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The burden of occupational cancer in Great Britain

Nasopharynx/Pharynx

Prepared by the **Institute of Environment and Health**, the **Institute of Occupational Medicine** and **Imperial College London** for the Health and Safety Executive 2012

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Nasopharynx/Pharynx

Rebecca Slack
Institute of Environment and Health
Cranfield University
Silsoe
Bedfordshire MK45 4DT

John Cherrie, Martie Van Tongeren
Institute of Occupational Medicine
Research Avenue North
Riccarton
Edinburgh EH14 4AP

Léa Fortunato, Sally Hutchings, Lesley Rushton
Department of Epidemiology and Biostatistics
Imperial College London
Norfolk Place
London W2 1PG

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for cancer of the nasopharynx that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) attributable fractions, deaths and registrations for nasopharyngeal cancer related to overall occupational exposure is 8.03% (95% Confidence Interval (CI)= 1.78-34.33), which equates to 8 (95%CI= 2-33) attributable deaths and 15 (95%CI= 3-65) attributable registrations.

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EXECUTIVE SUMMARY

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer used in this project was the attributable fraction i.e. the proportion of cases that would not have occurred in the absence of exposure; this was then used to estimate the attributable numbers. This involved obtaining data on the risk of the disease due to the exposure of interest, taking into account confounding factors and overlapping exposures, and the proportion of the target population exposed over the period in which relevant exposure occurred. Estimation was carried out for carcinogenic agents or exposure circumstances classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens. Here, we present estimates for cancer of the nasopharynx that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

Formaldehyde, mustard gas and wood dust have been classified by the IARC as definite human carcinogens for nasopharyngeal cancer. Mustard gas was used as a vesicant in chemical warfare during the First World War. Although use was prohibited in 1925, its use in warfare has been reported as recently as 1992. Formaldehyde exposure occurs during production, in pathology and embalming and in the plastics, plywood and textile industries. The highest exposures to wood dust occur in wood furniture and cabinet manufacture, especially during machine sanding and similar operations. Exposure also occurs in plywood and particleboard mills, sawmills, in joinery shops, window and door manufacture, wooden boat manufacture, installation and refinishing of wood floors, pattern and model making, pulp and paper manufacture, construction carpentry and logging.

Due to assumptions made about cancer latency and working age range, only cancers in ages 25+ in 2005/2004 could be attributable to occupation. For Great Britain in 2005, there were 65 total deaths in men aged 25+ and 32 in women aged 25+ from nasopharyngeal cancer; in 2004 there were 127 total registrations for nasopharyngeal cancer in men aged 25+ and 62 in women aged 25+.

The estimated total (male and female) attributable fractions, deaths and registrations for nasopharyngeal cancer related to occupational exposure is 8.03% (95% Confidence Interval (CI)=1.78-34.33), which equates to 8 (95%CI=2-33) attributable deaths and 15 (95%CI=3-65) attributable registrations. Results for individual carcinogenic agents for which the attributable fraction was determined are as follows:

- **Formaldehyde:** The estimated total (male and female) attributable fraction for nasopharyngeal cancer associated with occupational exposure to formaldehyde is 0.44% (95%CI=0.00-2.18), which equates to 0 (95%CI=0-2) attributable deaths and 1 (95%CI=0-4) attributable registration.

- **Wood dust**: The estimated total (male and female) attributable fraction for nasopharyngeal cancer associated with occupational exposure to wood dust is 7.62% (95%CI=1.08-17.98), which equates to 7 (95%CI=1-17), attributable deaths and 14 (95%CI=2-34), attributable registrations.

Other agents considered:

- **Mustard gas**: In the UK, manufacture of mustard gas ceased in the 1940s, with only 213 workers (research, health and educational services) possibly exposed to this chemical in 1990-1993. The attributable fraction and numbers of deaths and registrations due to occupational mustard gas exposure is thus negligible.

CONTENTS

1 INCIDENCE AND TRENDS

Pharyngeal cancer includes cancer of the oropharynx (ICD-10 C10; ICD-9 146), nasopharynx (ICD-10 C11; ICD-9 147), pyriform sinus (ICD-10 C12; ICD-9 148) and hypopharynx (or laryngopharynx) (ICD-10 C13; ICD-9 148) as well as much of the category described as other and ill-defined sites in lip, oral cavity and pharynx (ICD-10 C14; ICD-9 149); cancer of the tonsil (ICD-10 C09; ICD-9 146) is frequently considered alongside/within the oropharynx category due to ICD-9 dual classification. It is not uncommon for pharyngeal cancer to be considered alongside other cancers of the lip, oral cavity and pharynx, otherwise called oral cancer, (ICD-10 C00-C14) or in the more general category of head and neck cancer (ICD-10 C00-C14, C30-C32), and nasopharyngeal cancer (NPC) is frequently considered separately to the other pharyngeal cancers due to differences in epidemiology and aetiology. Pharyngeal cancers comprise 34% of all lip, mouth and pharyngeal (oral) cancers (Quinn *et al,* 2001). This report will consider NPC (ICD-10 C11; ICD-9 147) separately to 'other pharyngeal cancers', which will be considered to include cancers of the oropharynx (ICD-10 C10; ICD-9 146), hypopharynx (inclusive of pyriform sinus: ICD-10 C12-C13; ICD-9 148) and unspecified oral cavity/pharynx (ICD-10 C14; ICD-9 149). Generic reference to pharyngeal cancers will include NPC as well as the "other pharyngeal cancers", unless otherwise stated. Unfortunately, the IARC Monographs and papers referred to in this report tend not to utilise the ICD (International Classification of Diseases) coding when discussing cancer sites and hence, in certain circumstances, it may not be apparent which pharyngeal cancer categories are under consideration.

More than 90% of oral cancers (pharyngeal cancers except nasopharynx) are papillary and squamous cell carcinomas (Daley and Darling 2003); epithelial neoplasms and adenocarcinomas/adenoid cystic carcinomas are much less common (Quinn *et al,* 2001; Cancer Research UK 2007). Survival of patients with keratinising squamous cell nasopharyngeal carcinoma was shown to be worse than for those with non-keratinising nasopharyngeal carcinoma, the more common form of NPC (Dietz *et al,* 2004; Hildesheim *et al,* 2001).

Tables 1 and 2 (ONS, 2006a; 2006b) provide an indication of pharyngeal cancer trends over the period from the mid-1990s to the mid-2000s in England and Wales. Note that the 1994 figures include cases for England and Wales; subsequent years refer to England only. While there was an increase in cases of lip, mouth and pharyngeal cancer diagnosed in both males and females between 1971 and 1997 (24% and 21% respectively) (Quinn *et al,* 2001), it is clear from Tables 1 and 2 that incidence and mortality rates relating to pharyngeal cancers only have been very consistent over the last ten years, with mortality rates for males in the 1971-2000 period increasing very slightly but declining for females over the same period (Table 3). Generally, oral/pharyngeal cancer incidence and mortality decreased rapidly in cohorts born in the late 19th century, before stabilising in those born up to the 1930s; subsequent cohorts have demonstrated an increasing risk for males from Scotland (Robinson and Macfarlane 2003) whilst males from England and Wales and all females have shown a further decline and/or stabilisation in both incidence and mortality (Moller and Brewster, 2005; Quinn *et al,* 2001). Lip, mouth and pharyngeal cancer incidence and mortality appear to correlate with socio-economic status (Moller and Brewster, 2005). For males, incidence in the most deprived groups was found to be three times higher than for the more affluent groups. The variations were similar, if less pronounced, for females (Moller and Brewster, 2005).

Survival for cancers of the lip and mouth is generally better than for those of the pharynx and is dependent on stage at time of diagnosis (Quinn *et al,* 2001). Five-year survival for patients diagnosed in 1986-1990 was higher in females than males, with rates around 37% for females and 33% for males surviving oropharyneal cancer and 38% females and 29% males in the case of nasopharyngeal cancer. Hypopharyngeal cancer has the lowest survival over-all, at 30.9% (Mayne *et al,* 2006). Survival increased in the period 1971-1990 for most pharyngeal cancers although survival was linked with deprivation (lower for most deprived) and age at diagnosis (lower with older patient) (Jones *et al,* 1998; Coleman *et al,* 1999; Black *et al,* 2000).

Table 1 Number of pharyngeal cancer registrations in England and Wales 1994, England 1995-2004, by ICD-10 and (ICD-9) category.

MALE		Total registrations per pharyngeal cancer category					% Total					Crude rate /100,000				
Year	Total cancer registrations*	C10 (146)	C11 (147)	C12 (148)	C13 (148)	C14 (149)	C10 (146)	C11 (147)	C12 (148)	C13 (148)	C14 (149)	C10 (146)	C11 (147)	C12 (148)	C13 (148)	C14 (149)
1994	112145	311	122	n/a	244	125	0.28	0.11	n/a	0.22	0.11	1.2	0.5	n/a	1	0.5
1995	103986	86	122	176	65	124	0.08	0.12	0.17	0.06	0.12	0.4	0.5	0.7	0.3	0.5
1996	104103	88	145	162	56	113	0.08	0.14	0.16	0.05	0.11	0.4	0.6	0.7	0.2	0.5
1997	104335	76	130	148	79	107	0.07	0.12	0.14	0.08	0.10	0.3	0.5	0.6	0.3	0.4
1998	106745	88	113	169	71	113	0.08	0.11	0.16	0.07	0.11	0.4	0.5	0.7	0.3	0.5
1999	108827	100	142	208	72	129	0.09	0.13	0.19	0.07	0.12	0.4	0.6	0.8	0.3	0.5
2000	111543	90	114	195	75	140	0.08	0.10	0.17	0.07	0.13	0.4	0.5	0.8	0.3	0.6
2001	112516	104	107	165	78	115	0.09	0.10	0.15	0.07	0.10	0.4	0.4	0.7	0.3	0.5
2002	112579	88	128	178	70	145	0.08	0.11	0.16	0.06	0.13	0.4	0.5	0.7	0.3	0.6
2003	112732	89	131	176	80	127	0.08	0.12	0.16	0.07	0.11	0.4	0.5	0.7	0.3	0.5
2004	117805	113	128	193	76	124	0.10	0.11	0.16	0.06	0.11	0.5	0.5	0.8	0.3	0.5
Average 1994-2004	**109756.0**	**112.1**	**125.6**	**177.0**	**87.8**	**123.8**	**0.10**	**0.11**	**0.16**	**0.08**	**0.11**	**0.5**	**0.5**	**0.7**	**0.4**	**0.5**
FEMALE																
1994	112175	142	61	n/a	123	58	0.13	0.05	n/a	0.11	0.05	0.5	0.2	n/a	0.5	0.2
1995	105151	34	59	41	78	55	0.03	0.06	0.04	0.07	0.05	0.1	0.2	0.2	0.3	0.2
1996	105461	24	73	44	64	57	0.02	0.07	0.04	0.06	0.05	0.1	0.3	0.2	0.3	0.2
1997	107289	38	62	47	66	60	0.04	0.06	0.04	0.06	0.06	0.2	0.2	0.2	0.3	0.2
1998	109957	39	49	39	70	57	0.04	0.04	0.04	0.06	0.05	0.2	0.2	0.2	0.3	0.2
1999	112237	30	63	41	61	65	0.03	0.06	0.04	0.05	0.06	0.1	0.2	0.2	0.2	0.3
2000	112066	29	76	45	47	64	0.03	0.07	0.04	0.04	0.06	0.1	0.3	0.2	0.2	0.3
2001	112134	29	64	36	69	61	0.03	0.06	0.03	0.06	0.05	0.1	0.3	0.1	0.3	0.2
2002	111210	32	53	54	45	57	0.03	0.05	0.05	0.04	0.05	0.1	0.2	0.2	0.2	0.2
2003	114740	32	70	43	66	52	0.03	0.06	0.04	0.06	0.05	0.1	0.3	0.2	0.3	0.2
2004	115816	42	59	43	35	56	0.04	0.05	0.04	0.03	0.05	0.2	0.2	0.2	0.1	0.2
Average 1994-2004	**110748.7**	**42.8**	**62.6**	**43.3**	**65.8**	**58.4**	**0.04**	**0.06**	**0.04**	**0.06**	**0.05**	**0.2**	**0.2**	**0.2**	**0.3**	**0.2**

*All cancers excluding non-melanoma skin cancer (NMSC)
Source: adapted from ONS (2006a; 2005a,b; 2004a; 2003a; 2002a,b; 2001a; 2000a)

Table 2 Number of pharyngeal cancer deaths in England and Wales 1999-2005, by ICD-10 (and ICD-9) category.

