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The burden of occupational cancer in Great Britain

Oesophageal cancer

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

RR929
Research Report

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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 oesophagus that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for oesophageal cancer associated with overall occupational exposure is 2.54% (95% Confidence Interval (CI)= 1.07-5.58), which equates to 184 (95%CI=78-429) attributable deaths and 188 (95%CI=80-439) attributable registrations.

This report and the work it describes were funded by the Health and Safety Executive (HSE). Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

HSE Books

First published 2012

ACKNOWLEDGEMENTS

Funding was obtained from the Health and Safety Executive (HSE). Andrew Darnton from the HSE was responsible for the work on mesothelioma. The contributions to the project and advice received from many other HSE and Health and Safety Laboratory staff is gratefully acknowledged. Two workshops were held during the project bringing together experts from the UK and around the world. We would like to thank all those who participated and have continued to give advice and comment on the project. We would also like to thank Helen Pedersen and Gareth Evans for their help in editing and formatting the reports.

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 oesophagus that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

Soot has been classified by the IARC as a definite human carcinogen for oesophageal cancer and tetrachloroethylene has been classified by IARC as a probable human carcinogen. Soots are black particulate matter formed as by-products of incomplete combustion of organic (carbon-containing) materials and are known to contain various potentially carcinogenic substances, including arsenic, nickel and several polycyclic aromatic hydrocarbons such as benzo[a]pyrene. The highest occupational exposure to soot is likely to occur among chimney sweeps. Other occupational exposure may occur among heating unit personnel, insulators, firefighters, metallurgical workers, horticulturists and anyone who works where organic materials are burned. Occupational exposure to tetrachloroethylene occurs in the dry cleaning industry and during metal degreasing in manufacturing industries.

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 4750 total deaths in men aged 25+ and 2536 in women aged 25+ from oesophageal cancer; in 2004 there were 4837 total registrations for oesophageal cancer in men aged 25+ and 2661 in women aged 25+. Only a few women are chimney sweeps and an estimate was therefore not made.

The estimated total (male and female) attributable fraction (AF) for oesophageal cancer associated with occupational exposure is 2.54% (95% Confidence Interval (CI)=1.07-5.58), which equates to 184 (95%CI=78-429) attributable deaths and 188 (95%CI=80-439) attributable registrations. Results for individual carcinogenic agents for which the attributable fraction was determined are as follows:

The estimated total (males only) attributable fraction (AF) for oesophageal cancer associated with exposure to soot during occupation as a chimney sweep is 0.81% (95% CI=0.29-1.75). This equates to 59 attributable deaths (95% CI=21-128) and 60 attributable registrations (95% CI= 22-130) from oesophageal cancer.

The estimated total (male and female) attributable fraction for oesophageal cancer associated with occupational exposure to tetrachloroethylene is 1.74% (95% CI=0.41-5.05). This equates to 126 (95% CI=30-368) attributable deaths and 130 (95%=CI 31-377) attributable registrations of oesophageal cancer.

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1 INCIDENCE AND TRENDS

Cancer of the oesophagus (ICD-10 C15; ICD-9 150) is the eighth most common cancer worldwide, with an estimated 462,000 new cases (4.2% of the world total) in 2002 (Parkin *et al,* 2005). It is also the sixth most common cause of death from cancer with 386,000 deaths (5.7% of the world total) in 2002. In most parts of the world the condition is relatively uncommon. However, for the area termed the Asian 'oesophageal cancer belt', which stretches from northern Iran through southern Russia to northern China, south-eastern Africa and areas of western Europe, this profile alters, resulting in these areas having the highest reported incidence rates worldwide.

Squamous cell carcinomas mostly occur in the middle third of the oesophagus whereas the majority of adenocarcinomas arise in the lower third (Blot *et al,* 2006). However, similarities in the risk of adenocarcinoma of the middle and lower thirds of the oesophagus have been observed (Wood *et al,* 2001). Tobacco smoking is causally associated with the condition; typically an increase of risk is associated with high numbers of cigarettes smoked and a long duration. However, in England and Wales, recent trends indicate that even though tobacco smoking has reduced, the incidence of this cancer has risen. Alcohol consumption and the subsequent multiplicative relationship with smoking, has been suggested as an explanation for this trend.

In males about 40% of oesophageal cancers are adenocarcinomas, and squamous cell carcinomas account for approximately 20%. This pattern is reversed in females (20% adenocarcinomas and 40% squamous cell carcinomas). In both males and females the remaining 40% are due to unspecified carcinomas (Wood *et al,* 2005).

In the UK and Ireland in the 1990s, oesophageal cancer accounted for around 1 in 40 diagnosed cancer cases, with males being more than twice as likely to be diagnosed than females, and 1 in 25 cancer deaths. Overall, the age-standardised incidence rates were 13 per 100,000 for males and 5.9 per 100,000 for females, and the age-standardised mortality rates were 12.8 per 100,000 for males and 5.3 per 100,000 for females (Wood *et al,* 2005).

Currently the condition is the ninth most common cancer in the UK, and is responsible for around 5% of all cancer deaths. In Great Britain, the total numbers diagnosed (new cases) steadily increased from 6,668 in 1995 to 7,499 in 2004 (Table 1). This increase was only evident among men (approximately from 4,000 to 5,000 cases per year), the incidence in women tended to be stable at around 2,700 cases per year. On average between 1995 and 2004, 7,109 patients (4,369 men and 2,740 women) were diagnosed with oesophageal cancer in Great Britain. Males appear to have the highest annual crude rate, which is increasing in England and is currently in excess of 16 per 100,000.

Table 1 Number of oesophageal cancer registrations in England, Wales and Scotland for 1995-2004.

