10.02% (95% CI=3.85–19.60%), with 11 (95% CI=4–22) attributable deaths and 39 (95% CI=15–76) attributable registrations.

Exposures affecting SNC only

Over the REP, 446917 men and 244475 women were ‘ever exposed’ to Cr VI. The total AF for SNC associated with Cr VI was 5.69% (95% CI=2.16–15.50%), with 7 deaths (95% CI=2–18) and 22 (95% CI=8–59) registrations for SNC. Approximately 72% of the deaths and registrations that could be attributable to chromium were for men. Chromium VI exposure in manufacture of machinery (except electrical) had the most attributable registrations and deaths for both men (four and one, respectively) and women (one registration). Manufacture of fabricated metal products, except machinery and equipment also had three male and one female registration and one male death.

There were an estimated 216,814 men and 384,132 women ‘ever exposed’ to leather dust over the REP. The overall AF for SNC from leather dust was 8.39% (95% CI=4.17–15.19%), resulting in 10 (95% CI=5–17) attributable deaths and 31 (95% CI=16–57) attributable registrations. Individuals involved in the manufacture of footwear had the most registrations and deaths attributable to occupation for both men (9 and 3, respectively) and women (13 and 4, respectively).

The total AF for SNC associated with nickel exposure was 0.00% (95% CI=0.00–0.02%). For the Clydach factory alone there were 164 men ever potentially exposed to nickel over the relevant exposure period, resulting in no attributable deaths or registrations.

There were an estimated 4 426 581 men and 466 252 women ‘ever exposed’ to mineral oils over the REP. The total AF was 13.84% (95% CI=1.37–38.97%), with 16 (95% CI=2–45) deaths and 55 (95% CI=5–154) registrations. Metal workers were at the most risk (43 male and 5 female registrations), particularly machine tool operators for both men (18 registrations and 5 deaths) and women (4 registrations and 1 death).

DISCUSSION

These results for SNC update those previously published (HSE, 2007). Because of the availability of more recent data, the overall AF estimated for men has reduced from 64 to 43% and has risen slightly for women from 18 to 20%. Our estimate of the overall AF for SNC of 33% is greater than those of Doll and Peto (1981) (25% men and 5% women) and Nurminen and Karjalainen (2001) (24% men and 7% women), but is at the lower end of the range given by Steenland *et al* (2003) (33–46%) and lower than those for Europe, given by Kogevinas *et al* (1998) (41%) and Mannetje *et al* (1999) (39%). Our estimate of the overall AF for NPC of 8.0% is also greater than that of Nurminen and Karjalainen (2001) (<0.01%).

Occupational exposures contribute greatly to SNC incidence and mortality compared with NPC. Mineral oils for SNC and wood dust for NPC are responsible for the greatest number of cancer

registration/deaths. However, establishing risk estimates for NPC and SNC and exposure to formaldehyde is complicated by the unclear definitions in many studies of cancer sites, variation in magnitude and direction of effect and the effects of confounding from other risk factors, notably wood dust. In addition to the carcinogens evaluated, there are other occupational agents and factors that may also have a role in NPC and SNC incidence and mortality. Exposures that have not been evaluated in this study include ionising radiation (particularly in radium dial

painters) that has recently been identified as a Group 1 carcinogen for SNC (unlikely to contribute to the UK burden due to small numbers), and asbestos and environmental tobacco smoke as Group 2A carcinogens for pharyngeal cancers (Straif *et al*, 2009).