		Total deaths per pharyngeal cancer category					% Total					Crude rate /100,000				
Year	**Total cancer registrations***	**C10 (146)**	**C11 (147)**	**C12 (148)**	**C13 (148)**	**C14 (149)**	**C10 (146)**	**C11 (147)**	**C12 (148)**	**C13 (148)**	**C14 (149)**	**C10 (146)**	**C11 (147)**	**C12 (148)**	**C13 (148)**	**C14 (149)**
MALE																
1999	264299	204	88	n/a	89	123	0.08	0.03	n/a	0.03	0.05	0.79	0.34	n/a	0.34	0.47
2000	255547	141	81	n/a	93	125	0.06	0.03	n/a	0.04	0.05	0.53	0.31	n/a	0.35	0.47
2001	252426	84	60	55	49	120	0.03	0.02	0.02	0.02	0.05	0.33	0.24	0.22	0.19	0.47
2002	253144	68	68	64	59	112	0.03	0.03	0.03	0.02	0.04	0.27	0.27	0.25	0.23	0.44
2003	253852	82	71	50	39	100	0.03	0.03	0.02	0.02	0.04	0.32	0.27	0.19	0.15	0.39
2004	244130	67	84	46	38	120	0.03	0.03	0.02	0.02	0.05	0.26	0.32	0.18	0.15	0.46
2005	243324	85	64	51	52	159	0.03	0.03	0.02	0.02	0.07	0.32	0.24	0.19	0.20	0.61
Average 1999-2005	**252388.9**	**104.4**	**73.7**	**53.2**	**59.9**	**122.7**	**0.04**	**0.03**	**0.02**	**0.02**	**0.05**	**0.40**	**0.28**	**0.21**	**0.23**	**0.47**
FEMALE																
1999	291819	73	35	n/a	53	48	0.03	0.01	n/a	0.02	0.02	0.27	0.13	n/a	0.20	0.18
2000	280117	61	37	n/a	60	62	0.02	0.01	n/a	0.02	0.02	0.23	0.14	n/a	0.22	0.23
2001	277947	35	21	9	35	48	0.01	0.01	0.00	0.01	0.02	0.13	0.08	0.03	0.13	0.18
2002	280383	21	33	11	29	53	0.01	0.01	0.00	0.01	0.02	0.08	0.12	0.04	0.11	0.20
2003	284402	27	40	16	35	52	0.01	0.01	0.01	0.01	0.02	0.10	0.15	0.06	0.13	0.19
2004	268411	31	36	12	32	48	0.01	0.01	0.00	0.01	0.02	0.11	0.13	0.04	0.12	0.18
2005	269368	37	30	7	33	44	0.01	0.01	0.00	0.01	0.02	0.14	0.11	0.03	0.12	0.16
Average 1999-2005	**278921.00**	**40.7**	**33.1**	**11.0**	**39.6**	**50.7**	**0.01**	**0.01**	**0.00**	**0.01**	**0.02**	**0.15**	**0.12**	**0.04**	**0.15**	**0.19**

*All causes including all cancers

Source: adapted from ONS (2006b; 2005c; 2004b; 2003b; 2002c; 2001b; 2000b)

Table 3 Cancer mortality trends 1971-2000 in England and Wales and proportions associated with all categories of malignant neoplasm of pharynx (ICD-10 C10-C14; ICD-9 146-149, inclusive).

	Male			Female		
Year	**Total neoplasms**	**Pharyngeal neoplasms**	**% Total**	**Total neoplasms**	**Pharyngeal neoplasms**	**% Total**
1971-1975	326838	2134	0.65	279710	1459	0.52
1976-1980	343180	2030	0.59	298261	1457	0.49
1981-1985	359493	2207	0.61	320635	1426	0.44
1986-1990	374103	2152	0.58	343106	1283	0.37
1991-1995	374029	2284	0.61	342716	1139	0.33
1996-2000	355943	2397	0.67	330414	1111	0.34

Source: adapted from ONS (2001b)

In the UK, approximately 1800 people are diagnosed with pharyngeal cancer including cancer of the tonsil (Table 4). In the UK and Ireland in the 1990s, incidences of lip, mouth and pharynx cancer were about 5000 cases (1 in 60 cancer cases) (Moller and Brewster 2005). Pharyngeal cancer is the 15th most commonly registered cancer for the combined UK population, although it is higher for men (ranked 12th with a crude rate of 4.5 cases per 100,000 males) then females (ranked 17th with a crude rate of 1.6 cases per 100,000 females) (Table 4; Cancer Research UK, 2007). The age-standardised incidence rates (European) have been determined for all oral cancers to be 9.8 and 4.2 per 100,000 in males and females respectively, producing a ratio of 2.3:1 male-to-female (Table 4; Cancer Research UK 2007). Incidence rates increase with age and are highest in the oldest age groups. For the individual cancer types falling within the term 'pharyngeal cancer', cancer of the pyriform sinus is markedly higher in men then women, with a male-to-female ratio of 4.8:1 new cases in 2004 (Cancer Research 2007). For Great Britain (England, Scotland and Wales) in 2004, there were 1278 total pharyngeal cancer registrations in males and 474 in females generating a total incidence of 1752 cases. Of these cases, 207 were for nasopharyngeal cancer (16% of pharyngeal registrations), with 141 male cases and 66 female registrations.

Geographical patterns of incidence in Great Britain reveal that there are more pharyngeal cancer registrations per head of population in Scotland than any other of the British regions (Table 4), a pattern supported by age-standardised incidence rates for oral cancers (Moller and Brewster 2005). Within England and Wales, registration rates are higher in northern than in southern areas, with the exception of some areas in the south of Wales and central London. This difference is particularly evident for males but the pattern is similar, although less pronounced, for females. There are similarities between the geographical patterns in the incidence of cancers of the lip, mouth and pharynx and those of the larynx, lung and oesophagus.

In the UK, pharyngeal cancer (including tonsil cancer) results in more than 800 deaths per year (Table 4); in the 1990s, about 2000 deaths (1 in 80 cancer deaths) per year in the UK and Ireland were from lip, mouth and pharynx cancer (Moller and Brewster 2005). Pharyngeal cancer is the 18th commonest cancer resulting in death, mortality rates being higher in males than females (Table 4; Cancer Research UK 2007). The age-standardised mortality rates (European) for all oral cancers including pharyngeal cancer are 3.4 and 1.3 per 100,000 in

males and females respectively, generating a male-to-female ratio of 2.6:1. As is the case when incidence is considered, mortality rates increase with age and are highest in the oldest age groups. Mortality also reflects the geographical patterns exhibited by oral cancer registrations, although the rates are lower and variations less pronounced, with Scotland and the northern regions of England having higher mortality rates than southern England (Moller and Brewster 2005). Across Great Britain, there were 848 deaths from all pharyngeal cancers in 2005, of which 73% (619 deaths) were men and 27% (229) women. Deaths from nasopharyngeal cancer accounted for 12% of all deaths from pharyngeal cancers, with a total of 101 people (33 women and 68 men) succumbing to NPC in Great Britain in 2005.

Table 4 Incidence of and mortality from pharyngeal cancer (ICD-10 C09-C14, inclusive) in UK, 2004-2005.[1]

	England	**Wales**	**Scotland**	**NI**	**UK**	**Rank***	**%***	**EASR***
Incidence: Number of cases, 2004								
Males	1054 [128]	69 [4]	155 [9]	36 [10]	1314 [151]	12 [28]	2.2	9.8
Females	387 [59]	27 [2]	60 [5]	7 [0]	481 [66]	17 [30]	1.1	4.2
Persons	1441 [187]	96 [6]	215 [14]	43 [10]	1795 [217]	15 [33]	1.7	6.9
Incidence: Crude rate per 100,000 population, 2004 (ICD-10 C09-C14)								
Males	4.3	4.8	6.4	4.3	4.5			
Females	1.5	1.8	2.3	0.8	1.6			
Persons	2.9	3.2	4.2	2.5	3.0			
Mortality: Number of deaths, 2005								
Males	513 [61]	33 [4]	73 [3]	13 [1]	632 [69]	16 [29]	1.4	3.4
Females	183 [29]	15 [1]	31 [3]	6 [1]	235 [34]	18 [32]	0.8	1.3
Persons	696 [90]	48 [5]	104 [6]	19 [2]	867 [103]	18 [32]	1.1	2.3
Mortality: Crude rate per 100,000 population, 2005 (ICD-10 C09-C14)								
Males	2.1	2.3	3.0	1.5	2.2			
Females	0.7	1.0	1.2	0.7	0.8			
Persons	1.4	1.6	2.1	1.1	1.4			

*Based on UK oral cancer rates (ICD-10 C00-C06+C09+C10+C12-C14)
Source: adapted from Cancer Research UK (2007)

[1] Note that the figures for the UK regions also include malignant neoplasm of the tonsil (ICD-10 C09) for which rates are frequently higher than for the individual pharyngeal cancers defined by ICD-10 C10-C14; for instance, in England in 2004, there were 420 cases of tonsil cancer in men and 152 cases in women representing 40% of the total for cancers in the category ICD-10 C09-C14. Figures in square brackets refer to incidence of and mortality from nasopharyngeal cancer (ICD-10 C11) only.

The incidence of and mortality from lip, mouth and pharyngeal cancer in England and Wales are amongst the lowest internationally. Oral and oro-/hypopharyngeal cancers rank as the 11th most common worldwide cancer (20th when considering cancer of the oro-/hypopharynx alone), with 390,000 new cases per year, while nasopharyngeal cancer is much less common with an estimated 65,000 new cases per year (0.6% of all cancers). The highest worldwide incidence of oral/pharyngeal cancer has been reported to be among males in Bas-Rhin and Calvados in France, where the annual incidence rate in the mid-1980s was 55.5 per 100,000 population (Zatonski *et al,* 1996); 60% of the incidence is due to pharyngeal cancer alone, although it is usual in other regions for oral cancers to exceed incidence of pharyngeal carcinomas (Mayne *et al,* 2006). High levels are also observed in the Indian subcontinent where occurrence among females is highest (10 in 100,000 per year), Australia (although mortality is low), Brazil and southern African countries (Stewart and Kleihues 2003). Pharyngeal cancers are common in both males and females in developed countries including Central and Eastern European countries such as Hungary; levels of incidence and mortality in Northern Europe, Latin America, Japan, the Middle East and Western Africa are lower. Whilst oral/pharyngeal cancer incidence and mortality rates have been stable in many countries, there have been sharp increases reported in Hungary, Germany, Denmark, Central and Eastern Europe, Japan, Australia, New Zealand, and in the USA among non-whites (Stewart and Kleihues 2003; Dobrossy 2007). Nasopharyngeal cancer has a very distinctive geographic distribution, with high age-standardised incidence rates recorded for populations living in or originating from Southern China, particularly Guangdong province of which Hong Kong is a part, and Singapore (Chang and Adami 2006; Yu and Yuan 2002). For pharyngeal and nasopharyngeal cancers, the male-to-female ratio is >2:1 and there is a general increase in risk with age, although high incidence and mortality in early and middle adult years from NPC in high risk areas such as Singapore is more common (Armstrong *et al,* 2000). Socioeconomic associations have also been described (Maier *et al,* 2002), with more deprived groups having higher rates, and there are differences reported for different American racial-ethnic groups for nasopharyngeal and pharyngeal cancers (Mayne *et al,* 2006; Yu and Yuan 2006).

Many of these trends, particularly pharyngeal cancer incidence rates over time and associations with socio-economic factors, are closely linked to alcohol consumption and tobacco use. Nasopharyngeal cancer has also been associated with Epstein-Barr virus infection and consumption of preserved foods. The aetiology of pharyngeal/nasopharyngeal neoplasms is considered further in Section 2.