Year	Men			Women		
	England	**Wales**	**Scotland**	**England**	**Wales**	**Scotland**
1995	3276 (13.6)	224 (16.0)	452 (17.1)	2221 (8.9)	160 (10.8)	335 (8.4)
1996	3320 (13.8)	203 (14.5)	484 (18.5)	2156 (8.6)	184 (12.4)	353 (8.7)
1997	3456 (14.3)	247 (17.7)	436 (16.6)	2216 (8.9)	175 (11.8)	319 (7.9)
1998	3444 (14.1)	236 (16.8)	477 (17.7)	2286 (9.1)	168 (11.3)	291 (7.2)
1999	3538 (14.4)	229 (16.3)	459 (16.9)	2355 (9.3)	166 (11.1)	331 (8.2)
2000	3700 (15.5)	264 (18.8)	454 (16.6)	2333 (9.3)	186 (12.4)	294 (7.0)
2001	3806 (15.8)	297 (21.2)	485 (17.4)	2274 (9.0)	165 (11.0)	299 (6.9)
2002	3861 (15.9)	253 (17.9)	518 (18.3)	2224 (8.8)	188 (12.5)	314 (7.4)
2003	3951 (16.2)	274 (19.2)	507 (17.7)	2279 (9.0)	159 (10.5)	300 (6.9)
2004	4047 (16.5)	254 (17.7)	536 (18.4)	2171 (8.5)	155 (10.2)	336 (7.9)
Average	**3640 (15.0)**	**248 (17.6)**	**481 (17.5)**	**2252 (8.9)**	**171 (11.4)**	**317 (7.7)**

Source: ONS MB1 Series (ONS 2007a), Welsh Cancer Intelligence and Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008). Numbers in brackets are crude rates per 100,000

The numbers that die from the condition consistently increased from 6,816 in 1999 to 7,288 in 2005 (Table 2). On average over this period 7,018 patients (4,456 men and 2,570 women) die from oesophageal cancer in Great Britain and similar rates are observed for England/Wales and Scotland. Like incidence, the numbers dying is increasing in males and remaining stable for females. The crude rates for males appear to be relatively stable (around 135 per 1,000,000 in England/Wales and 17 per 100,000 in Scotland). In contrast, the crude rates for females are steadily decreasing (from 85 to 48 per 1,000,000 in England/Wales and from 8.0 to 6.8 in Scotland). The annual mortality rates for men are consistently twice those for women. Oesophageal cancer is commonly a disease of the elderly, and cases are rare below the age of 50 (Cancer Research UK 2007). In 2004, incidence (and mortality) peaked between 70 and 80 years of age for males and over 85 years of age for females.

Table 2 Number of oesophageal cancer deaths in England, Wales and Scotland 1999-2005.

Year	Men		Women	
	England and Wales	**Scotland**	**England and Wales**	**Scotland**
1999	3730 (138)	443 (16.3)	2310 (85)	333 (8.0)
2000	3782 (137)	427 (15.5)	2279 (84)	281 (6.5)
2001	3898 (140)	472 (17.0)	2209 (81)	280 (6.2)
2002	4001 (143)	462 (16.1)	2329 (85)	301 (6.9)
2003	4142 (134)	501 (17.3)	2285 (50)	275 (6.0)
2004	4071 (129)	511 (17.2)	2227 (48)	290 (6.5)
2005	4257 (132)	495 (16.5)	2233 (48)	303 (6.8)
Average	**3983 (136)**	**473 (16.6)**	**2267 (69)**	**295 (6.7)**

Source: ONS DH2 Series (ONS 2007b), Welsh Cancer Intelligence and Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008). Numbers in brackets are crude rates per 1,000,000 for England/Wales and per 100,000 for Scotland

For patients diagnosed with this cancer in 2000-2001 in England and Wales, the population-based five-year relative survival rate was extremely poor at about 8%, with corresponding one-year survival rates of 30% for males and 27% for females; these low rates result in the time trends for mortality closely following the time trends for incidence (Cancer Research UK 2007). The low survival rates can be related to the late stages at which the cancer is typically diagnosed (Blot *et al*, 2006). In 2004, cancer mortality to incidence ratios for cancer of the oesophagus was 0.95 for both men and women (ONS 2006).

2 OVERVIEW OF AETIOLOGY

The two main histological types of oesophageal cancer have distinct aetiologies. However, tobacco smoking has been shown to be a potential risk factor for both. The elevated relative risks due to smoking for adenocarcinoma are not as high as those for squamous cell carcinoma. The link between tobacco smoking and alcohol intake has been observed to be primarily associated with squamous cell carcinoma (IARC 2004). Ethanol and acetaldehyde, commonly found in alcoholic beverages have been suggested as the underlying reason for the increase in cancer risk. Other non-occupational risk factors for squamous cell carcinoma and adenocarcinoma include low consumption of fresh fruit and vegetables, consumption of exceptionally hot drinks and obesity. A significant relationship with obesity has been observed only for adenocarcinoma (Blot *et al,* 2006).

Epidemiological studies have consistently reported elevated risks associated with oesophageal cancer and smoking. In most of the studies the risk for all types of oesophageal cancer increased with numbers of cigarettes smoked daily and the duration of smoking. However, the studies also showed the risk remains elevated after cessation of smoking (IARC 2004). Several retrospective cohort studies and case-control studies showed increased risks associated with alcohol consumption. Some studies found increased relative risks with level of intake of alcoholic beverages. These increased risks were found to persist after tobacco smoking was taken into account (IARC 1988). In Europe and North America over 90% of cases can be attributed to tobacco and alcohol (Parkin *et al,* 2005). Smoking for over 35 years and heavy alcohol consumption is associated with ORs of 8.8 and 3.1 respectively for squamous cell carcinoma and ORs of 2 and 0.6 respectively for adenocarcinoma (Cancer Research UK 2007). The combined effect of heavy smoking and alcohol consumption gave ORs of 23.1 for squamous cell carcinoma and 2.3 for adenocarcinoma, however odds ratios as high as 50 and 130 have been reported. In terms of the combined amount (in grams) smoked and drunk per day, relative risks could vary from 3.2 up to 155.6 (Blot *et al,* 2006). Therefore, tobacco and alcohol consumption must be taken into account, if possible, when assessing the associations between oesophageal cancer and occupational exposures.

The Occupational Health Decennial Supplement examined mortality (1979-1980, 1982-1990) and cancer incidence (1981-1987) in men and women aged 20-74 years in England (Drever 1995). For oesophageal cancer it was observed that the risk was greatest in mains and service layers, and electrical plant operators for males, and butchers and clergy staff for women, which was reflected by the elevated PRRs and PMRs (Table 3). Exposure to occupational soot has also been shown to cause this condition and again PRRs and PMRs were elevated in fire service personnel, masons and builders. Other exposures that have been shown to be associated include chlorinated hydrocarbons such as tetrachloroethylene and trichloroethylene, radiation and possibly asbestos (Blot *et al,* 2006, Siemiatycki *et al,* 2004).

Table 3 Job codes with significantly high PRRs and PMRs for cancer of the oesophagus. Men and women aged 20-74 years, England.

