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Occupational cancer in Britain
Respiratory cancer sites: larynx, lung and mesothelioma

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OVERVIEW OF RESPIRATORY CANCER

Laryngeal cancer

Most laryngeal cancers are squamous in origin and originate in the glottis. Supraglottic and subglottic tumours are rare. This disease is markedly more frequent in men than in women (Rafferty *et al*, 2001), and there is a large geographical variability in disease frequency. In the United Kingdom in the 1990s, laryngeal cancer accounted for around 1 in 70 diagnosed cases of cancer. Moreover, the disease mainly affects elderly people. On the basis of male patients diagnosed in 2000–2001, the age-standardised 1-year relative survival rate was 84% and after 5 years was 64% (Rachet *et al*, 2008a), and has improved significantly since the early 1980s. Survival was poorer for women than for men (Quinn *et al*, 2005).

The main risk factors for cancer of the larynx are tobacco and alcohol, which together have a synergistic effect on the risk of laryngeal cancer (IARC, 2004; Altieri *et al*, 2005; Pelucchi *et al*, 2006a). For smoking, the reported effect estimates have been generally strong, consistent and show a pronounced exposure–response relationship (Olshan, 2006). The aetiological role of alcohol is less clear, but evidence suggests both a weaker association and a joint effect with tobacco.

Lung cancer

Lung cancer is the most common malignant neoplasm among men in most countries and is increasing among women, notably in western countries. Lung cancer is rapidly fatal, and thus the trends in incidence and mortality are closely similar. Survival in the United Kingdom in 1986–1990 was very poor, only around 21% after 1 year and 6% after 5 years in both men and women, and has only marginally improved over the last 20 years (Rachet *et al*, 2008b). In men in England, Wales and Scotland, both incidence and mortality reached a plateau in the early 1970s, and both have since steadily decreased (Quinn *et al*, 2005). However, in women, increasing trends were seen up to the end of the 1980s, since when rates have been fairly stable. Lung cancer accounted for 23.4% of cancer deaths among men, and 17.9% of such deaths in women in 2005.

The overwhelming determinant of the occurrence of lung cancer is cigarette smoking, which is now estimated to account for $\sim$90% of the burden in developed countries (Peto *et al*, 1994), either independently or by synergistic associations with other risk factors. The geographical and temporal patterns are determined chiefly by the consumption of tobacco (Boffetta and Trichopoulos, 2002).

MESOTHELIOMA

Mesothelioma is a rare form of cancer that develops from the mesothelium, the protective lining that covers many of the body's internal organs. Its most common site is the pleura, but it may also occur in the peritoneum and the pericardium. The number of mesothelioma deaths each year has increased markedly since the late 1960s. In 2005, there were 2046 mesothelioma deaths – $>$1% of all malignant cancer deaths in Great Britain – compared with 153 in 1968 (HSE, 2010), the first full year for which data are available from the mesothelioma register. This cancer is more common in men who typically account for about 85% of mesothelioma-related deaths each year (McElvenny *et al*, 2005). The long latency of the disease – typically 30–40 years – also means that most cases occur at older ages, with around two-thirds of cases occurring at ages 60–80 years (HSE, 2010). Survival remains very poor; median survival is $<$12 months (CRUK, 2011).

METHODS

Occupational risk factors

Group 1 and 2A human carcinogens The agents that the International Agency for Research on Cancer (IARC) has classified as either causing (Group 1 agents) or possibly causing (Group 2A agents) mesothelioma, and lung and laryngeal cancer, and for which estimation has been carried out, are summarised in Table 1. Up to the end of 2008, there were 32 occupational carcinogens or circumstances for lung cancer classified by IARC as Group 1 and

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

Table 1 Occupational agents, groups of agents, mixtures and exposure circumstances classified by the IARC monographs, vols 1–77 (IARC, 1972–2001), into Groups 1 and 2A, which targets the respiratory system and for which burden was estimated

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Source of data for estimation of numbers ever exposed over REP	Comments
Group 1: Carcinogenic to humans				
Agents and groups of agents and exposure circumstances				
Arsenic and arsenic compounds	Non-ferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fibre production; mining or ores containing arsenic	Lung *sufficient*	CAREX	
Asbestos	Mining and milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry	Lung *sufficient* Larynx *sufficient* Mesothelioma *sufficient*	UK Mesothelioma Register, CAREX	
Beryllium	Extraction and processing; aircraft, aerospace, electronics and nuclear industries; jewellers	Lung *sufficient*	CAREX	
Bis(chloromethyl)ether, chloromethyl methyl ether	Production, chemical intermediate, alkylating agent; laboratory reagent; plastic manufacturing; ion-exchange resins and polymers	Lung *sufficient*		Small numbers exposed
Cadmium and cadmium compounds	Smelter workers; battery production workers; cadmium-copper alloy workers; dyes and pigments production; electroplating processes	Lung *sufficient*	CAREX	
Chromium (VI) compounds	Production plants; dyes and pigments; plating and engraving; chromium ferro-alloy production; stainless steel welding; in wood preservatives; leather tanning; water treatment; inks; photography; lithography; drilling muds; synthetic perfumes; pyrotechnics; corrosion resistance	Lung *sufficient*	CAREX	
Dioxin (TCDD)	Production; use of chlorophenols & chlorophenoxy herbicides; waste incineration; PCB production; pulp and paper bleaching	Lung *limited*	LFS, COE	
Environmental tobacco smoke		Lung *sufficient* Larynx *limited*	CAREX	
Ionising radiation	Radiologists, technologists, nuclear workers, radium-dial painters, underground miners, plutonium workers, cleanup workers following nuclear accidents, aircraft crew	Lung *sufficient*	CIDI, LFS, British Airways Stewards and Stewardesses Association	
Mineral oils	Production; used as a lubricant by metal workers, machinists, engineers; printing industry (ink formulation); used in cosmetics; medicinal and pharmaceutical preparations	Lung *limited*	LFS	
Mustard gas	Production; used in research laboratories; military personnel	Lung *limited* Larynx *sufficient*		Small numbers exposed
Nickel compounds	Nickel miners; metal fabrication; grinding; electroplating, and welding	Lung *sufficient*	CAREX	Clydach refinery only