2 OVERVIEW OF AETIOLOGY

2.1 INTRODUCTION

The main risk factors for cancer of the pharynx, particularly oro- and hypopharyngeal cancers, are tobacco use and alcohol consumption, which have been shown to have a multiplicative or synergistic effect (e.g. Baan *et al,* 2007; Mayne *et al,* 2006; Vlajinac *et al,* 2006; Busquets *et al,* 2003; Zeka *et al,* 2003; Znaor *et al,* 2003; IARC 2004a; Wasnik *et al,* 1998; Franceschi *et al,*, 1991; Yu *et al*., 1990; Blot *et al,* 1988; IARC 1988; Young *et al,* 1986; Elwood *et al,* 1984; IARC In prep.). Smoking exhibits a strong positive dose-response relationship, with a steady decline in risk apparent after smoking cessation (Blot *et al,* 1988), and has been estimated to be responsible for about 41% of laryngeal and oral/pharyngeal cancer in men and 15% in women worldwide (Stewart and Kleihues 2003). In the Indian subcontinent, chewing tobacco in the form of betel quid (with or without tobacco) and bidi smoking contribute to oral/pharyngeal cancer (IARC 2004b; Stewart and Kleihues 2003; Merchant *et al,* 2000), as do cigar and pipe smoking elsewhere in the world (Garrote *et al,* 2001), marijuana smoking, 'reverse' smoking, exposure to environmental tobacco smoke and use of other 'smokeless' tobacco products (Mayne *et al,* 2006; Znaor *et al,* 2003; Secretan *et al,* 2009). Risk increases with increasing frequency of alcohol consumption and cumulative lifetime exposure, but declines after cessation (Bagnardi *et al,* 2001).

A meta-analysis of 229 studies determined that alcohol most strongly increases the risks for cancers of the oral cavity and pharynx even at a relatively low intake of 25 g alcohol per day, or two standard drinks (relative risk (RR) = 1.73; 95% CI, 1.67-1.78). At higher alcohol consumption levels of 100g alcohol per day, the risk factor is considerably greater (RR = 5.75; 95% CI = 5.22-6.34) (Bagnardi *et al,* 2001). This meta-analysis also suggested that a combination of alcohol and tobacco raise the RR values higher, with an RR for oral cavity and pharyngeal cancer, based on highest exposure levels for both alcohol and tobacco, of 80.

Oral human papillomavirus (HPV or herpes simplex virus) infection by HPV-16 type has been associated with an increased risk of squamous cell carcinoma development in the head and neck region, particularly the oropharynx (Gillison *et al,* 1999). The presence of the virus does not imply a causal link but women with prior cervical malignancies have higher rates of incidence of oral/pharyngeal carcinoma (Spitz *et al,* 1992). However, data linking HPV-16 infection to pharyngeal cancers has largely been considered inadequate and more research is required to examine whether HPV is a causal factor I pharyngeal cancers (IARC 1995a; Bouvard *et al,* 2009). Oral hygiene and the use of alcohol-based mouthwashes have also been associated with pharyngeal cancer but evidence is not substantial (Mayne *et al,* 2006). Genetic predisposition, primary cancer at other sites in the body, and mutagenic sensitivity have also been considered as causal factors in pharyngeal cancer (Yu and Yuan 2006).

For nasopharyngeal cancer (NPC), Epstein-Barr virus (EBV) infection, consumption of preserved food such as salt-preserved fish/meat, a family history of cancer of the nasopharynx, certain human leukocyte antigen class I genotypes and nitrosamine-metabolising genotypes increase the risk of this disease (Chang and Ademi, 2006; Yu and Yuan, 2002; 2006; IARC 1997; 1993). There is strong evidence that EBV is not capable of inducing NPC alone; nitrosamines/precursors and EBV-activating substances have been detected in a number of preserved foods (Yu and Yuan, 2006). The use of preserved food for weaning and feeding of young children has been associated with increased risk in early adult-hood in high-risk NPC areas such as southern China (Yu and Yuan, 2006). Although cohort and case-control studies sometimes indicate that smoking and alcohol consumption are not considered to be major risk factors in NPC (Yu and Yuan 2006), IARC consider there to be sufficient evidence in humans that tobacco smoking and alcohol causes cancer of the nasopharynx as well as oro- and hypopharynx (Baan *et al,* 2007; IARC 2004a). NPC incidence in high-risk areas has been shown to peak in middle age

Consumption of fresh fruits and vegetables can assist in decreasing risk factors (Maier *et al,* 2002; Garrote *et al,* 2001; Franceschi *et al,*, 1991), with associations found between pharyngeal cancer and diets low in vitamins and minerals (Negri *et al,* 2000; Steinmatz and Potter, 1991). Case-control studies conducted among Southern Chinese report a statistically significant deficit in intake of fresh fruit and vegetables among cases relative to control subjects, particularly for vitamin C rich fruits (Yu and Yuan 2006) and orange/yellow fruit/vegetables with high levels of carotenoids (Mayne *at al*. 2006), and a significant positive association between meat intake and oral/pharyngeal cancer risk has also been reported (Garrote *et al,* 2001).

There are a number of occupational agents/exposures associated with pharyngeal/nasopharyngeal cancers. These include NPC with formaldehyde (Hildesheim *et al,* 2001; Armstrong *et al,* 2000; Blair *et al,* 1990; IARC 2006), wood dust and wood preservatives such as chlorophenols (Hildesheim *et al,* 2001; Armstrong *et al,* 2000; Mirabelli *et al,* 2000; Demers et al 1995) and smoke particles/dust (Armstrong et al 2000). In addition, pharyngeal cancer and cancer of the oral cavity have been associated with a number of work-related exposure scenarios including hairdressing, construction and metalworking industries, particularly as painters, carpenters and machine operators, as well as the paper and rubber industries and a variety of blue-collar jobs that lead to exposure to dusts and organic/inorganic agents (Mayne *at al*. 2006: Ji and Hemminki 2005; Riechelmann 2002; Rix *et al,* 1998). However, occupation is generally deemed to play a minor role, with tobacco and alcohol key to the aetiology of pharyngeal cancer. This is disputed by Menvielle *et al,* (2004) who found that hypopharyngeal cancer incidence could not be completely explained by alcohol consumption; after adjustment for such lifestyle factors, occupational exposure was still significant (odds ratio (OR) for manual worker = 1.91; 95%CI=1.23-2.95).

The Occupational Health Decennial Supplement (Drever 1995) examined cancer incidence (1981-1987) in England and cancer mortality (1979-1980, 1982-1990) in England and Wales in men and women aged 20-74 years. Table 5a shows that pharyngeal cancer incidence is related to occupations where elevated smoking and alcohol consumption can be expected such as publicans and bar staff for both men and women, as shown by significantly high proportional registration risks (PRRs). As nasopharyngeal cancer is associated with the preparation and consumption of preserved foods, it is perhaps not unsurprising that levels of pharyngeal and nasopharyngeal cancers are highly associated with men employed as cooks and kitchen porters, caterers, and possibly even those more likely to eat preserved foods such as seafarers (Table 5). The aforementioned occupations also record significant mortality rates (using proportional mortality ratios or PMRs). As naso- and other pharyngeal cancers are closely associated with such lifestyle factors, it is difficult to assess the causal factors resulting from the other occupations, although dust (lorry drivers; lathe turners; bakers) and solvents/fumes (fire service personnel; launderers; painters and decorators; artistic occupations) could possibly be factors. Exposure to formaldehyde may be associated to the elevated cancer incidence in doctors, nurses (if both pathology), rubber manufacture, electrical and electronic assemblers, and electrical engineers. Table 5b shows cancer mortality data for the period 1991-2000 (Coggon *et al,* 2009). Similar occupational groups to Table 5a occur, reinforcing the potential causal factors discussed earlier.

Several studies report different risk estimates for the different cancer cell types and the various associated environmental and occupational agents. Squamous cell NPC is less well associated with a diet of preserved food than non-keratinising or undifferentiated NPC (Yu and Yuan 2002) but is more closely associated with formaldehyde exposure (Vaughan *et al,* 2000). All studies assessing pharyngeal cancer and NPC must overcome the difficulty of assessing generally rare cancers.

Table 5a Job codes with significantly high PRRs and PMRs for pharyngeal/nasopharyngeal cancer. Men and women aged 20-74 years, England. Unless otherwise specified, figures correspond to cancer of the pharynx (ICD-9 146-148) (Drever 1995).

Job group		Registration	PRR*	95% CI	Deaths	PMR**	95% CI
SIC code	Description	(1981-87)			(1979-1980 and 1982-90)		
Men							
015	Doctors	9	137	63-262			
024	Literary and artistic occupations	13	115	62-198	33	166	114-234
036	Seafarers	18	214	127-339	45	290	212-388
041	Office managers‡	9	229	105-435			
044	Retailers and dealers	62 (20†)	131 (184†)	101-169 (112-284†)			
045	Publicans and bar staff	48 (14§)	334 (613§)	247-444 (336-1030§)	71	230	180-291
046	Caterers	15 (9†)	235 (520†)	132-389 (238-988†)	36	243	170-336
050	Fire service personnel$	4	469	128-1203			
051	Launderers and dry cleaners	4 (3‡)	277 (580‡)	76-711 (120-1695‡)			
059	Cooks and kitchen porters	37 (18†)	397 (847†)	280-548 (502-1340†)	54	334	251-435
066	Fishing & related workers	3	190	39-558			
076	Bakers†	4	366	100-939			
077	Brewery workers	6	311	114-678			
085	Rubber manufacturers	6	190	70-415			
122	Centre lathe turners§	5	777	253-1815			
145	Sheet metal workers				22	167	105-254
160	Painters and decorators‡	18	174	103-275			
161	Electrical, electronic assemblers	3	556	115-1628			
183	Lorry drivers§	17	176	103-283			
Women							
017	Nurses†	13	204	109-350			
040	Managers in transport, utilities and mining	2	759	92-2745			
045	Publicans and bar staff	12 (8$)	201 (524$)	104-351 (227-1034$)	22	251	157-380
143	Electrical engineers	1	1049	27-5848			

*p<0.05 based on at least 3 registrations; adjusted for age, social class and registration region.
**p<0.05 based on at least 3 registrations; adjusted for age and social class
‡Hypopharynx only (ICD-9 148)
†Nasopharynx only (ICD-9 147)
§Ill-defined mouth and pharynx only (ICD-9 149)
$Oropharynx only (ICD-9 146)

Table 5b Job codes with significantly high PMRs for pharyngeal/nasopharyngeal cancer 1991-2000. Men and women aged 20-74 years, England. Figures correspond to cancer of the pharynx (Coggon *et al,* 2009)

Job group					95% CI	
SIC code	Description	Obs	Exp	PMR	Lower CI	Upper CI
Men						
036	Seafarers	39	14.6	267.2	190.0	365.3
045	Publicans and Bar staff	67	28.2	238.0	184.4	302.2
046	Caterers	47	16.0	294.3	216.2	391.3
059	Cooks and Kitchen Porters	40	20.3	196.6	140.4	267.7
143	Electrical Engineers (not professional)	22	13.8	160.0	100.2	242.2
148	Scaffolders, Stagers, Steeplejacks, Riggers	18	7.8	231.0	136.9	365.1
165	Bricklayers, Masons	36	24.7	145.7	102.1	201.8
Women						
045	Publicans and Bar staff	16	8.5	187.2	107	303.9
052	Hairdressers	8	3.3	241.6	104	476.1

IARC have classified a number of occupational agents as definitely (Group 1) or possibly (group 2A) causing pharyngeal and nasopharyngeal cancers (Table 6). Siemiatycki *et al.* (2004) summarised the evidence used in the classification of these agents and substances as strong or suggestive (Table 6). There is suggestive evidence that the following Group 1 agents are occupational carcinogens for pharyngeal cancers: formaldehyde and mustard gas. Although not considered by Siemiatycki *et al* (2009) IARC state that there is suggestive evidence that exposure to wood dust is associated with an increased risk of work-related nasopharyngeal cancer but there is a lack of evidence of causal factors in pharyngeal cancer (IARC 1995b). A number of other chemicals not classified as Group 1 or 2A pharynx/nasopharynx carcinogens, may be associated with pharyngeal/nasopharyngeal carcinoma, including cement and mine dusts (e.g. Armstrong *et al*, 2000).

Table 6 Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1-88, into Groups 1 and 2A, which have the pharynx and nasopharynx as target.