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

- Armstrong RW, Imrey PB, Lye MS, Armstrong MJ, Yu MC, Sani S (2000) Nasopharyngeal carcinoma in Malaysian Chinese: occupational exposures to particles, formaldehyde and heat. *Int J Epidemiol* **29**: 991–998
- Blair A, Kazerouni N (1997) Reactive chemicals and cancer. *Cancer Cause Control* **8**: 473–490
- Cancer Research UK (2012) Cancer Research UK. Available at <http://info.cancerresearchuk.org/> (accessed 17 April 2012)
- Coggon D, Harris EC, Poole J, Palmer KT (2003) Extended follow-up of a cohort of British chemical workers exposed to formaldehyde. *J Natl Cancer Inst* **95**: 1608–1615
- Daley T, Darling M (2003) Non-squamous cell malignant tumours of the oral cavity: an overview. *J Can Dent Asso* **69**: 577–582
- Dell L, Teta MJ (1995) Mortality among workers at a plastics manufacturing and research and development facility: 1946–1988. *Am J Ind Med* **28**: 373–384
- Demers PA, Boffetta P, Kogevinas M, Blair A, Miller BA, Robinson CF, Roscoe RJ, Winter PD, Colin D, Matos E (1995) Pooled reanalysis of cancer mortality among 5 cohorts of workers in wood-related industries. *Scand J Work Env Health* **21**: 179–190
- Dilworth M (2000) *Wood Dust Survey 1999/2000*. Health and Safety Laboratory: Buxton
- Doll R, Peto R (1981) *The Cause of Cancer*. Oxford University Press: Oxford
- Elwood JM (1981) Wood exposure and smoking: association with cancer of the nasal cavity and paranasal sinuses in British Columbia. *Can Med Assoc* **124**: 1573–1577
- Fu H, Demers PA, Costantini AS, Winter P, Colin D, Kogevinas M, Boffetta P (1996) Cancer mortality among shoe manufacturing workers: an analysis of two cohorts. *Occup Environ Med* **53**: 394–398
- Grimsrud TK, Peto J (2006) Persisting risk of nickel related lung cancer and nasal cancer among Clydach refiners. *Occup Environ Med* **63**: 365–366
- Hansen J, Olsen JH (1995) Formaldehyde and cancer morbidity among male employees in Denmark. *Cancer Cause Control* **6**: 354–360
- Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A (2004) Mortality from solid cancers among workers in formaldehyde industries. *Am J Epidemiol* **159**: 1117–1130
- Hayes RB, Blair A, Stewart PA, Herrick RF, Mahar H (1990) Mortality of US embalmers and funeral directors. *Am J Ind Med* **18**: 641–652
- Hayes RB, Gerin M, Raatgever JW, de Bruyn A (1986) Wood-related occupations, wood dust exposure, and sinonasal cancer. *Am J Epidemiol* **124**: 569–577
- Hildesheim A, Dosemeci M, Chan CC, Chen CJ, Cheng YJ, Hsu MM, Chen IH, Mittl BF, Sun B, Levine PH, Chen JY (2001) Occupational exposure to wood, formaldehyde, and solvents and risk of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers* **10**: 1145–1153
- HSE (2007) The burden of occupational cancer in Great Britain: Technical Annex 2: Sinonasal cancer. RR 595, Health and Safety Executive: <http://www.hse.gov.uk/research/rrpdf/rr595ann2.pdf>
- HSE (2012a) The burden of occupational cancer in Great Britain – technical report: pharyngeal and nasopharyngeal cancer. Health and Safety Executive: <http://www.hse.gov.uk/cancer/>
- HSE (2012b) The burden of occupational cancer in Great Britain – technical report: sino-nasal cancer. Health and Safety Executive: <http://www.hse.gov.uk/cancer/>
- IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to humans: overall Evaluations of Carcinogenicity – An Updating of IARC Monographs*, Vols 1–42. International Agency for Research on Cancer: Lyon
- IARC (1995) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Wood Dust and Formaldehyde*, Vol. 62. International Agency for Research on Cancer: Lyon