Job Group		Registrations	PRR	95% CI	Deaths	PMR	95% CI
SIC code	Description	(1981 – 1987)			(1979 – 1980 and 1982 – 1990)		
Men							
045	Publicans and bar staff				261	116	102-131
049	Police				129	150	125-178
050	Fire service personnel				46	135	99-180
108	Woodworking machinists	24	165	106-246			
138	Electrical plant operators				52	161	120-211
148	Scaffolders	14	187	102-314			
150	Riggers				38	177	125-243
166	Masons and stonecutters				40	145	103-197
169	Builders				298	114	102-128
171	Road construction workers and paviors				77	132	104-165
173	Mains and service layers	16	194	111-317			
182	Bus and coach drivers	59	132	101-171	166	118	101-138
Women							
014	Clergy				16	187	107-303
024	Literary and artistic occupations				31	146	99-208
042	Butchers	5	402	131-940			
057	Sales representatives	9	228	104-434			
091	Other occupations – glass and ceramics				15	182	102-300

Source: Drever *et al.* (1995) Occupational Health Decennial Supplement

The recent Occupational Health Decennial Supplement examined mortality for the period 1991-2000 in men and women aged 20-74 years in England (Table 4) (Coggon *et al*, 2009). For oesophageal cancer it was observed that the risk was greatest in petrol pump forecourt attendants and government inspectors for males, and bookbinders for females. In comparison to the previous supplement, police and fire service personnel are the only occupations that re-appear, with a lower PMR in police and a higher PMR in fire service personnel.

Table 4 Job codes with significantly high PMRs for cancer of the oesophagus. Men and women aged 20-74 years, England.

Job Group		Deaths	Expected deaths	PMR	Lower 95% CI	Upper 95% CI
SIC code	Description	1991 - 2000				
Men						
007	Government Inspectors	43	26.1	164.9	119.4	222.2
047	Farmers	772	709.9	108.7	101.2	116.7
049	Police	166	136.4	121.7	103.9	141.7
050	Fire Service Personnel	73	48.6	150.4	117.9	189.0
055	Petrol Pump Forecourt Attendants	15	8.2	183.8	102.9	303.2
062	Ambulance Staff	54	35.3	153.1	115.0	199.7
065	Forestry Workers	30	18.5	162.2	109.4	231.5
137	Electricians, Electrical Maintenance Fitters	371	332.9	111.4	100.4	123.4
139	Telephone Fitters	93	67.2	138.5	111.8	169.6
165	Bricklayers, Masons	243	212.2	114.5	100.6	129.9
192	Refuse and Salvage Collectors	79	62.4	126.6	100.2	157.8
Women						
010	Teachers in Higher Education	30	19.1	157.0	106	224.1
080	Bookbinders	17	7.6	224.2	131	358.9

Source: Coggon *et* al. (2009) Occupational mortality in England and Wales, 1991-2000

IARC have assessed the carcinogenicity of a number of chemicals and those classified as causing oesophageal cancer (Group 1), or possibly causing oesophageal cancer (Group 2A), are given in Table 5. From the information included in the IARC assessments Siemiatycki *et al.* (2004) further classified the evidence as strong or suggestive, which can also be found in Table 5. There is suggestive evidence that exposures to soot and tetrachloroethylene are associated with an increased risk of work-related oesophageal cancer.

Table 5 Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1-77 (IARC, 1972-2001), into Groups 1 and 2A, which have the oesophagus as the target organ.

Agents, Mixture, Circumstance	Main industry, Use	Evidence of carcinogenicity in humans*	Strength of evidence[$]	Other target organs
Group 1: Carcinogenic to Humans				
Agents and **groups of agents**				
Soots	Chimney sweeps; heating unit service personnel; brick masons and helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials	Sufficient	Suggestive	Skin Lung
Exposure circumstances				
None identified				
Group 2A: Probably Carcinogenic to Humans				
Agents and **groups of agents**				
Tetrachloroethylene	Production; dry cleaning; metal degreasing	Limited	Suggestive	NHL Cervix
Exposure circumstances				
None identified				

* Evidence according to the IARC monograph evaluation; [$] taken from Siemiatycki *et al.* (2004)

2.1 EXPOSURES

2.1.1 Soots

Soots are black particulate matter formed as by-products of incomplete combustion of organic (carbon-containing) materials, such as coal, wood, fuel oil, waste oil, paper, plastics and household refuse. Soots are known to contain various potentially carcinogenic substances, including arsenic, nickel and several polycyclic aromatic hydrocarbons (PAHs) such as benzo[a]pyrene.

The highest occupational exposure to soot is likely to occur among chimney sweeps. Other occupational exposure may occur among heating unit personnel, insulators, firefighters, metallurgical workers, horticulturists and anyone who works where organic materials are burned. Exposure from soot can be by inhalation, ingestion or skin contact; with respect to oesophageal cancer exposure via inhalation and ingestion is most likely.

Various soots and extracts, namely coal-soot, wood-soot and oil-shale, have been tested for carcinogenity in experimental animals. Coal-soot extract and oil-shale extract yielded sufficient evidence for carcinogenity. However, limited evidence was found from dermal implanted wood soot and whole body exposure to coal-soot. In terms of human data, a study revealed statistically significant excess mortality from oesophageal cancer among chimney sweeps. This led to soots being classified, by IARC, as a group 1 carcinogen for humans in 1985 (IARC 1985).

Beaumont *et al.* (1991) conducted an epidemiologic study of mortality among 3,066 firefighters from San Francisco employed between 1940 and 1970 that had been employed for at least 3 years. They followed up the cohort to 1982, and discovered significant excess for number of deaths from oesophageal cancer, compared to the general US population. The risk ratio was standardised for age, year, gender and race, giving an RR of 2.04 (95% CI=1.05-3.57, n=12). Time since first

employment was elevated for all year categories although not significantly (3-19years: RR=5.22, n=2, 20-29years: RR=1.41, n=2, 30-39years: RR=2.34, n=5 and 40+years: RR=1.55, n=3), as was length of employment (10-19years: RR=3.47, n=2, 20-29years: RR=2.10, n=6 and 30+years: RR=1.82, n=4). However, firefighters can be exposed to various substances, such as silica and asbestos, not solely soots, and confounding from alcohol consumption and subsequent interactions were not taken into account.