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Strength of evidence	Other target organs
Group 1: carcinogenic to humans				
Agents, groups of agents				
Formaldehyde	Production; pathologists; medical laboratory technicians; plastics; textile industry	Sufficient (nasopharynx) / limited (other pharynx)	Suggestive	Nasal sinuses Leukaemia
Mustard gas	Production; used in research laboratories; military personnel	Sufficient	Suggestive	Lung Larynx
Wood dust	Logging & sawmill workers; pulp & paper & paperboard industry; woodworking trades (e.g. furniture industries, cabinet-making, carpentry & construction); used as a filler in plastic and linoleum production	Suggestive (nasopharynx) / limited (other pharynx)	n/d	Nasal sinuses
Exposure circumstances				
None identified				
Group 2A: probably carcinogenic to humans				
None identified				

Source: adapted from Siemiatycki *et al,* (2004) and IARC (2006; 1995b; 1987; 1975)

2.2 EXPOSURES

2.2.1 Agents or groups of agents

Mustard Gas

Mustard gas (bis[2-chloroethyl]sulphide), or sulphur mustard, was used as a vesicant in chemical warfare during the First World War but use was prohibited thereafter by the Geneva Convention of 1925, although its use in warfare has been reported as recently as 1992 (Iyriboz 2004). Currently, this chemical is only produced for use in military research although it has had application in medicine as an antineoplastic agent. The main routes of potential human exposure to mustard gas are inhalation and dermal contact. However, the general population is typically not exposed. A number of studies have assessed exposure retrospectively following warfare and using volunteer servicemen (Balali-Mood 2006; Iyriboz 2004; Khateri *et al,* 2003); these reports also acknowledge the mutagenic potential of mustard gas first identified by Auerbach and Robson (1946). Studies of poisoned veterans demonstrate lower cancer incidence and mortality rates than workers in mustard gas production, suggesting that chronic exposure may be a greater cancer hazard than a single acute exposure (Blair and Kazerouni, 1997), with the possible exception of lung cancer (Reutter, 1999).

Based on the studies of workers involved in its manufacture, mustard gas is clearly carcinogenic in humans (Blair and Kazerouni, 1997; Yanagida *et al,* 1988; IARC, 1987; IARC 1975). Pharyngeal cancer among workers engaged in the manufacture of mustard gas has been studied in Japan (Nishimoto *et al,*, 1988; Yamada 1963) and in England (Easton *et al,*, 1988), and their findings are discussed below.

Nishimoto *et al,* (1988) followed 1632 workers employed at a mustard gas factory between 1929 and 1945 through to 1980. There appeared to be an excess of cancer of the pharynx but the standardised mortality ratio (SMR) was not presented.

In a cohort study of 2498 men and 1032 women in England followed for mortality through 1985, there was a significant increase in mortality from pharyngeal cancer (SMR = 5.5, 13 deaths) in workers employed in the manufacture of mustard gas during the Second World War, compared with national death rates (Blair and Kazerouni 1997; Easton *et al,* 1988). The risks for cancers of the pharynx were significantly associated with duration of employment, although the effect of smoking could not be controlled. In an earlier study to assess the long-term health effects resulting from employment in mustard gas manufacture between 1939-1945, Manning *et al,* (1981) followed 428 workers until 1974 and reported increased mortality due to laryngeal cancer but not pharyngeal cancer.

In the UK, manufacture of mustard gas ceased in the 1940s, and it is unlikely that attributable cases now occur in any number (Coggon, 1999). CAREX estimated there were only 213 workers possibly exposed to this chemical in 1990-1993, deriving from educational services (122 people), research and scientific institutes (44 people), and medical, dental or other health and veterinary services (47 people).

Formaldehyde

Formaldehyde is used mainly in the production of phenolics, urea, melamine and polyacetal resins. These have wide uses as adhesives and binders for the wood products, pulp and paper, and synthetic vitreous fibre industries and in the production of plastics and coatings and in textile finishing. It is also used extensively as an intermediate in the manufacture of industrial chemicals, and directly in aqueous solution (as formalin) as a disinfectant and preservative in many applications. Occupational exposure occurs in a wide range of occupations and industries, the highest occurring during the varnishing of furniture and wooden floors, in the finishing of textiles, the garment industry, treatment of fur and in certain jobs within manufactured board mills and foundries. Short-term high exposure episodes have been reported for embalmers, pathologists and paper workers.

The most recent IARC monograph concerned with formaldehyde (IARC 2006) stated that there is sufficient evidence of carcinogenicity in humans and hence re-classified formaldehyde from Group 2A (IARC 1995b) to Group 1. The IARC Working Group concluded that the positive findings from a number of cohort and case-control studies provided sufficient epidemiological support that formaldehyde causes nasopharyngeal cancer but evidence was not considered sufficient with regard to a causal role for formaldehyde in relation to oro- and hypopharyngeal cancers. The evidence base included a number of case-control studies (Berrino *et al,* 2003; Hildesheim *et al,* 2001, 1992; Armstrong *et al,* 2000; Laforest *et al,* 2000; Vaughan *et al,* 2000, 1986; Gustavsson *et al,* 1998; West *et al,* 1993; Roush *et al,* 1987; Olsen *et al,* 1984) and cohort studies of industrial workers and professional groups (Marsh and Youk 2005; Hauptmann *et al,* 2004; Pinkerton *et al,* 2004; Coggon *et al,* 2003; Andjelkovich *et al,* 1995; Hansen and Olsen 1995; Hayes *et al,* 1990; Edling *et al,* 1987). Collins *et al,* (1997) provide a meta-analysis of 47 studies assessing formaldehyde exposure and cancer of the nasopharynx. The main studies are summarised in Table 7.

The most recent update on the National Cancer Institute (NCI) Cohort, by Hauptmann *et al,* (2004), assessed mortality rates among workers in formaldehyde industries in the USA between 1966-1994. Ten US facilities were included in the study, manufacturing formaldehyde (three plants), formaldehyde resins (six plants), moulding compounds (six plants), moulded plastic products (two plants), photographic film (two plants) and plywood (one plant). Mortality from nasopharyngeal cancer was significantly higher among formaldehyde-exposed workers than the national population (SMR, 2.10; 95%CI=1.05-4.21), with a highly statistically significant peak exposure-response relationship ($p<0.001$). A non-significant dose-response relationship provided relative risks of 0.38 for mid-exposures (0.5-

<1.0 ppm) and 1.67 for high exposures (≥1.0 ppm); there were no deaths in the low exposure category but two in the no exposure category. Marsh *et al,* (2002) considered exposure through to 1995 and mortality through to 1998 for 7328 workers employed at one formaldehyde using plant (Wallingford, CT, USA) included in the NCI cohort study during 1941-1984. Compared with local mortality rates, SMR was high for cancers of the nasopharynx (SMR, 5.00; 95%CI=2.01-10.30) and showed an increase with cumulative exposure to formaldehyde. The SMRs for other pharyngeal cancers were also elevated (SMR, 2.23; 95%CI, 1.40-3.38). In a case-control study nested within this cohort, deaths from cancer of the oro-, naso- and hypopharynx, as well as other pharyngeal cancers, were not associated with exposure to formaldehyde, and it was considered that the observed differences may reflect the influence of lifestyle factors or other occupational risk factors. A further paper in 2007 indicated that occupational exposures to sulphuric acid mists, mineral acid, metal dusts and heat may show a closer association to NPC than formaldehyde exposure (Marsh *et al,* 2007). Furthermore, Marsh *et al,* (2002, 2007) and Marsh and Youk (2005) dispute the reported strength of association between formaldehyde exposure and nasopharyngeal cancer identified by Hauptmann *et al,* (2004). Removal of the Wallingford plant from the NCI cohort reduces the SMR for nasopharyngeal cancer at the remaining nine plants to 0.65 (95% CI0.08-2.3). These authors argue that the decision to amend the status of formaldehyde from a Group 2A to Group 1 carcinogen was overly reliant on the Hauptmann *et al* (2004) study, where the reported statistically significant NPC mortality excess was largely due to effects seen at the Wallingford NCI site. Exclusion of this one factory from meta-analyses of case-control and cohort studies caused the pooled RR to decline from 1.33 (95%CI=0.61-2.53) to 0.49 (no 95% CI provided) (Bosetti *et al*. 2008) and to 1.22 (95%CI=1.00-1.50) for case-control studies only and 0.72 (95%CI=0.40-1.29) for cohort-only analyses (Bachand *et al.* 2010). Blair and Kazerouni (1997) also note that a number of studies have not found an association between NPC and formaldehyde, while Blair et al. (1990) report a meta relative risk of 1.3.

Table 7 Studies of formaldehyde and nasopharyngeal cancer (with or without adjustments for lifestyle factors). Where data exist, results for other pharyngeal cancers have also been included.

Reference	Industry/product	Country	Design	Study size	Results
Bachand et al. (2010)	Varied	Varied	Meta analysis	15 studies	Cohort metaRR= 0.72; Case-control metaRR= 1.22
Bosetti et al. (2008)	Varied	Varied	Meta analysis	11 studies	Pooled RR=0.49 (excluding 1 study)
Collins *et al.* (1997)	Varied	Varied	Meta analysis	47 studies	Cohort metaRR= 1.0; Case-control metaRR=1.3
Hauptmann *et al.* (2004)	Manufacture of formaldehyde and users	USA	Cohort	25,619	SMR = 2.10 (95% CI= 0.91-4.14; 8 deaths)
Marsh *et al.* (2002)	Plastics-producing factory	USA	Cohort	7,328	SMR = 5.00 [SMR = 2.23 ‡]
Marsh *et al.* (2007)	Plastics-producing factory	USA	Cohort	7,345	SMR = 4.43 (1.78-9.13) [SMR = 1.71 (1.01-2.72) ‡]
Coggon *et al.* (2003)	Chemical factories producing or using formaldehyde	UK	Cohort	14,014 male	SMR = 1.55 (0.87-2.56) #

Reference	Industry/product	Country	Design	Study size	Results
Andjelkovich *et al.* (1995)	Foundry	USA	Cohort†	3,929	SMR = 0 (no NPC deaths)
Blair *et al.* (1986)*	Producers, resin makers, other users	USA	Cohort†	26,561	SMR = 3.0 (6 observations)
Gardner *et al.* (1993)*	Manufacturing plants using formaldehyde	UK	Cohort	7,660	SMR = 0.0 (0.0 to 2.8) (1.3 expected)
Hayes *et al.* (1990)	Embalmers/funeral directors	USA	PMR	4,046	SMR=2.1 (0.6-5.4) [SMR=1.19 (0.78-1.74) ‡]
Olsen *et al.* (1984)	Work history	Denmark	Case-control†	266 cases; 2,465 controls	OR=0.7 (0.3-1.7), male OR=2.6 (0.3-22), female
Vaughan *et al.* (1986)	Work history	USA	Case-control†	27 [205‡] cases; 552 controls	OR=2.1 (0.6-7.8) [OR=1.5 (0.7-3) ‡], high exp.
Roush *et al.* (1987)	Work history	USA	Case-control	173 cases; 605 controls	OR=2.3 (0.9-6), high exp. >20 years
West *et al.* (1993)	Work history	Philippines	Case-control†	104 cases; 205 controls	OR=2.7 (1.1-1.7), exp. <15 years
Armstrong *et al.* (2000)	Work history	Malaysia	Case-control†	282 cases; 282 controls	OR=0.71 (0.34-1.41),adj. diet/smoking
Laforest *et al.* (2000) §	Work history	France	Case-control†	83 cases; 85 controls	OR=1.35 (0.86-2.14), ever exposed
Vaughan *et al.* (2000)	Work history	USA	Case-control†	196 cases; 244 controls	OR=1.3 (0.8-2.1), ever exposed
Hildesheim *et al.* (2001)	Work history	Taiwan	Case-control	375 cases; 325 controls	RR=1.4 (0.93-2.2), ever exposed
Berrino *et al.* (2003) §	Work history	Fr, I, Es, Swiss	Case-control†	100 cases; 819 controls	RR=0.5 (0.1-1.8), probable/certain exposure

PMR = Proportionate mortality ratio
‡Oro- and hypopharyngeal carcinoma ("all other pharyngeal")
†Confounders considered (various including smoking, wood dust, other occupational exposures), sometimes applicable to a sample in cohort
#All pharyngeal carcinomas
*Earlier studies of same/similar cohort as Hauptmann *et al,* (2004) for Blair *et al,* (1986) and Coggon *et al,* (2003) for Gardner *et al,* (1993)
§Hypopharyngeal carcinoma

A study of a cohort of approximately 14,000 workers from UK chemical facilities employed between 1937-1965 showed a statistically non-significant excess mortality from pharyngeal cancer (SMR, 1.55; 95%CI= 0.87-2.56) and fewer observed deaths from NPC than were expected (Coggon *et al,* 2003). The study concluded that formaldehyde exposure had a greater association with lung cancer than pharyngeal, particularly nasopharyngeal, cancer. This is supported by Andjelkovich *et al,* (1995) who reported no deaths from NPC/pharyngeal cancer in workers exposed to formaldehyde, despite elevated mortality from carcinoma of the buccal cavity among exposed workers and elevated NPC/pharyngeal mortality in unexposed workers. Laforest *et al.* (2000) did however report an association between hypopharyngeal

cancer and formaldehyde (OR 1.35) rising to OR=1.74 (95%CI=0.91-3.34) when adjusted for low probabilities (<10%) of occupational exposure and OR=3.78 (95%CI=1.50-9.49) for high exposure (>50%) probabilities, although the association was stronger with coal dust (OR 2.31; p<0.005).