- IARC (2006) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol*, Vol. 88. International Agency for Research on Cancer: Lyon
- Kogevinas M, Kauppinen T, Boffetta P, Saracci R (1998) *Estimation of the Burden of Occupational Cancer in Europe. Final Report to the European Commission Programme 'Europe Against Cancer'*. IMIM: Barcelona
- Mannetje A, Kogevinas M, Luce D, Demers PA, Begin D, Bolm-Audorf U, Comba P, Gerin M, Hardell L, Hayes RB, Leclerc A, Magnani C, Merler E, Tobias A, Boffetta P (1999) Sinonasal cancer, occupation, and tobacco smoking in European women and men. *Am J Ind Med* **36**: 101–107
- Marsh GM, Youk AO, Buchanich JM, Erdal S, Esmen NA (2007) Work in the metal industry and nasopharyngeal cancer mortality among formaldehyde-exposed workers. *Regul Toxicol Pharm* **48**: 308–319
- Mayne ST, Morse DE, Winn DM (2006) Cancers of the oral cavity and pharynx. In *Cancer Epidemiology and Cancer Schottenfeld D, Fraumeni JF* (eds) 3rd edn, pp 674–696. Oxford University Press: New York
- Merler E, Baldasseroni A, Laria R, Faravelli P, Agostini R, Pisa R, Berrino F (1986) On the causal association between exposure to leather dust and nasal cancer: further evidence from a case-control study. *Brit J Ind Med* **43**: 91–95
- Nurminen MM, Karjalainen A (2001) Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. *Scand J Work Env Health* **27**: 161–213
- Pinkerton LE, Hein MJ, Staynor LT (2004) Mortality among a cohort of garment workers exposed to formaldehyde: an update. *Occup Environ Med* **61**: 193–200
- Pippard EC, Acheson ED (1985) The mortality of boot and shoemakers with special reference to cancer. *Scand J Work Env Hlth* **11**: 249–255
- Quinn M, Babb P, Brock A, Kirby L, Jones J (2001) *Cancer Trends in England and Wales 1950–1999*, pp 240. ONS: TSO, London
- Rang EH, Acheson ED (1981) Cancer in furniture workers. *Int J Epidemiol* **10**: 253–261
- Rosenman KD, Stanbury M (1996) Risk of lung cancer among former chromium smelter workers. *Am J Ind Med* **29**: 491–500
- Roush GC (1996) Cancer of the nasal cavity and paranasal sinuses. In *Cancer Epidemiology and Prevention*, Schottenfeld D, Fraumeni JF (eds), pp 587–602. Oxford University Press: Oxford
- Roush GC, Meigs JA, Kelly JA, Flannery JT, Burdo H (1980) Sinonasal cancer and occupation: a case-control study. *Am J Epidemiol* **111**: 183–193
- Rutstein DD, Mullan RJ, Frazier TM, Halperin WE, Melius JM, Sestito JP (1984) Sentinel health events (occupational) – a basis for physician recognition and public health surveillance. *Arch Environ Health* **39**: 159–168
- Sorahan T, Williams SP (2005) Mortality of workers at a nickel carbonyl refinery, 1958–2000. *Occup Environ Med* **62**: 80–85
- Steenland K, Burnett C, Lulich N, Ward E, Hurrell J (2003) Dying for work: the magnitude of US mortality from selected causes of death associated with occupation. *Am J Ind Med* **43**: 461–482
- Straif K, Benbrahim-Tallaa L, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Guha N, Freeman C, Galichell L, Coglian V (2009) A review

of human carcinogens – Part C: metals, arsenic, dusts and fibres. *Lancet Oncol* 10: 453–454

Vaughan TL, Davis S (1991) Wood dust exposure and squamous cell cancers of the upper respiratory tract. *Am J Epidemiol* 133: 560–564

Vaughan TL, Stewart PA, Teschke K, Lynch CF, Swanson GM, Lyon JL, Berwick M (2000) Occupational exposure to formaldehyde and wood dust and nasopharyngeal carcinoma. *Occup Environ Med* 57: 376–384

Yu MC, Yuan J (2002) Epidemiology of nasopharyngeal carcinoma. *Semin Cancer Biol* 12: 421–429



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Appendix

British Occupational Cancer Burden Study Group

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