A meta-analysis of cancer risk among firefighters obtained a non-significant elevated summary risk estimate for oesophageal cancer of 1.16 (95% CI=0.86-1.57) (LeMasters *et al,* 2006). Various comparison groups were used in the studies, including internal, the local general population and the national general population. Of the eight studies included for evaluating oesophageal cancer risk, only one study reported significant estimates (Beaumont *et al,* 1991). Four were mortality studies with SMR results giving a meta-RR of 0.68 (95% CI=0.39-1.08), one study gave a mortality RR of 2.03 (95% CI=1.05-3.57), two incidence studies gave meta-SIR of 1.32 (95% CI=0.63-2.42) and one case-control mortality study gave an OR=0.90 (95% CI=0.70-1.30).

Evanoff *et al.* (1993) conducted an extended follow-up study amongst a cohort of 5,542 Swedish chimney sweeps involved in the trade union from 1918 to 1980. Two studies on the group were conducted: a mortality study covering the period 1951–1990 consisting of 5,313 workers, and a cancer incidence study covering the period 1958–1987 consisting of 5,242 workers. National rates for mortality and cancer incidence were used for comparison. After adjusting estimates for smoking and alcohol intake they found a significant increase in both incidence and mortality, SIR = 387 (95% CI=193-693, n=11) and SMR=386 (95% CI=200-675, n=12) respectively. In addition, a positive association between duration of employment and oesophageal cancer was discovered, with a significant estimate for over 30 years in active employment (SMR=674, n=6, $p<0.05$). When investigating latency (years since first exposure) a significant estimate was obtained for exposures in excess of 30 years (SMR=393, n=11, $p<0.05$). The authors conclude that the alcohol and tobacco consumption habits of the chimney sweeps cannot explain the excesses observed. Thus, the study supports a causal role for exposure to chimney soot.

Gustavsson *et al.* (1993) conducted a mortality study investigating increased risk of oesophageal cancer in relation to exposure to combustion products. Using the same chimney sweep cohort as Evanoff (n=5,542), along with three other cohorts (Waste incinerator workers (n=176), gas workers (n=296) and bus garage workers (n=695)), they discovered an overall SMR of 289 (95% CI=174-452, n=19). Two reference populations were used: Swedish males for the chimney sweeps and Stockholm males for the other three cohorts. However, evaluating the cohorts individually revealed the only statistically significant increase of oesophageal cancer was among the chimney sweeps (SMR=386, 95% CI=199-674, n=12), which could not be solely attributed to other known risk factors, such as smoking habits and alcohol consumption. The authors conclude that it is likely that occupational exposure to combustion products is associated with an increased risk of oesophageal cancer.

A mortality study was conducted by Salg and Alterman (2005), consisting of members of the International Union of Bricklayers and Allied Craftworkers (IUBAC). The study considered 10,386 members of the IUBAC who died in the period 1986-1991. The proportionate mortality experience of the US population was used for comparison. The mortality estimates were adjusted for age and race, revealing an increased risk of oesophageal cancer among white men, with an associated Proportional Mortality Ratio (PMR) of 134 (95% CI=106-167, n=77, $p<0.05$). Non-white men had a non-significant lower risk (PMR=78, 95% CI=25-181, n=5). No combined estimate for all males was published.

2.1.2 Tetrachloroethylene

Tetrachloroethylene, also known as perchloroethylene (PCE) or 'perc', is a non-flammable, colourless and volatile liquid with an ether-like odour. PCE is a manufactured chemical compound that is primarily used as a cleaning solvent instead of water for the dry cleaning of fabrics, metal degreasing in automotive and metalworking industries, and as a chemical precursor for fluorocarbons. In addition the compound is also used as an insulating fluid and cooling gas in electrical transformers, in the manufacture of rubber solutions, paint removers and printing inks.

The highest occupational exposure to PCE is likely to occur among dry cleaning and metal degreasing workers. Other occupational exposure may occur among workers involved in fluorocarbon production. Exposure from PCE is most likely by inhalation or ingestion but exposure via skin contact may occur.

PCE has been shown to be carcinogenic in experimental animals and possibly carcinogenic to humans (Group 2A), following two cohort studies that reported an elevated risk of oesophageal cancer after exposure (IARC 1995).

Ruder reported an update in 1994, on a study conducted in 1987 by Brown and Kaplan. The study consisted of 1,708 dry cleaners that were primarily exposed to PCE for at least one year in the period 1940-1960. Individuals were chosen from union records for four areas (California, Michigan, Illinois and New York), and classified as using only PCE (PCE only) or as using other substances as well (PCE plus). In the update, the cohort was followed to 1990. After adjusting for age, gender, race and calendar period, there was a statistically significant excess risk for cancer of the oesophagus with SMR=2.1 (95% CI=1.0-3.9, n=10), along with elevated mortality rates for the PCE only sub-group (SMR=2.6, n=4), and in workers with a duration of employment over 5 years, and with latency (time from first employment) of 20 or more years, with resulting SMR=5.4 (n=8) (Weiss 1995). Ruder *et al.* (2001) subsequently extended the study to 1996, with a continuation of the statistically significant excess. Three mortality rates, with different reference populations, were produced for the entire study period (1940-1996). National rates were used that cover the whole period, in the main analysis, giving a significant SMR of 2.47 (95% CI=1.35-4.14, $p<0.01$, n=14) for cancer of the oesophagus. Additional analyses were conducted for the four geographic sub cohorts using county rates (termed local rates) and national rates (termed US rates) for 1960-1996, again resulting in significant SMR estimates of 2.23 (95% CI=1.22-3.80, $p<0.05$, n=14) and 2.75 (95% CI=1.50-4.61, $p<0.01$, n=14) using local and US rates respectively. The results that follow all use national rates for 1940-1996. Statistically significant excess risks were also found for over 5 years duration of employment accompanied with over 20 years latency (SMR=5.03, 95% CI=2.41-9.47, n=10) and for the PCE plus sub-group (SMR=2.40, 95% CI=1.10-4.56, n=9). Elevated mortality estimates were discovered in all gender-race categories (non-white female: SMR=2.82, 95% CI=0.8-7.2, n=4, non-white male: SMR=1.92, 95% CI=0.6-4.5, n=5, white female: SMR=3.42, 95% CI=0.4-12.4, n=2, white male: SMR=2.68, 95% CI=0.6-7.8, n=3) and in the PCE only sub-group (SMR=2.65, 95% CI=0.85-6.20, n=5). With the extended follow-up period, Ruder was able to suggest that there was an association between oesophageal cancer and lengthy PCE exposure. Unfortunately, there was no data available on potential confounders. However, the authors noted that the magnitude of the results were greater than could be explained by smoking alone.