Pinkerton *et al.* (2004) and Dell and Teta (1995) did not observe any cases of nasopharyngeal cancer in retrospective cohort studies of mortality in garment workers and plastic manufacturing, respectively, exposed to formaldehyde. An association between formaldehyde exposure during fibreglass production and nasopharyngeal cancer has not been reported (IARC 2006). Edling *et al.* (1987) report one case of NPC in workers in the abrasives industry and Hansen and Olsen (1995) found very little difference between observed and expected cases of pharyngeal cancer for workers with mixed industrial exposures (SPIR 1.1; 95%CI=0.70-1.70) but a slightly elevated but non-significant risk of NPC (SPIR 1.3; 95%CI=0.30-3.20). Nasopharyngeal and pharyngeal cancer incidence and mortality have been reported to be associated with professions exposed to formaldehyde such as embalmers and funeral directors, with a reported SMR = 2.10 (95%CI= 0.6-5.4) based on 4046 workers (Hayes *et al,* 1990). Other studies on similarly exposed professions, including pathologists and anatomists, have either not reported any association with NPC or have not noted any difference in expected and observed cases (Walrath and Fraumeni 1983; 1984, Hall *et al,* 1991 and Stroup *et al,* 1986).

Formaldehyde exposure may occur during furniture production and in other wood industries. Partanen *et al.* (1985; 1990) conducted case control studies in a cohort of 3805 male workers, employed within the Finnish wood-working industry during 1944-1966, expanded to 7307 in a 1990 update study. One case of pharyngeal cancer was identified in the 1990 study but an odds ratio was not provided. Generally, a slight, non-significant increase in risk for all cancers (including lung cancer) combined was seen for workers exposed to at least 0.1 ppm (0.12 mg/m^3) formaldehyde (OR=1.44; 95%CI=0.6-3.5) compared with no exposure, after adjustment for smoking. IARC (2006) note that there were too few cancers at sites other than the lung to allow for a meaningful analysis. A number of case-control studies assessed formaldehyde co-exposure alongside wood dust, and are discussed in the wood dust section below.

The textile finishing industry frequently uses formaldehyde and hence offers a route of exposure to textile workers. A recent study reported by Li *et al.* (2006) did not identify any cases of NPC in workers exposed to formaldehyde. However, the study, which adjusted for smoking and alcohol consumption, did identify exposures to dyes, inks, acids and cotton dusts as causal factors for the disease, adjusted for smoking and alcohol consumption. The study did not adjusted for diet (particularly consumption of preserved foods) which could be a cofounding factor given the location of the cohort (Shanghai, China).

CAREX estimate about 94,000 workers were exposed to formaldehyde in GB between 1990 and 1993. Almost 40,000 workers (42% of total) were employed in the manufacture of furniture and fixtures, with a further 18,000 (19% of total) working in garment manufacture and 12,000 (or 13%) in the manufacture of wood products. The remaining 24,000 (25% of total) were employed in 19 other industry types.

Wood Dust

Occupational exposure to fine particulate wood dust is an established cause of adenocarcinoma of the nasal cavities and paranasal sinuses, and has been classified as carcinogenic to humans by IARC (IARC, 1995b). A number of case-control studies on NPC have reported an association with exposure to wood dust and/or employment in wood-related occupations (West *et al,* 1993; Hildesheim *et al,* 1992; Sriamporn *et al,* 1992; Vaughan and Davis 1991; Kawachi *et al,* 1989; Vaughan 1989). However, as confounding could not be

ruled out, these studies were considered by IARC as providing suggestive, but inconclusive evidence of a causal role of occupational exposure to wood dust in cancers of the nasopharynx (IARC, 1995b). IARC (1995b) also reported no indication that occupational exposure to wood dust has a causal role in other pharyngeal cancers (oro- and hypopharyngeal carcinomas) based on the results of five case-control studies assessing pharyngeal cancer incidence separately from other cancer sites (Huebner *et al,* 1992; Vaughan and Davis 1991; Haguenoer *et al,* 1990; Vaughan 1989; Elwood *et al,* 1984).

More recent studies provide additional information regarding the association between wood dust and naso-/pharyngeal cancers (Table 8). Hildesheim *et al.* (2001) determined that wood dust was closely correlated with NPC, particularly non-keratinizing and undifferentiated carcinomas, with formaldehyde showing a less clear association while solvents were not found to have an association with NPC incidence. Yu and Yuan (2002) found an association between NPC and wood dust, and Demers *et al.* (1995) reported a statistically significant excess in mortality for NPC in wood workers (especially furniture and plywood workers) but a statistically significant deficit for pharyngeal cancer overall. Armstrong *et al.* (2000) found a clear association between wood dust and NPC after adjustment for risk from diet, cigarette smoking and social class but did not identify any association between NPC and formaldehyde irrespective of any adjustment. This was supported by a meta-analysis described by Collins *et al.* (1997). Vaughan *et al.* (2000), however, report an association between squamous cell NPC and formaldehyde but not wood dust. Further more, an association between wood dust and oropharyngeal cancer has been indicated by a study in Belgrade (Serbia and Montenegro) but the researchers indicated that further work is required to investigate the association between pharyngeal cancer and wood dust (Vlajinac *et al,* 2006).

The highest exposures have generally been reported for occupations in the furniture making industry although carpenters, machine operators, construction industry and logging/forestry operations also result in exposure to wood dust (Boffetta *et al,* 2003; Riechelmann 2002; Goldberg *et al,* 1997; Demers *et al,* 1995; Sriamporn *et al,* 1992; Kawachi *et al,* 1989; Reif *et al,* 1989; Hardell *et al,* 1982). An association with paper manufacture has also been suggested (Rix *et al,* 1998; 1997).

Within the wood industries, exposure to solvents and formaldehyde in glues and surface coatings, phenol, wood preservatives, engine exhausts and fungal spores may also occur. Formaldehyde exposures have been considered separately (see above). Mirabelli *et al.* (2000) and Hardell *et al.* (1982) have suggested exposure to chlorophenols (used as a wood preservative) as a causal factor for NPC. Hildesheim *et al.* (2000) suggested that chlorophenol exposure may explain the stronger effects observed from exposure to softwood as opposed to hardwood dust. Maier *et al.* (1997) did not find an association between paint, lacquer and solvents and pharyngeal cancer.

Table 8 Studies of wood dust and nasopharyngeal cancer (with or without adjustments for lifestyle factors). Where data exist, results for other pharyngeal cancers have also been included

Reference	Industry/product	Country	Design	Study size	Results
Demers *et al,* (1995)	Furniture makers and plywood workers	UK/USA	Pooled cohort	5 cohorts = 28,704	SMR=2.4 (1.1-4.5) [SMR=0.8 (0.5-1.3) ‡]
Hardell *et al,* (1982)	Carpenter, cabinet-maker, sawmill worker	Sweden	Case-control	27 cases; 541 controls	RR=1.3 (0.6-2.9)
Kawachi *et al,* (1989)	Woodworkers, foresters/loggers, carpenters	New Zealand	Case-control	Cases not reported; 19,858 controls	OR=2.5 (0.9-6.6), OR=6 (1.0-28), OR=2.5 (0.6-8.5)
Vaughan (1989); Vaughan and Davis (1991)	Carpenters and other wood-related occupations	USA	Case-control	21 cases; 552 controls	OR=3.3 (0.8-13) carpenter; OR=1.2 (0.2-4.6) other work
Sriamporn *et al,* (1992)	Wood cutting +/- agriculture	Thailand	Case-control	120 cases; 120 controls	OR=4.1 (0.8-22); OR=8 (2.3-28)
Armstrong *et al,* (2000)	Work history	Malaysia	Case-control†	282 cases; 282 controls	OR=2.36 (1.33-4.19), adj. diet/smoking
Laforest *et al,* (2000) §	Work history	France	Case-control†	33 cases; 36 controls	RR=0.89 (0.47-1.68), ever exposed
Vaughan *et al,*(2000)	Work history	USA	Case-control†	196 cases; 244 controls	OR=1.3 (0.8-2.1)
Hildesheim *et al,* (2001)	Work history	Taiwan	Case-control	375 cases; 325 controls	RR=1.7 (1.00 – 3.0), ever exposed
Vlajinac *et al,* (2006)*	Work history	Serbia and Montenegro	Case-control†	100 cases; 100 controls	OR=4.16 (1.45-11.91)*

‡Oro- and hypopharyngeal carcinoma ("all other pharyngeal")
† Confounders considered (various including smoking, alcohol consumption, formaldehyde, other occupational exposures), sometimes applicable to a sample in cohort
*Oropharyngeal carcinoma only

According to CAREX there were about 430,000 people exposed to wood dust in various industries in Great Britain (GB) in 1990-93, with workers in the construction industry dominating with almost 230,000 people (53% of total) exposed to wood dust. Employment in the manufacture of furniture and fixtures is the next largest group with 94,000 people exposed (22% of total), followed by manufacture of primary wood products (56,000 people or 13% of total) and forestry and logging occupations (11,000 people or 3% of total); a further 33 occupation types, including paper manufacture, are reported to have fewer people exposed to wood dust, accounting for 9% of total people exposed in GB.

Other dusts

Shangina *et al.* (2006) indentified that coal dust exposure was an important causal factor for hypopharyngeal cancers, with the possibility of mild steel dust/iron compounds and associated fumes also being factors. Laforest *et al.* (2000) report an association between coal dust and hypopharyngeal cancer, with a significant increase in risk with probability and level of exposure. Purdue *et al.* (2006) found a potential association between pharyngeal cancer and cement dust exposure but suggested that more work was required to determine the strength of the association. Work by Maier *et al,* (2002) provided some support for the existence of such

an association and also indicated an association with asbestos exposure. However, this study considered laryngeal, as well as oral cavity and pharyngeal, cancers. Asbestos as a causal factor has also been suggested by Marchand *et al.* (2000) who reported a significant association between hypopharyngeal cancer and asbestos exposure. Su *et al.* (2006) found an association between iron mine dust and nasopharyngeal cancer. Uzcudun *et al.* (2002), whilst noting that smoking, alcohol consumption and socioeconomic factors exert predominate effects, report a number of occupational risk factors associated with the incidence of oropharyngeal and hypopharyngeal cancers; these included employment as manual workers in agriculture and construction, and occupational exposure to pesticides, solvents and dusts. Zhang *et al.* (2004) report that dust as a causal factor for NPC shows a stronger association than smoking with NPC. Li *et al.* (2006) found an increased risk of NPC in female textile workers exposed to dyes, inks, acids and cotton dusts, an association originally suggested by Moss and Lee (1974) in a population drawn from England and Wales.

2.2.2 Occupations

Boffetta *et al.* (2003) found evidence of elevated larynx and hypopharynx cancer risk in workers engaged in occupations associated with construction, metal, textile, ceramic, and food industries and in railway transport, barbers, butchers, shoe finishers and loggers. The same cancers were evaluated by Goldberg *et al.* (1997) who reported associations with service workers, agricultural and animal husbandry workers, miners and quarrymen, transport workers and various other skilled and unskilled workers. These authors also suggested a risk to machine operators among woodworkers. A different methodological approach to the same dataset revealed that occupational exposure to solvents and asbestos were associated with increased risks of hypopharyngeal/laryngeal cancer; formaldehyde was suggested as a factor for laryngeal cancer and wood dust for subjects over 55 years of age (Berrino *et al,* 2003). Nasopharyngeal cancer is reported to be one of the top three causes of death in industrial workers in China (Chen and Liu, 2002. However this study, which was carried out in the city of Guangzhou in southern China, did not adjust for confounders such as salted fish consumption. Riechelmann (2002) reviewed several tobacco- and alcohol-adjusted case-control and cohort studies and found an association between cancers of the oral cavity and pharynx and employment in the construction and metalworking industries, particularly as painters, carpenters and machine operators, and in the paper and rubber industries; findings for textile and woodworking were inconclusive. Li *et al.* (2006) did, however, identify an association for female workers in the textile industry exposed to textile dusts and NPC. Liu *et al.* (2002) provide evidence of an association between NPC and employment in the printing industry and nasopharyngeal cancer, while Rix *et al.* (1998) reported an association between male paper mill workers and incidence of pharyngeal cancer. A significant association between nitrosamine exposure (rubber industry) and cancers of the oral cavity and pharynx has also been reported (Straif *et al,* 2000a, 2000b, 1998). Zhu *et al.* (2002) reported that occupational exposure to cutting oils was associated with nasopharyngeal cancer. Low concentrations of sulphuric acid vapour were found to be associated with NPC incidence (Ho *et al,* 1999) and welding fumes have been associated with pharyngeal cancer (Gustavsson *et al,* 1998). Marsh *et al.* (2007) suggest that the elevated levels of NPC mortality rates reportedly associated to formaldehyde exposure at the Wallingford plastics-producing plant may be due instead to other employment in the ferrous and non-ferrous metal industries.