Table 1 (*Continued*)

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Source of data for estimation of numbers ever exposed over REP	Comments
PAHs: benzo(a)pyrene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Lung *limited*		Included with PAHs
Coal-tar and pitches	Production of refined chemicals and coal tar products (patent-fuel); coke production; coal gasification; aluminium production; foundries; road paving and construction (roofers and slaters)	Lung *sufficient*		Included with PAHs
Soots	Chimney sweeps; heating-unit service personnel; brick masons and helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials	Lung *sufficient*		Included with PAHs
Radon and its decay products		Lung *sufficient*	NRPB	
Crystalline silica	Granite and stone industries; ceramics, glass and related industries; foundries and metallurgical industries; abrasives; construction; farming	Lung *sufficient*	CAREX	
Strong inorganic acid mists containing sulphuric acid	Pickling operations; steel industry; petrochemical industry; phosphate acid fertilizer manufacturing	Lung *limited* Larynx *sufficient*	CAREX	
Talc containing asbestiform fibres	Manufacture of pottery, paper, paint and cosmetics	Lung *sufficient*		Included with asbestos
Exposure circumstances				
Aluminium production	Pitch volatiles; aromatic amines	Lung *sufficient*		Included with PAHs
Coal gasification	Coal tar; coal-tar fumes; PAHs	Lung *sufficient*		Included with PAHs
Coke production	Coal-tar fumes	Lung *sufficient*		Included with PAHs
Hematite mining (underground) with exposure to radon	Radon; silica	Lung *sufficient*		Small numbers exposed
Iron and steel founding	PAHs; silica; metal fumes; formaldehyde	Lung *sufficient*	LFS	
Painter		Lung *sufficient*	LFS	
Tin miners		Lung *strong*		Cornish tin miners included because of exposure to radon
Group 2A: Probably carcinogenic to humans				
Agents and groups of agents and exposure circumstances				
α-chlorinated toluenes and benzoyl chloride (combined exposure)	Production; dye and pesticide manufacture	Lung *limited*		Small numbers exposed
Cobalt metal with tungsten carbide	Miners; processing of copper and nickel ore; glass and ceramic production	Lung *limited*	CAREX	
Diesel engine exhaust	Railroad workers; professional drivers; dock workers; mechanics	Lung *limited*	CAREX	
Epichlorohydrin	Production and use of resins, glycerine and propylene-based rubbers; used as a solvent	Lung *limited*		Unknown number of workers exposed
Inorganic lead	Smelters; plumbers; solderers; occupations in battery recycling smelters	Lung *limited*	CAREX	

Table 1 (*Continued*)

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Source of data for estimation of numbers ever exposed over REP	Comments
Non-arsenical insecticides	Production; pest control and agricultural workers; flour and grain mill workers	Lung *limited*		Included with dioxins
PAHs: Dibenz(a,h)anthracene Cyclopenta(c,d)pyrene, Dibenzo(a,l)pyrene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Lung *limited*	CAREX	
Exposure circumstances				
Art glass, glass containers and pressed ware (manufacture)	Lead; arsenic; antimony oxides; silica; asbestos; other metal oxides; PAHs	Lung *limited*		Included with arsenic, asbestos, silica, PAHs
Hairdressers and barbers	Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols	Lung *limited*		Included with ETS
Isopropyl alcohol manufacture, strong acid process	Diisopropyl sulphate	Lung *limited* Larynx *sufficient*		Included with strong acids
Rubber industry		Lung *limited* Larynx *limited*		British study gives negative risk estimates
Welders[a]		Lung *limited*	LFS	

Abbreviations: CAREX = CARcinogen EXposure Database; CIDI = Central Index of Dose Information; CoE = Census of Employment; LFS = Labour Force Survey; NRPB = National Radiological Protection Board; REP = risk exposure period. [a]Welders are classified by IARC as Group 2B.