In 1990, Blair *et al.* conducted two analyses on a cohort of 5,365 dry cleaners who were employed for at least 1 year between 1945 and 1978, with a follow-up period from 1948 to 1978. The first analysis included all dry cleaning workers and the second included only those employed after 1960. Members of the cohort were identified by union records and were included for analysis if their age, gender and race were known. Each worker was assigned an exposure status according to the job(s) they held; results of the first analysis were reported by Weiss (1995). US mortality rates were used

for the external analysis and an internal group was used for cumulative exposure comparison. After adjusting risk estimates for the pre mentioned demographics, there was a statistically significant excess mortality risk with SMR=2.1 (95% CI=1.1-3.6, n=13), together with an elevated mortality rate in workers with the highest cumulative exposure (SMR=2.8). Blair *et al.* (2003) reported results on an extension of this study to 1993, which included four more individuals than the earlier study, due to demographic information being available. Again, the general US population was used for reference. In the second study period (1979-1993) there continued to be a significant excess mortality risk, SMR=2.4 (95% CI=1.3-4.1, n=13). The two study periods resulted in a combined estimate for the whole study period being statistically significant with SMR=2.2 (95% CI=1.5-3.3, n=26). Elevated risks were found in three of the gender-race sub cohorts (white male, non-white male and white female), but the excess was found to be only significant in the non-white male sub-cohort (SMR=3.1, 95% CI=1.9-5.0, n=18). On investigating exposure levels between two groups (little or no exposure and medium or high exposure) there was little difference between the estimates, SMR=2.1 (95% CI=0.9-4.4, n=7) and SMR=2.2 (95% CI=1.2-3.5, n=16) respectively. For the second analysis, Blair considered the date individuals joined the union, based on the assumption that individuals who joined after 1960 were more likely to be exposed to PCE; again there was little difference between the estimates, SMR=2.2 for joining before 1960 and SMR=2.3 for joining after 1960. Tobacco usage was not taken into account in this study but the authors conclude that confounding by smoking is unlikely to fully explain the observed two-fold excess.

A study of cancer incidence and work in dry cleaning, showed a strong association between employment in dry cleaning and oesophageal squamous cell carcinomas, particularly after adjustment for cigarette and alcohol intake (Vaughan *et al*, 1997). From two population based case-control studies conducted between September 1983 and November 1990, 1,130 cancer cases (404 oesophageal), aged between 20 and 74 years, and 724 matched (on age and gender) controls, were identified. From each subjects decade of work the probability of exposure to tetrachloroethylene was estimated as “unlikely” (before 1940), “medium” (1940-1959) or “high” (1960-1989). For squamous cell carcinoma a crude estimate of the risk of exposure was RR=1.7 (95% CI=0.2-8.5), whereas after adjusting for other risk factors, including smoking and alcohol consumption, the estimate increased to 3.6 (95% CI=0.5-27.0, n=2). After adjustment for potential confounders, elevated risk estimates were found for duration employed (1-9 years, OR=4.6, 95% CI=0.5-39.4, n=2) and probable exposure level (“medium” and “high”, OR=3.6, 95% CI=0.5-27, n=2, and “high”, OR=6.4, 95% CI=0.6-68.9, n=2). In addition borderline significance was found for cumulative exposure based on job title (1-29 ppm-y), OR=11.9 (95% CI=1.1-124, n=2). For adenocarcinoma (n=2) none of the estimates were significantly elevated. These results are based on only 4 exposed cases and should be carefully interpreted. However, the authors note that results of other studies that are unable to take account of potential confounding may actually underestimate the risk between occupational exposure and oesophageal cancer.

In a study investigating cancer mortality among 8,163 laundry and dry cleaning workers from the NOMS system, Walker *et al.* (1997) found a significant increase in mortality risk amongst black men aged 15-64 years (PMR=215, 95% CI=111-376 and PCMR=168, 95% CI=87-294, n=12), and an elevated risk in women aged 15-64 (black women: PMR=184, 95% CI=84-349, PCMR=164, 95% CI=75-311, n=9; white women: PMR=189, 95% CI=51-483, PCMR=205, 95% CI=56-526, n=4). All other occupations in the NOMS system were used for comparison. There were also elevated mortality risks for the same gender-race sub-cohorts in the over 65 years of age group (black men: PMR=140, 95% CI=45-326, PCMR=134, 95% CI=44-314, n=5; black women: PMR=148, 95% CI=60-305, PCMR=140, 95% CI=56-289, n=7; white women: PMR=106, 95% CI=43-218, PCMR=126, 95% CI=51-259, n=7). Although there was no information on smoking or alcohol use, length of employment or possible exposure, his findings support other evidence that there is an excess risk of oesophageal cancer amongst laundry and dry cleaning workers.

A recently published case-control study of cancer in 46,768 dry cleaning workers in the Nordic countries was conducted during the period when PCE was the dominant solvent (Lynge *et al*, 2006). The cohort consisted of all laundry and dry cleaning workers from Denmark, Finland, Norway and Sweden contained in the 1970 censuses. Follow-up started in 1970/1971 and concluded in the period 1997-2001. For each of the seventy-two oesophageal cancer cases, six controls were matched by country, gender, age and calendar period from the whole cohort. Exposure status was defined by job(s) held and the duration of employment (at the place of work in 1970). Unfortunately some individuals could not be correctly classified as dry cleaners or laundry workers. Using laundry workers (as they were assumed to be unexposed) as a reference group gave non-significant RRs of 0.76 (95% CI=0.34-1.69, n=8), 1.22 (95% CI=0.41-3.63, n=5) and 2.04 (95% CI=0.91-4.62, n=18) for "dry cleaners", "others in dry cleaning" and "unclassifiable", respectively. Combining Denmark and Norway only (these two countries had no unclassifiable oesophageal cancer cases) again gave non-significant RRs of 0.91 (95% CI=0.38-2.20, n=7) and 0.66 (95% CI=0.14-3.01, n=2) for "dry cleaners" and "others in dry cleaning", respectively. There was one estimate that was elevated for length of employment, corresponding to working as a dry cleaner for 2-4 years (RR=1.20, 95% CI=0.14-10.41, n=1). However, the estimates for longer lengths of employment showed no increased risk. In this study information on smoking and alcohol consumption were obtained for Norway and Sweden but no separate risk estimates were carried out. The authors concluded that the use of PCE was not associated with an increased risk of oesophageal cancer, but the results were hampered by unclassifiable cases and the potential differences in exposure levels compared to the US studies.

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 oesophagus are those outlined in Table 6.