Increased incidence of pharyngeal cancer, particularly of the oropharynx and nasopharynx, has also been reported for vehicle maintenance workers (Andreotti *et al,* 2006), female hairdressers and male dry cleaners (Ji and Hemminki 2005), and waiters/waitresses in Chinese restaurants (Yu *et al,* 2004). Agricultural work was not identified as having a significant association with pharyngeal cancer (Coble *et al,* 2003; Settimi *et al,* 2001). Armstrong *et al.* (2000) reported an association between NPC and industrial heat. A large number of these studies, however, failed to adjust for lifestyle factors (such as smoking, alcohol and preserved food consumption, or Epstein-Barr viral load).

Other than workers in industry, the professional occupations of pathology, anatomy, embalming and funeral organisation have also been linked to cancers of the naso-/pharynx with exposure to formaldehyde being identified as the important factor. Nonetheless, it is important to note that evidence of an association between occupational exposure to formaldehyde and cancer of the nasopharynx is uncertain, with some studies finding elevated risk (Hayes *et al,* 1990) and others showing no increase (Walrath and Fraumeni 1983; 1984, Hall *et al,* 1991 and Stroup *et al,* 1986).

2.2.3 Exposure concentrations

Coggon *et al.* (2003) estimate background exposure to formaldehyde in their study as corresponding to a time-weighted average (TWA) concentration of less than 0.1 ppm; low exposure to 0.1-0.5 ppm; moderate exposure to 0.6-2.0 ppm; and high exposure greater than 2.0 ppm.

Workplace exposure limits for formaldehyde in the UK are 8-hour and 15-minute time-weighted averages (TWA) of 2 ppm (2.5 mg/m^3) (HSE 2005). In the US, the OSHA permissible exposure limit for an 8-hour TWA is 0.75 ppm and, for 15-minute STEL, is 2 ppm with a threshold limit value of 0.3 ppm. The NIOSH recommended exposure limit for 10-hour TWA is 0.016 ppm with a 15-minute ceiling limit of 0.1 ppm. Formaldehyde is considered to be immediately dangerous to life at 20 ppm (HSDB 2006).

3 ATTRIBUTABLE FRACTION ESTIMATION

3.1 GENERAL CONSIDERATIONS

Substances and Occupations

The substances considered in the estimation of the attributable fraction (AF) for cancer of the nasopharynx are those outlined in Table 9.

Table 9 Substances considered in the estimation of the attributable fraction for cancer of the nasopharynx

Agents, mixture, circumstance	AF calculation	Strength of evidence	Comments
Group 1: carcinogenic to humans			
Agents, groups of agents			
Formaldehyde	Y	Suggestive	
Mustard gas	N	Suggestive	Few workers possibly exposed
Wood dust	Y		Possible co-exposure to formaldehyde
Group 2A: probably carcinogenic to humans			
None identified			

Data Relevant to the Calculation of AF

The two data elements required are an estimate of relative risk (RR), and either (1) an estimate of the proportion of the population exposed (Pr(E)) from independent data for Great Britain, or (2) an estimate of the proportion of cases exposed (Pr(E|D)) from population based study data.

The RR chosen from a 'best study' source is described for each exposure, with justification of its suitability. Information on the 'best study' and independent data sources for the proportion of the population exposed are also summarised for each exposure in the appropriate section below. In the absence of more precise knowledge of cancer latency, for solid tumours a latency of up to 50 years and at least 10 years has been assumed for all types of the cancer. Therefore it is assumed that exposure at any time between 1956 and 1995 (the Risk Exposure Period, REP) can result in a cancer being recorded in 2004 as a registration or in 2005 as an underlying cause of death. Although strictly speaking the REP for cancer registrations recorded in 2004, the year for which estimation has been carried out, would be 1955-1994, for simplification the years 1956 to 1995 have also been used, as for deaths, as the proportion exposed will not be affected. For an independent estimate of the proportion of the population exposed, numbers of workers ever exposed during this period are estimated by extrapolating from a point estimate of exposed workers taken from the period. If this is from CAREX relating to 1990-93, an adjustment is made to take account of gross changes in employment levels which have occurred particularly in manufacturing industry and the service sector across the REP. Otherwise a point estimate that represents numbers employed as close as possible to about 35 years before the target year of 2005 is used, as this is thought to represent a 'peak' latency for the solid tumours, and is also close to the mid-point of the REP for estimating numbers ever exposed across the period (for which a linear change in employment levels is implicitly assumed). Where the Census of Employment is used, the point estimate data are for 1971. Where the LFS is used, the first year available is 1979 and was used. A turnover factor is applied to estimate numbers ever exposed during the REP, determined mainly by the estimate of staff turnover per year during the period. For each exposure

therefore, if an AF has been based on independent estimates of numbers exposed, the table of results includes the point estimate of numbers employed, the adjustment factor for CAREX if applicable, the staff turnover estimate, and the resulting estimate of numbers ever exposed during the REP. Other estimates used in the calculations that remain constant across exposures (unless otherwise stated) are given below:

- Number of years in REP = 40
- Proportion in the workplace ever exposed is set to one, i.e. all are assumed to be exposed, in the absence of more detailed information. Where sources other than CAREX are used for the point estimate of numbers exposed, such as the LFS or Census of Employment, a precise as possible definition of workers exposed is sought.
- Numbers ever of working age during the target REP = 19.4 million men, 21.0 million women. This is the denominator for the proportion of the population exposed, and is based on population estimates by age cohort in the target year.
- Total deaths from nasopharyngeal cancer in GB in 2005 = 65 for men aged 25+ (62 England and Wales and 3 Scotland), 32 for women aged 25+ (29 England and Wales and 3 Scotland).
- Total registrations from nasopharyngeal cancer in GB in 2004 = 127 aged 25+ for men (114 England, 4 Wales and 9 Scotland), 62 for women aged 25+ (56 England, 1 Wales and 5 Scotland).

Attributable numbers are estimated by multiplying the AF by the total number of cancers in GB. Only cancers which could have been initiated during the risk exposure period are counted, taking normal retirement age into account. Therefore for solid tumour cancers, total deaths or registrations recorded at all adult ages (25+) are used to estimate attributable numbers, and for short latency cancers, deaths and registrations for ages 15-84 for men and 15-79 for women are used.

For each agent where data on worker numbers are only available for men and women combined (CAREX data), the assumed percentage of men is given in addition to the numbers exposed. The allocation to high and low, and occasionally negligible, exposure level categories, or division into separate exposure scenarios, is also included in these tables. Where no separate estimate of relative risk is available for the low exposure level category, an estimate is based on an average of the high/low ratios for cancer-exposure pairs for which data were available.

Full details of the derivation of the above factors and the methods of calculating AF are published separately. Unless otherwise stated, Levin's method is used for estimates using independent estimates of numbers exposed, and Miettinen's method is used for study based estimates. A summary of the methodology is given in the Statistical Appendix.

3.2 FORMALDEHYDE

(a) Risk estimate There remains considerable uncertainty regarding the importance of formaldehyde as a causal factor in naso-/pharyngeal cancer. IARC (2006) consider there to be sufficient evidence of an association between formaldehyde exposure and NPC. However, evidence of formaldehyde as a causal factor in other pharyngeal cancers has not been considered to be adequate. Despite the IARC acknowledgement of the relationship between formaldehyde exposure and NPC, a large number of case-control and cohort studies dispute the strength of association identified by workers such as Blair *et al.* (1986) and Hauptmann *et al.* (2004) (Duhayon et al. 2008). Marsh *et al.* (2007; 2002) and Marsh and Youk (2005) re-

analysed the NCI data reported by Blair *et al.* (1986) and Hauptmann *et al.* (2004) and suggest that the SMR calculated may be biased due to one of the ten factories included in the NCI cohort study and may be heavily influenced by external employment in metal industries rather than formaldehyde exposure. Due to the uncertainty regarding the NCI data, the cohort study reported by Coggon *et al.* (2003) could be used to derive the risk estimate for industrial workers (industry sector C-E); this study has the added benefits of being UK-based and of relating to a large number of workers with limited co-exposures. A number of case-control studies provide risk estimates for other occupations including embalming/pathology (Hayes *et al,* 1990), wood workers (Hildesheim *et al,* 2001) and textile workers (Li *et al,* 2006).

A cohort of British chemical workers exposed to formaldehyde was established in the early 1980s (Coggon *et al,* 2003). Five of the six companies involved produced their own formaldehyde on site and either used it to manufacture resins and adhesives or exported the product as formalin, paraformaldehyde or alcoforms. The last company imported formalin to produce resins. The cohort comprised 14,014 men who were followed up to 2000. Between 1941 and 2000 the SMR for pharyngeal cancer (ICD-9 146-149.1) was 1.55 (95%CI=0.87 – 2.56) based on 15 cases observed (low or background exposures). Six deaths occurred in men with high exposure, giving a SMR of 1.91 (95%CI=0.70 – 4.17) (high exposures > 2 ppm). It should be noted that IARC consider formaldehyde to be a causal factor for nasopharyngeal cancer but not other pharyngeal carcinomas. Only one death from NPC was observed (2.0 expected) and the man concerned had not had high occupational exposure to formaldehyde; Coggon *et al.* (2003) do not provide a SMR for NPC. Marsh *et al.* (2007) and Hauptmann *et al.* (2004) indicate 4.43-fold (95%CI=1.05 - 4.21) and 2.10-fold (95%CI=1.78 – 9.13) excesses, respectively, for NPC. The SMR for NPC provided by Hauptmann *et al.* (2004) is derived from a cohort study of 25,619 US workers employed at ten plants prior to 1966 (employed between 1934-1958) through to 1994. The ten plants either manufactured formaldehyde or used formaldehyde in the manufacture of other products. The SMR value of 2.1 (95%CI=1.78–9.13) is derived from mortality across all ten plants, including the largest, a plastics-producing plant at Wallingford, Connecticut. Marsh *et al.* (2007) suggest that this SMR is influenced by the large, statistically significant 10.3-fold excess in NPC deaths (95% CI, 3.8-22.5) for formaldehyde-exposed workers employed at the Wallingford plant; in contrast, a SMR of 0.65 (95%CI=0.08-2.3) was determined for exposed workers at the nine other plants. The Wallingford plant NPC rate was recalculated by Marsh *et al.* (2007) to 4.43 (95%CI=1.05-4.21). Hauptmann *et al.* (2004) provide relative risks by variations of exposure to formaldehyde; a non-significant RR of 1.67 (no 95% CI provided) was calculated for the high exposures ≥1 ppm. Except for a RR of 1.83 (no 95% CI provided) for peak exposure ≥4 ppm, all other risks were also non-significant.

Hayes *et al.* (1990) describe a cohort study of 4046 male embalmers/funeral directors (3649 white and 397 non-white) identified from mortality records between 1975 and 1985. Proportionate mortality ratios (PMRs) for cancer of the buccal cavity and pharynx were 1.19 (95%CI=0.78 – 1.74; 26 deaths) and 1.25 (95%CI=0.34 – 3.20; four deaths) for white and non-white men respectively. For nasopharyngeal cancer, PMRs of 1.89 (95%CI=0.39 – 5.48; three deaths) and 4.00 (95%CI=0.10 – 22.3; one death) were reported for the same respective groups. Combined, the two groups had a SMR for NPC of 2.1 (95%CI=0.6 – 5.4; four deaths). These risk estimates were used for the AF estimate in this study, for the high level exposure group and industry categories G-Q. Note that other studies, including Walrath and Fraumeni (1983; 1984), Hall *et al.* (1991) and Stroup *et al,* (1986) do not report any cases of nasopharyngeal cancer (although unspecified cancers of the buccal cavity and pharynx are described).