Table 6 Substances considered in the estimation of the attributable fraction for cancer of the oesophagus

Agents, Mixture, Circumstance	AF calculation	Strength of evidence	Comments
Group 1: Carcinogenic to Humans			
Agents, groups of agents			
Soots	Yes	Suggestive	Only chimney sweeps exposed
Exposure circumstances			
None identified			
Group 2A: Probably Carcinogenic to Humans			
Agents and **groups of agents**			
Tetrachloroethylene	Yes	Suggestive	Primarily studies on dry cleaners
Exposure circumstances			
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 counted using 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 is 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 cancer of the oesophagus in GB in 2005 = 4750 for men (4255 England and Wales and 495 Scotland), 2536 for women (2233 England and Wales and 303 Scotland).
- Total registrations from cancer of the oesophagus in GB in 2004 = 4837 for men (4047 England, 254 Wales and 536 Scotland), 2661 for women (2170 England, 155 Wales and 336 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 SOOTS

(a) Risk Estimate:

With the exception of studies of chimney sweeps, the effects of exposure to soot are not directly evaluated in many epidemiological studies. Soot exposure may be included as part of an evaluation of polycyclic aromatic hydrocarbon (PAH) exposure or may be just one of many possible concurrent exposures, for example, to firefighters. In the evaluation of the burden of occupationally related lung cancer, soots were included with PAHs. IARC (1985) report that exposure to chimney sweep soots is related to excess mortality. Within the lung cancer report, a review and meta-analysis (Armstrong *et al*, 2004) identified two cohort studies conducted on chimney sweeps that were likely to be exposed to soots, the first by Evanoff *et al*, (1993) and the second by Hansen (1983). Of these two, the study by Evanoff explicitly mentioned an elevated risk from oesophageal cancer, whereas the study by Hansen gave no mention of specific cancer sites. Although Siemiatycki *et al.* (2004) identified several occupations, other than chimney sweeps, that may be

exposed to soots, the studies investigated in this report do not explicitly mention soots as the predominant exposure (LeMasters *et al,* 2006, Beaumont *et al,* 1991, Salg and Alterman 2005). Thus no meaningful risk estimates can be calculated for these occupations, and the subsequent analysis will base calculations on numbers employed as chimney sweeps. The two remaining studies are conducted on the same chimney sweep cohort, with the Evanoff study giving more information about the cohort and analysis conducted (Evanoff *et al,* 1993, Gustavsson *et al,* 1993). Therefore this study was chosen as the best study for the statistical analysis, with incidence and mortality risk estimates of SIR=387 (95% CI=193-693) and SMR=386 (95% CI=200-675), respectively. The estimates reported by Evanoff were adjusted for both smoking and alcohol consumption. Percentages of current, former and non-smokers in ten-year age classes were available from a 1972 cohort of active chimney sweeps and from national smoking data for 1963 and 1977, from which national smoking habits were estimated for 1972. Risk ratios for smoking were also obtained and estimated from published studies. Smoking adjusted RRs were obtained by calculating the expected numbers of cases from national data and adjusting them to take into account the difference between smoking habits of chimney sweeps and the national population, producing an age specific RR which was subsequently weighted using the relative risks for smoking. Adjustments for alcohol consumption were done by using information on alcohol abuse collected from the National Psychiatric Discharge Registry for 1973-1983 (patients discharged with alcohol psychosis or alcoholism). An expected number of stays in hospital due to alcohol abuse was calculated with a background rate calculated from the national population. Observed stays by the chimney sweeps was divided by age-adjusted expected values from the general population to obtain a ratio that represents the RR of stays in hospital due to alcohol abuse among the sweeps compared to the general population.

The chosen study conducted a cancer incidence and mortality study on 5,542 Swedish chimney sweeps involved in the trade union from 1918 to 1980 (Evanoff *et al,* 1993). National rates for mortality and cancer incidence from Statistics Sweden and the National Cancer Registry were used for comparison. Years of active work as a chimney sweep (until 1980) were used as a measure of cumulative exposure. The incidence study covered the period 1958-1987 and included 5,242 chimney sweeps. The mortality study covered the period 1951-1990 and included 5,313 chimney sweeps. The estimates produced were adjusted for potential confounding from alcohol intake and smoking.

(b) Numbers Exposed:

There are estimated to be approximately 2500 chimney sweeps in the UK in 2006 with 250 affiliated to a representative trade association (McAlinden 2006). Of these chimney sweeps it is expected that 99.5% (2,488) of them were male. According to the 2006 LFS data chimney sweeps were included under the SOC2000 classification 9232: Road Sweepers. In this classification 12,421 males were employed, with there being too few females in the occupation to report. The proportion of this category estimated to be chimney sweeps in 2006 is 2488/12421 = 0.20. Applying this proportion to the most relevant category in the 1979 LFS data: 72.2 cleaners, gave an estimated 20,246 male chimney sweeps employed/exposed to soots in 1979. Chimney sweeps are included under the main industry sector corresponding to service industries.

(a) AF Calculation:

The estimated total (males only) AF for oesophageal cancer attributable to work as a chimney sweep is 1.24% (95%CI=0.45-2.69). This equates to 59 attributable deaths (95%CI=21-128) and 60 attributable registrations (95%CI=22-130) (Table 7).

Table 7 Summary results for occupational exposure to soots

				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]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	Evanoff *et al.* (1993)	H	G-Q	3.87	20246	0.11	84585	0.0044	0.0124	0.0045	0.0269	59	21	128	60	22	130
		H	All		20246		84585	0.0044	0.0124	0.0045	0.0269	59	21	128	60	22	130
		All	All		20246		84585	0.0044	0.0124	0.0045	0.0269	59	21	128	60	22	130

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 TETRACHLOROETHYLENE

(a) Risk Estimate:

Tetrachloroethylene exposure has consistently been associated with an increased risk of oesophageal cancer (Blair *et al,* 2003, Ruder *et al,* 2001, Walker *et al,* 1997, Vaughan *et al,* 1997). For the purposes of the calculations that follow, the US study followed by Ruder *et al.* (2001) was chosen as the best study to base risk estimates on. The two population case-control studies were excluded due to the small numbers of exposed cases, and the study by Walker was considered inappropriate, as there was no overall mixed-race estimate given (Lynge *et al,* 2006, Walker *et al,* 1997, Vaughan *et al,* 1997). The two larger American studies had extended follow-up periods with larger numbers of exposed cases (Blair *et al,* 2003; Ruder *et al,* 2001). However, overall, the study by Ruder was chosen because this had the most recent follow-up (until 1996 vs 1993), involved good exposure assessment (from visiting the workplaces where possible), and excluded any individuals that had ever been exposed to carbon tetrachloride (the primary solvent used in dry cleaning until the 1950s). The corresponding risk estimate to be used is SMR=2.47 (95% CI=1.35-4.14) (This is similar to the risk estimate of 2.3 found by Blair *et al.* (2003) for workers joining after 1960 who were more likely to have been exposed to PCE). All the studies mentioned in this report relating to PCE are based on cohorts of dry cleaning and laundry workers. However, IARC (1995) state that workers in dry cleaning and degreasing are the most heavily exposed. Also, in a European Union report it is believed that metalworking is the second major industrial use of the chemical in the EU and UK (European Chemicals Bureau 2005). Therefore, the subsequent analysis will be based on all workers exposed to tetrachloroethylene, not just dry cleaners.

As stated previously, the highest occupational exposure to PCE is likely to occur among dry cleaning and metal degreasing workers, with lower exposures in other occupations and industries. However, two of the other studies did attempt this investigation (Table 8). Unfortunately, these studies provide little information on a dose-response mechanism, since the first shows very little difference between the two exposure categories and the second, is based on only four cases and does not combine the estimates for all oesophageal cancer. In addition, these studies present results on the “probability” of exposure to PCE not direct and explicit exposure.

The chosen study therefore is Ruder *et al,* (2001) who conducted a mortality study on 1,708 dry cleaners in the USA that were primarily exposed to PCE for at least one year in the period 1940-1960. The follow-up period was from 1940 through 1996. Exposed individuals were chosen from union records and national rates were used for comparison. Exposure was determined by workplace visits and each individual was subsequently classified as using only PCE (PCE only), or as using other substances as well (PCE plus). Any individuals that had ever used carbon tetrachloride were excluded from the study. The estimate of 2.47 (95%CI=1.35-4.14) was adjusted for age, gender, race and calendar period but not for smoking, although as noted in a similar study by Blair *et al.* (2003), confounding by smoking is unlikely to fully explain the two fold excess. This has been used for the higher category. An RR = 1.63 (95%CI=0.24-3.8 5) has been estimated for the low exposure level category. This was based on a harmonic mean of the high/low ratios across all other cancer-exposures pairs in the overall project for which data were available.

Table 8: Summary of Dose-Response Studies

Authors	Exposure	Number of Cases	Reference Category	Risk Estimate	Adjustment Factors
Blair *et al.* (2003)	Assigned to exposure category based on job title. **High**: Cleaners **Medium**: Pressers, Sewers, Counter workers **Little/No**: Pick-up point workers	7 Little/No Exposure 16 Medium/High Exposure	General USA Population	**Little/No** SMR=2.1 95% CI=0.9-4.4 **Medium/High** SMR=2.2 95% CI=1.2-3.5	Age Gender Calendar Time
Vaughan *et al.* (1997)	Assigned a probability for exposure to PCE based on decade of work. **High**: 1960-1989 **Medium**: 1940-1959 **Unlikely**: <1940 Medium and High probability further assigned a cumulative exposure from an 8-hr time weighted average exposure based on job title. (No estimates are given for individuals with unlikely exposure)	2 Squamous Cell Both High Probability of Exposure Both Cumulative Exposure of 1-29 ppm-y 2 Adenocarcinoma One High Probability of Exposure One Cumulative Exposure 1-29 ppm-y	Individuals Never Worked in Dry Cleaning	**Medium/High** OR=3.6 95% CI=0.5-27.0 **High** OR=6.4 95% CI=0.6-68.9 **1-29ppm-y** OR=11.9 95% CI=1.1-124 **Medium/High** OR=1.1 95% CI=0.2-5.7 **High** OR=0.9 95% CI=0.1-10.0 **1-29ppm-y** OR=2.0 95% CI=0.2-21.7 **30+ppm-y** OR=0.7 95% CI=0.1-6.8	Age Gender Education Study Period Alcohol Consumption Cigarette Smoking

(b) Numbers Exposed:

CAREX estimated about 120,000 workers were exposed to tetrachloroethylene in Great Britain between 1990 and 1993. Table 9 shows the numbers of workers exposed to tetrachloroethylene in the various industries. For the male/female split all are assumed to be ‘blue collar’ workers in SOC major groups 5, 8 and 9.

Table 9 Numbers of workers exposed to tetrachloroethylene; CAREX in 1990-1993.

Code	Industry		CAREX Data 1990-1993		
			Number Exposed	Number in Industry	Exposure Level
22	Crude petroleum and natural gas production		62	53300	L
311-2	Food manufacturing		2236	414150	L
313	Beverage industries		351	88100	L
314	Tobacco manufacture		24	9950	L
321	Manufacture of textiles		3182	182000	L
322	Manufacture of wearing apparel, except footwear		4127	189500	L
323	Manufacture of leather and products of leather or of its substitutes		114	16825	L
341	Manufacture of paper and paper products		2206	119050	L
342	Printing, publishing and allied industries		2826	354750	L
353	Petroleum refineries		4	18075	L
361	Manufacture of pottery, china and earthenware		30	54450	L
362	Manufacture of glass and glass products		230	43275	L
371	Iron and steel basic industries		942	48425	L
372	Non-ferrous metal basic industries		675	79325	L
381	Manufacture of fabricated metal products, except machinery and equipment		6002	292200	H
382	Manufacture of machinery except electrical		8566	692275	H
383	Manufacture of electrical machinery, apparatus, appliances and supplies		3238	473750	H
384	Manufacture of transport equipment		2626	456900	H
41	Electricity, gas and steam		3173	140975	L
42	Water works and supply		332	45175	L
5	Construction		15085	1753450	L
711	Land transport		5970	671050	L
712	Water transport		171	68175	L
713	Air transport		1325	95700	L
719	Services allied to transport		324	180725	L
72	Communication		340	459425	L
931	Education services		61	1455875	L
932	Research and scientific institutes		88	91100	L
95	Personal and household services		55165	686750	H
	TOTAL		**119475**	**9234700**	
	Main Industry Sector			% Male	
A-B	Agriculture, hunting and forestry; fishing	High	0		
		Low	0		
C-E	Mining/quarrying, electricity/gas/steam, manufacturing industry	High	20432	76%	
		Low	20514		
F	Construction	High	0	99%	
		Low	15085		
G-Q	Service industries	High	55165	65%	
		Low	8279		

(c) AF Calculation:

The estimated total (male and female) AF for oesophageal cancer (all attributable to exposure to tetrachloroethylene) is 1.74% (95%CI=0.41-5.05). This equates to 126 (95%CI=30-368) attributable deaths and 130 (95%CI=31-377) attributable registrations of oesophageal cancer. The estimated AF for men is 2.08% (95%CI=0.46-6.26) resulting in 99 (95%CI=- 22- 297) attributable deaths and 101 (95%CI=- 22-303) attributable registrations; for women the estimated AF is 1.09% (95%CI=- 0.32-2.78) resulting in 28 (95%CI=8-70) attributable deaths and 29 (95%CI=9-74) attributable registrations.