Occupational exposure of workers to formaldehyde in wood industries (carpentry, furniture making, sawmills, etc.) is not a well studied area and there are no suitable risk estimates available from the literature (Partanen *et al.* 1985; 1990). Similarly, the exposure of textile workers to formaldehyde is not well reported, with studies evaluating exposures to other

agents such as textile dusts, dyes and inks, more commonly available. The recent paper by Li *et al.* (2006) quoted a hazard ratio of 3.6 (95%CI=1.8-7.2) for NPC cases associated with high level exposure to cotton dust. Exposure during manufacture of fibreglass is also not reported for NPC (IARC 2006).

Establishing a risk estimate for occupational exposure to formaldehyde and naso-/pharyngeal cancer is complicated by the frequently unclear definitions of the type of pharyngeal cancers included in the study. This is an important consideration as IARC only consider formaldehyde to be a causal factor for NPC; evidence is insufficient regarding other pharyngeal cancers. (IARC 2006). While Coggon *et al.* (2003) provide SMRs for low and high formaldehyde exposure in industrial workers, the risk estimates refer to all pharyngeal cancers including NPC; a value for NPC alone is not provided. For NPC, the Hauptmann *et al.* (2004) SMR of 2.10 (95%CI=1.78 – 9.13) may be used to determine the AF estimate for workers exposed to formaldehyde (high exposures (H) in Table 10). This includes embalmers and other professional services due to similarity of mortality ratio (SMR=2.1, 95%CI=0.6 – 5.4) as provided by Hayes *et al,* (1990), and other industrial occupations such as textile manufacture due to absence in the literature of appropriate relative risks. Given the uncertainty about the risk of nasopharyngeal cancer and exposure to formaldehyde, particularly at low levels, the relative risk for low (L) or background (B) exposures to formaldehyde have been set to 1.00 for AF estimation.

(b) Numbers exposed: The number of workers exposed to formaldehyde in 1990-1993 according to CAREX is given in Table 10. Embalmers and related professions are considered to be included in the 'personal and household services' category based on the SOC 'personal service occupations' (SOC major group 6 and minor group 629). According to the British Institute of Embalmers (BIOE), there are currently 1400 registered embalmers in the UK and Ireland, 100 of whom work overseas (BIOE, Pers. Comm.). However, not all registered embalmers will be working at one time, with many retired or employed elsewhere. As the occupation is unregulated, there is no requirement for workers to qualify and hence register, and there may be many more employed in the embalming services than current estimates allow (BIOE, Pers. Comm.). It is also uncertain how many embalmers were employed in the past although it is thought that numbers are increasing. In the AF estimate the CAREX figure for personal and household services has thus been used.

In order to split the CAREX exposed numbers between men and women, it is assumed that all the exposed occupations in manufacturing and in construction were in skilled trades, shop floor and transport operatives (SOC major groups 5, 8 and 9), and that the exposed occupations in the service sector were in professional, associated professional and technical and personal and protective service occupations (SOC groups 2, 3 and 6), except workers employed in personal and household services. For this industry, it assumes that workers are mainly embalmers and according to BIOE, 78% are male. These data were used to estimate Pr(E) for Levin's calculation of AF, as an alternative to the European population based studies.

(c) AF calculation: The estimated total (male and female) attributable fraction for nasopharyngeal cancer associated with occupational exposure to formaldehyde is 0.44% (95%Confidence Interval (CI)=0.00-2.18), which equates to 0 (95%CI=0-2) attributable death and 1 (95%CI= 0-4) attributable registration. The estimated AF for men is 0.51% (95% CI=0.0-2.56) resulting in 0 (95%CI=0-2) attributable deaths and 1 (95%CI=0-3) attributable registration; and for women the AF is 0.29% (95% CI=0.0-1.41) resulting in 0 (95%CI= 0-0) attributable deaths and 0 (95%CI=0-1) attributable registrations (Table 11).

Table 10 Numbers of workers exposed to formaldehyde according to CAREX in 1990-1993

Main sector industry	Industry	Carex Data 1990-1993		Exposure level
		Number exposed	Number in industry	
C-E	Crude petroleum and natural gas production	656	53,300	B
	Beverage industries	881	88,100	B
	Manufacture of textiles	4,730	182,000	H
	Manufacture of wearing apparel, except footwear	17,992	189,500	H
	Manufacture of wood and wood and cork product, except furniture	12,430	132,975	L
	Manufacture of furniture and fixtures, except primary use of metal	39,772	144,325	L
	Manufacture of paper and paper products	722	119,050	B
	Manufacture of industrial chemicals	1,006	130,000	L
	Manufacture of other chemical products	360	175,175	L
	Manufacture of plastics products nec	2,021	136,900	L
	Manufacture of glass and glass products	278	43,275	H
	Manufacture of other non-metallic mineral products	585	70,875	L
	Iron and steel basic industries	1,870	48,425	L
	Non-ferrous metal basic industries	1,254	79,325	L
	Manufacture of fabricated metal products, except machinery and equipment	535	292,200	L
	Manufacture of machinery except electrical	760	692,275	L
F	Construction	4,511	1,753,450	L
G-Q	Education services	122	1,455,875	H
	Research and scientific institutes	176	91,100	H
	Medical, dental, other health and veterinary services	2,796	1,435,675	H
	Recreational and cultural services	74	534,600	B
	Personal and household services	276	686,750	H
	Total	**93,807**	**2,687,375**	

	Main sector industry		% Male	
A-B	Agriculture, hunting and forestry; fishing			
	High	0		
	Low	0		
C-E	Mining/quarrying, electricity/gas/steam, manufacturing industry			
	High	23,000	76	
	Low	60,593	76	
	Background	2,259	76	
F	Construction			
	Low	4,511	99	
G-Q	Service industries			
	High (except Personal and household services)	3,094	45	
	High (only Personal and household services)	276	78	
	Background	74	45	

Table 11 Results for nasopharyngeal cancer and exposure to formaldehyde

				Data		Calculations				Attributable Fraction (Levins[8]) and Monte Carlo Confidence Interval			Attributable Deaths			Attributable Registrations		
	Risk Estimate Reference	Exposure	Main Industry Sector[1]	RR[2]	Ne[3]	Carex adj[4]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	Hauptmann *et al.* (2004)	H	C-E	2.1	17480	1.4	0.09	84552	0.00436	0.0048	0.0000	0.0244	0	0	2	1	0	3
		H	G-Q	2.1	1608	0.9	0.11	6045	0.0003	0.0003	0.0000	0.0011	0	0	0	0	0	0
		H	All		19088			90596	0.0047	0.0051	0.0000	0.0256	0	0	2	1	0	3
		L	C-E	1	46051	1.4	0.09	222750	0.0115	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	F	1	4466	1	0.12	20272	0.0010	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		50517			243022	0.0125	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	C-E	1	1717	1.4	0.09	8304	0.0004	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	G-Q	1	33	0.9	0.11	125	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	All		1750			8430	0.0004	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		71354			342048	0.0176	0.0051	0.0000	0.0256	0	0	2	1	0	3
Women	Hauptmann *et al.* (2004)	H	C-E	2.1	5520	1.5	0.14	46438	0.0022	0.0024	0.0000	0.0126	0	0	0	0	0	1
		H	G-Q	2.1	1762	0.8	0.15	8439	0.0004	0.0004	0.0000	0.0015	0	0	0	0	0	0
		H	All		10266			54877	0.0026	0.0029	0.0000	0.0141	0	0	0	0	0	1
		L	C-E	1	14542	1.5	0.14	122339	0.0058	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	F	1	45	0.67	0.15	181	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		14587			122520	0.0058	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	C-E	1	542	1.5	0.14	4756	0.0002	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	G-Q	1	41	0.8	0.15	194	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		B	All		583			4755	0.0002	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		**22453**			182153	0.0087	0.0029	0.0000	0.0141	0	0	0	0	0	1

1. Specific scenario or main industry code (Table A1)
2. Relative risks selected from the best study
3. Numbers exposed, allocated to men/women
4. CAREX adjustment factor to mid-REP (Table A1)
5. Staff turnover (TO, Table A1)
6. Number ever exposed during the REP (Statistical Appendix equation 3)
7. Proportion of the population exposed (Pr(E), Statistical Appendix equation 4)
8. Statistical Appendix equation 1

3.3 MUSTARD GAS

(a) Risk estimate: A suggestive association between naso-/pharyngeal cancer and exposure to mustard gas has been reported (see Section 2). However, subjects were workers employed in manufacturing before and during the Second World War.

(b) Number exposed: According to CAREX, 213 workers were exposed to mustard gas for the period 1990-1993. This number exposed in the GB was therefore expected to be negligible.

(c) AF calculation: The AF calculation is therefore omitted.

3.4 WOOD DUST

(a) Risk estimate: While wood dust is not listed by Siemiatycki *et al.* (2004) as a causal factor for naso-/pharyngeal cancer, IARC have recently stated that that there is sufficient evidence of a causal role of occupational exposure to wood dust in cancers of the nasopharynx (Straif *et al,* 2009). There is, however, no indication of a causal role in cancers of the oro- and hypopharynx (IARC, 1995). Demers *et al*. (1995) provide an updated analysis of workers in the furniture industry in a pooled analysis that also assessed the plywood industry. They observed a statistically significant increase in NPC mortality in workers exposed to wood dust but a deficit for pharyngeal cancer generally. This analysis resulted in an overall summary SMR of 2.4 (95% CI 1.1-4.5) for NPC for woodworkers in all industries. By industry, there were seven deaths from NPC amongst furniture workers (SMR = 2.9, 95% CI 1.2-5.9) and two deaths amongst plywood workers (SMR = 4.6, 95% CI 0.6-16.4). Study subjects having the highest probability of wood dust exposure had elevated relative risks for NPC:

- Possible exposure SMR = 2.9, 95% CI 0.8-7.5
- Probable exposure SMR = 0.0, 95% CI 0.0-3.8
- Definite exposure SMR = 5.3, 95% CI 1.7-12.4

It is problematic converting SMR values based on the probability of exposure (possible to definite) to values corresponding to level of exposure (low to high). Application of the overall summary SMR of 2.4 (95% CI 1.1-4.5) for all woodworkers will be used for high exposures in the AF calculation using Levin's formula and CAREX exposed numbers for the proportion of the population exposed (Pr(E)). The literature suggests that risks at low exposures are very uncertain and also low; therefore the low estimate is set to 1.
.

(b) Numbers exposed: The numbers of workers exposed to wood in various industries according to CAREX for 1990-93 are given in Table 12. Exposure in construction was allocated to the 'higher' category, as it was assumed that these were all carpenters/joiners.

Table 12 Numbers of workers exposed to wood dust according to CAREX in 1990-1993

Main sector industry	Industry	CAREX Data 1990-1993		Exposure Level
		Number Exposed	Number in Industry	
A-B	Forestry and logging	10,887	14,500	H
C-E	Crude petroleum and natural gas production	68	53,300	L
	Food manufacturing	412	414,150	L
	Beverage industries	9	88,100	L
	Tobacco manufacture	7	9,950	L
	Manufacture of textiles	58	182,000	L
	Manufacture of wearing apparel, except footwear	50	189,500	L
	Manufacture of leather and products of leather or of its substitutes	32	16,825	L
	Manufacture of footwear	11	38,500	L
	Manufacture of wood and wood and cork products, except	55,930	132,975	H
	Manufacture of furniture and fixture, except primary of metal	94,196	144,325	H
	Manufacture of paper and paper products	4,308	119,050	L
	Printing, publishing and allied industries	2,126	354,750	L
	Manufacture of industrial chemicals	620	130,000	L
	Manufacture of other chemical products	1,151	175,175	L
	Petroleum refineries	24	18,075	L
	Manufacture of rubber products	25	53,025	L
	Manufacture of plastic products nec	415	136,900	L
	Manufacture of glass and glass products	206	43,275	L
	Manufacture of other non-metallic mineral products	1,498	70,875	L
	Iron and steel basic industries	188	48,425	L
	Non-ferrous metal basic industries	260	79,325	L
	Manufacture of fabricated metal products, except machinery and equipment	2,104	292,200	L
	Manufacture of machinery except electrical	4,939	692,275	L
	Manufacture of electrical machinery, apparatus, appliances and	684	473,750	L
	Manufacture of transport equipment	7,272	456,900	L
	Manufacture of instruments, photographic and optical goods	132	8,6225	L
	Other manufacturing industries	1,953	59,375	L
	Electricity, gas and steam	24	140,975	L
F	Construction	228,115	1,753,450	H
G-Q	Land transport	5,114	671,050	L
	Water transport	58	68,175	L
	Air transport	558	95,700	L
	Services allied to transport	3,805	180,725	L
	Communication	7	459,425	L
	Sanitary and similar services	4,150	274,225	L
	Education services	2,438	1,455,875	L
	Total	**433,834**	**9,673,325**	
	Main Industry Sector		**Male %**	
A-B	Agriculture, hunting and forestry; fishing High	10,887	78	

C-E	Mining/quarrying, electricity/gas/steam, manufacturing industry	High Low	150,126 28,576	76 76	
F	Construction	High	228115	99	
G-Q	Service industries	Low	16130	65	

(c) AF calculation: The estimated total (male and female) attributable fraction for nasopharyngeal cancer associated with occupational exposure to wood dust is 7.62% (95%CI=1.08-17.98), which equates to 7 (95%CI=1-17), attributable deaths and 14 (95%CI=2-34), attributable registrations. The estimated AF for men is 10.35% (95%CI=1.48-24.1) resulting in 7 (95%CI=1-16) attributable deaths and 13 (95%CI=2-31) attributable registrations; and for women the AF is 2.09% (95% CI=0.28-5.54) resulting in 1 (95%CI=0-2), attributable death and 1 (95%CI=0-3) attributable registration (Table 13).