Table 10 Summary results for occupational exposure to tetrachloroethylene

				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	Ruder *et al.* (2001)	H	C-E	2.47	15528	1.4	0.09	75111	0.0039	0.0056	0.0016	0.0123	26	7	58	27	8	59
		H	G-Q	2.47	35857	0.9	0.11	134827	0.0069	0.0100	0.0028	0.0220	48	13	105	48	14	106
		H	All		51386			209938	0.0108	0.0156	0.0044	0.0343	74	21	163	75	21	166
		L	C-E	1.63	15591	1.4	0.09	75413	0.0039	0.0024	0.0000	0.0204	11	0	97	12	0	99
		L	F	1.63	14934	1	0.12	67791	0.0035	0.0022	0.0000	0.0184	10	0	87	10	0	89
		L	G-Q	1.63	5381	0.9	0.11	20234	0.0010	0.0006	0.0000	0.0055	3	0	26	3	0	26
		L	All		35906			163438	0.0084	0.0052	0.0000	0.0443	25	0	210	25	0	214
		All	All		87292			373376	0.0192	0.0208	0.0046	0.0626	99	22	297	101	22	303
Women	Ruder *et al.* (2001)	H	C-E	2.47	4904	1.5	0.14	41253	0.0020	0.0029	0.0008	0.0064	7	2	16	8	2	17
		H	G-Q	2.47	19308	0.8	0.15	92453	0.0044	0.0064	0.0018	0.0144	16	5	36	17	5	38
		H	All		24211			133706	0.0064	0.0093	0.0026	0.0208	23	7	53	25	7	55
		L	C-E	1.63	4923	1.5	0.14	41419	0.0020	0.0012	0.0000	0.0106	3	0	27	3	0	28
		L	F	1.63	151	0.67	0.15	605	0.0000	0.0000	0.0000	0.0002	0	0	0	0	0	0
		L	G-Q	1.63	2898	0.8	0.15	13875	0.0007	0.0004	0.0000	0.0036	1	0	9	1	0	9
		L	All		7972			55899	0.0027	0.0017	0.0000	0.0143	4	0	36	4	0	38
		All	All		32183			189605	0.0090	0.0109	0.0032	0.0278	28	8	70	29	9	74

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

4 OVERALL ATTRIBUTABLE FRACTION

4.1 EXPOSURE MAP

No exposure map is given since the two exposures; soots and tetrachloroethylene, do not overlap in the working population.

4.2 SUMMARY OF RESULTS

The results are summarised in Table 11 and Table 12.

Table 11 Summary of relative risks used to calculate AF

Agent	Exposure	RR	LL	UL
Soots	H	3.87	1.93	6.93
Tetrachloroethylene	H	2.47	1.35	4.14
Tetrachloroethylene	L	1.63	0.24	3.85

Table 12 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)
Soots	84585	0	0.0044	0.0000	0.0124	0.0045	0.0269	0.0000	0.0000	0.0000	59	0	60	0
Tetrachloroethylene	373376	189605	0.0192	0.0090	0.0208	0.0046	0.0626	0.0109	0.0032	0.0278	99	28	101	29
Totals*					**0.0329**	**0.0148**	**0.0754**	**0.0109**	**0.0032**	**0.0278**	**156**	**28**	**159**	**29**

***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.

EXPOSURES BY INDUSTRY/JOB

Table 13 shows for industry categories from CAREX and job categories from LFS, attributable registrations in 2004 and attributable deaths in 2005 by agent.

Table 13 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)
Soots	Chimney sweep	84,585	0	60	59	0	0	60	59
Tetrachloroethylene	Food manufacturing	8,220	4,515	1	1	0	0	2	2
Tetrachloroethylene	Manufacture of textiles	11,698	6,425	2	2	1	0	2	2
Tetrachloroethylene	Manufacture of wearing apparel. except footwear	15,172	8,333	2	2	1	1	3	3
Tetrachloroethylene	Manufacture of paper and paper products	8,110	4,454	1	1	0	0	2	2
Tetrachloroethylene	Printing, publishing and allied industries	10,389	5,706	2	2	0	0	2	2
Tetrachloroethylene	Iron and steel basic industries	3,463	1,902	1	1	0	0	1	1
Tetrachloroethylene	Manufacture of fabricated metal products except machinery and equipment	22,064	12,118	8	8	2	2	10	10
Tetrachloroethylene	Manufacture of machinery except electrical	31,490	17,295	11	11	3	3	14	14
Tetrachloroethylene	Manufacture of electrical machinery, apparatus, appliances	11,903	6,538	4	4	1	1	5	5
Tetrachloroethylene	Manufacture of transport equipment	9,654	5,302	3	3	1	1	4	4
Tetrachloroethylene	Electricity, gas and steam	11,664	6,406	2	2	1	0	2	2
Tetrachloroethylene	Construction	67,791	605	10	10	0	0	10	10
Tetrachloroethylene	Land transport	14,591	10,005	2	2	1	1	3	3
Tetrachloroethylene	Air transport	3,238	2,221	0	0	0	0	1	1
Tetrachloroethylene	Personal and household services	134,827	92,453	48	48	17	16	65	64
Tetrachloroethylene	Total	373,376	189,605	101	99	29	28	130	126

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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

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

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).

Published by the Health and Safety Executive 06/12

Health and Safety Executive

The burden of occupational cancer in Great Britain

Oesophageal cancer

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 oesophagus that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for oesophageal cancer associated with overall occupational exposure is 2.54% (95% Confidence Interval (CI)= 1.07-5.58), which equates to 184 (95%CI=78-429) attributable deaths and 188 (95%CI=80-439) attributable registrations.

This report and the work it describes were funded by the Health and Safety Executive (HSE). Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

RR929

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