Table 13 AF calculation for wood dust

				Data		Calculations				Attributable Fraction (Levins[8]) and Monte Carlo Confidence Interval			Attributable Deaths			Attributable Registrations		
	Risk Estimate Reference	Exposure	Main Industry Sector[1]	RR[2]	Ne[3]	Carex adj[4]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	Demers *et al*. (1995)	H	A-B	2.4	8492	1	0.07	23201	0.0012	0.0015	0.0002	0.0035	0	0	0	0	0	0
		H	C-E	2.4	114096	1.4	0.09	551887	0.0284	0.0357	0.0051	0.0831	2	0	5	5	1	11
		H	F	2.4	225834	1	0.12	1025129	0.0528	0.0663	0.0095	0.1544	4	1	10	8	1	20
		H	All		348421			1600217	0.0825	0.1035	0.0148	0.2410	7	1	16	13	2	31
		L	C-E	1	21718	1.4	0.09	105050	0.0054	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	G-Q	1	10485	0.9	0.11	39423	0.0020	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		32202			144473	0.0074	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		380624			1744690	0.0899	0.1035	0.0148	0.2410	7	1	16	13	2	31
Women	Demers *et al*. (1995)	H	A-B	2.4	2395	0.75	0.1	7365	0.0004	0.0005	0.0001	0.0013	0	0	0	0	0	0
		H	C-E	2.4	36030	1.5	0.14	303110	0.0144	0.0198	0.0027	0.0526	1	0	2	1	0	3
		H	F	2.4	2281	0.67	0.15	9148	0.0004	0.0006	0.0001	0.0016	0	0	0	0	0	0
		H	All		40707			319623	0.0152	0.0209	0.0028	0.0554	1	0	2	1	0	3
		L	C-E	1	6858	1.5	0.14	57696	0.0027	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	G-Q	1	5646	0.8	0.15	27033	0.0013	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		12504			84729	0.0040	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		53210			404352	0.0193	0.0209	0.0028	0.0554	1	0	2	1	0	3

1. Specific scenario or main industry code (Table A1)
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4. CAREX adjustment factor to mid-REP (Table A1)
5. Staff turnover (TO, Table A1)
6. Number ever exposed during the REP (Statistical Appendix equation 3)
7. Proportion of the population exposed (Pr(E), Statistical Appendix equation 4)
8. Statistical Appendix equation 1

4 OVERALL ATTRIBUTABLE FRACTION

4.1 EXPOSURE MAP

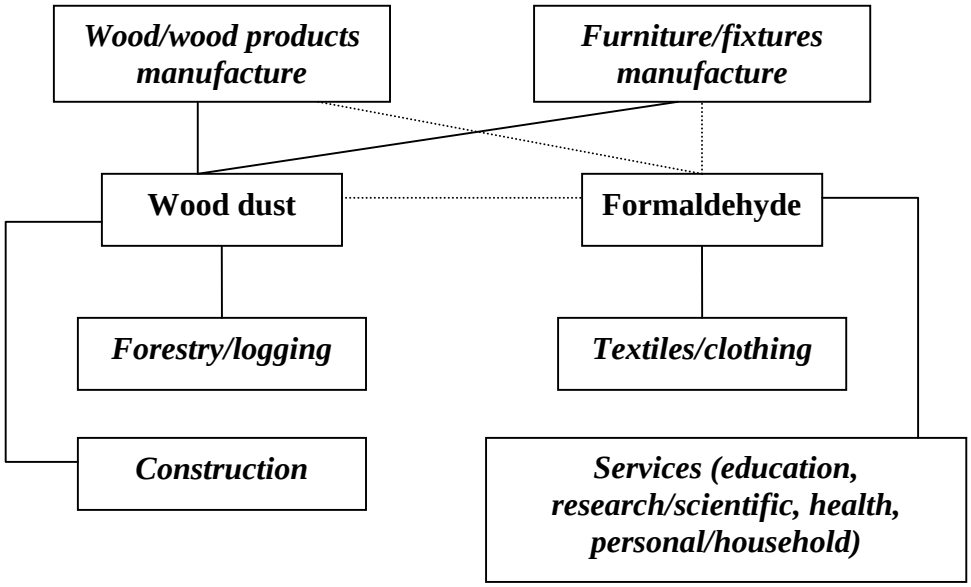

Figure 1 Nasopharynx cancer exposure map

The exposure map (Figure 1) gives an indication of how exposures overlap in the working population. It illustrates the potential for double counting of the exposed population to occur when an overall AF is calculated, and facilitates strategies to avoid this. For a given cancer, the map entries consist of either an agent (or group of agents such as PAHs), or an exposure scenario (i.e. an industry or occupation in which such exposure occurs). Agents are in plain type, exposure scenarios in italics, from Table 6; entries from Table 6 are in bold type to distinguish from extrapolated occupations/agents.

The dotted lines indicate the potential for overlap in the exposed populations e.g. for wood/wood products manufacture although different roles within this industry are likely to prevent high exposures to both wood dust and formaldehyde. There is no overlap in the exposed populations as occupational exposure of workers to formaldehyde in wood industries (carpentry, furniture making, other wood industries, etc.) is considered to be low compared to the high exposure of the same workers to wood dust.

4.2 SUMMARY OF RESULTS

The results are summarised in Tables 14 and 15.

Table 14 Summary of relative risks used to calculate AF

Agent	Exposure	RR	LL	UL
Formaldehyde	H	2.1	1.78	9.13
Formaldehyde	L	1	1	1
Formaldehyde	B	1	1	1
Wood dust	H	2.4	1.1	4.5
Wood dust	L	1	1	1

Table 15 Results

Agent	Numbers of Men Ever Exposed	Numbers of Women Ever Exposed	Proportion of Men Ever Exposed	Proportion of Women Ever Exposed	AF Men	MCLL Men	MCUL Men	AF Women	MCLL Women	MCUL Women	Attributable Deaths (Men)	Attributable Deaths (Women)	Attributable Registrations (Men)	Attributable Registrations (Women)
Formaldehyde	342048	182153	0.0176	0.0087	0.0051	0.0000	0.0256	0.0029	0.0000	0.0141	0	0	1	0
Wood dust	1744690	404352	0.0899	0.0193	0.1035	0.0148	0.2410	0.0209	0.0028	0.0554	7	1	13	1
Totals*					**0.1081**	**0.0234**	**0.4787**	**0.0237**	**0.0064**	**0.0684**	**7**	**1**	**14**	**1**

*Totals are the product sums and are not therefore equal to the sums of the separate estimates of attributable fraction, deaths and registrations for each agent. The difference is especially notable where the constituent AFs are large.

4.3 EXPOSURES BY INDUSTRY/JOB

Table 16 shows for industry categories from CAREX and job categories from LFS, attributable registrations in 2004 and attributable deaths in 2005 by agent.

Table 16 Industry/occupation codes by agent

Agent	Industry	Number Ever Exposed over REP (Men)	Number Ever Exposed over REP (Women)	Attributable Registrations (Men) (2004)	Attributable Deaths (Men) (2005)	Attributable Registrations (Women) (2004)	Attributable Deaths (Women) (2005)	Attributable Registrations (Total) (2004)	Attributable Deaths (Total) (2005)
Formaldehyde	Manufacture of wearing apparel, except footwear	66141	36327	0	0	0	0	1	0
Formaldehyde	**Total**	**342048**	**182153**	**1**	**0**	**0**	**0**	**1**	**0**
Wood dust	Manufacture of wood and wood and cork products, except furniture	205608	112925	2	1	0	0	2	1
Wood dust	Manufacture of furniture and fixture, except primary of metal	3462806	190185	3	1	1	0	4	2
Wood dust	Construction	1025129	9148	8	4	0	0	8	4
Wood dust	**Total**	**1,744,690**	**404,352**	**13**	**7**	**1**	**1**	**14**	**7**

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6 STATISTICAL APPENDIX

Formulae used in the estimation of AF

Levin's equation

$$AF = Pr(E)*(RR-1)/\{1+Pr(E)*(RR-1)\} \quad (1)$$

where RR = relative risk, Pr(E) = proportion of the population exposed

A common denominator is used across exposure levels and industries for each exposure

Miettinen's equation

$$AF = Pr(E|D)*(RR-1)/RR \quad (2)$$

where Pr(E|D) = proportion of cases exposed (E = exposed, D = case)

Turnover equation to estimate numbers ever employed during the REP

$$N_{e(REP)} = \sum_{i=a}^{i=b} l_{(adj15)i} * n_0/(R-15)\} + \sum_{k=0}^{k=(age(u)-age(l))} \sum_{j=c+k}^{j=d+k} \{l_{(adj15)j} * n_0 * TO /(age(u)-age(l)+1)\} \quad (3)$$

where $N_{e(REP)}$ = numbers ever employed in the REP

n_0 = numbers employed in the exposed job/industry at a mid-point in the REP

TO = staff turnover per year

R = retirement age (65 for men, 60 for women)

$l_{(adj15)i}$ = the proportion of survivors to age i of those alive at age 15 (from GB life tables)

a to b = age range achieved by the original cohort members by the target year (2004) (e.g. 65 to 100 for the solid tumour REP)

c to d = age range achieved by the turnover recruited cohort members by the target year (25 to 64 for the solid tumour REP)

age(u) and age(l) = upper and lower recruitment age limits (24 and 15)

The derivation and assumptions underlying this formula are described in the methodology technical report, available on the HSE website. The equation can be represented as a single factor acting as a multiplier for n_0, calculated by setting n_0 to 1 in the above equation, so that the factor varies only with TO see Table A1 below.

Equation to estimate the proportion of the population exposed

$$Pr(E) = N_{e(REP)} / N_{p(REP)} \quad (4)$$

where $N_{p(REP)}$ = numbers ever of working age during the REP from population estimates for the relevant age cohorts in the target year

Equation for combining AFs where exposed populations overlap but are independent and risk estimates are assumed to be multiplicative:

$$AF_{overall} = 1- \Pi_k(1-AF_k) \text{ for the k exposures in the set} \quad (5)$$

Table A1 Employment level adjustment and turnover factors used in the calculation of AF

		Main Industry Sector	Adjustment factor for change in employment levels*	Turnover per year
Men	A-B	Agriculture, hunting and forestry; fishing	1	7%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.4	9%
	F	Construction	1	12%
	G-Q	Service industries	0.9	11%
		Total	1	10%
Women	A-B	Agriculture, hunting and forestry; fishing	0.75	10%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.5	14%
	F	Construction	0.67	15%
	G-Q	Service industries	0.8	15%
		Total	0.9	14%

* Applied to CAREX data for the solid tumour REP only. Exposed numbers are obtained for a mid-point year in the REP where national employment data sources have been used (the LFS or CoE).

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The burden of occupational cancer in Great Britain

Nasopharynx/Pharynx

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for cancer of the nasopharynx that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) attributable fractions, deaths and registrations for nasopharyngeal cancer related to overall occupational exposure is 8.03% (95% Confidence Interval (CI)= 1.78-34.33), which equates to 8 (95%CI= 2-33) attributable deaths and 15 (95%CI= 3-65) attributable registrations.

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