2A agents. In the present study, burden estimation has been carried out for 21 of these agents/exposures. Welding fumes are classified as a Group 2B carcinogen; however, welders could potentially be exposed to several carcinogens, for which separate estimates have been made, including nickel, chromium, lead, polycyclic aromatic hydrocarbons (PAHs) and asbestos. It is not possible to identify and exclude welders specifically from the industry categories used by CAREX for these exposure estimates, and evidence suggests that other unidentified carcinogenic agents in welding fume may also be contributing to the observed lung cancer risk, or that synergism between the known risk agents may be operating to raise the risk in welders to above that observed in workers exposed to the agents separately (see below). For this reason, a separate estimate for welders as an occupation has been carried out. In addition, tin miners in Cornwall have been included because of exposure to radon.

As very few workers have been exposed to mustard gas, no estimation has been carried out for laryngeal or lung cancer. For the same reason, no estimation has been carried out for lung cancer for bis(chloromethyl)ether, haematite mining and α-chlorinated toluenes. Also excluded for lung cancer are: coal tars and pitches, soots, coal gasification, coke production, aluminium production (all included with the estimation for PAHs); hairdressers and barbers (included with environmental tobacco smoke (ETS)); isopropyl alcohol manufacture (included with strong acids and very small numbers exposed), art glass (included with arsenic); non-arsenical insecticides (included with 2,3,7,8-tetrachlorodibenzo-para-dioxin (dioxins)); talc containing asbestiform fibres (included with asbestos); epichlorohydrin (unknown number exposed) and work in the rubber industry (the British study shows no increased risk).

Choice of studies providing risk estimates for laryngeal and lung cancers and mesothelioma

A detailed review of occupational risk factor studies identified for these three cancers is provided in the relevant Health and Safety Executive (HSE) technical reports, including those carcinogens for which no estimation has been carried out (HSE, 2012a, b, c).

Occupational exposures common to laryngeal and lung cancers and mesothelioma

Asbestos All forms of asbestos, serpentine (chrysotile) and amphiboles (crocidolite, amosite, tremolite) are carcinogenic to humans, although the potency of chrysotile might be lower than that of other types (IARC, 1987; IPCS, 1998). Numerous studies and reviews have been published on workers exposed to asbestos. In Britain, heavy asbestos exposure in the past occurred in shipbuilding, railway engineering, asbestos product manufacture and construction. Workers with the highest risks today are likely to be those subject to incidental exposures during the course of their work; for example, building maintenance workers.

The role of asbestos and laryngeal cancer remains controversial (Siemiatycki *et al*, 2004). Recent reviews (Browne and Gee, 2000; Griffiths and Molony, 2003; Wight *et al*, 2003) concluded that the evidence is weak and that increases in risk may be because of insufficient adjustment for alcohol and tobacco consumption. In a review by Goodman *et al* (1999) of 69 cohorts, the overall meta-standardised mortality ratio (SMR) for laryngeal cancer, without taking into account latency and confounding factors (tobacco and alcohol), was 1.33 (95% confidence interval (CI) = 1.14–1.55), with a very high degree of homogeneity. In addition, a proxy of dosage exposure (using deaths from mesothelioma) showed no exposure–response in laryngeal cancer. A weak association between laryngeal cancer and asbestos was concluded. However, many of the industries included in this meta-analysis are no longer those where exposure to asbestos occurs in Britain.

A meta-analysis was therefore carried out by the study group on nine case–control studies (eight population-based and one industry-based study from Europe and the United States) that included adjustments for tobacco and alcohol consumption. The overall meta-standardised incidence ratio (SIR) of 1.38

(95% CI = 1.17–1.63) has been used to estimate the attributable fraction (AF) for the high exposure level. The relative risk for low exposure was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project for which data were available. As this was <1, the relative risk (RR) for low exposure has been set to 1.

The most comprehensive source of information on mesothelioma in Great Britain is the British Mesothelioma Register, set up in the late 1960s in response to reports associating the disease with asbestos exposure (McElvenny *et al*, 2005). A recent population-based case–control study of mesothelioma cases in Britain suggests that nearly half of currently occurring deaths in men are attributable to exposures in construction, such as those arising during the installation of asbestos building materials for fire protection purposes (Rake *et al*, 2009).

The authors also concluded that a substantial proportion of cases that were not attributable to identifiable sources of asbestos exposure (14% of male and 62% of female cases) were nevertheless caused by asbestos, and that the source was likely to be an increase in ambient asbestos exposure that coincided with the widespread occupational exposures of the 1960s and 1970s; 16% of female cases overall were attributable to domestic exposures. The AF for mesothelioma was derived directly from this study and several other UK mesothelioma studies. We have included the total proportion due to asbestos exposure (including the proportion of cases unattributed as such), as the distinction between para-occupational and environmental exposures is somewhat blurred in the case of a carcinogen that has been so widely used as a building product. On this basis, between 96% and 98% of male mesothelioma cases are due to asbestos exposure (Howel *et al*, 1997; Yates *et al*, 1997; Rake *et al*, 2009). Combining the results from Rake *et al* (2009) with those from two studies in which results were reported separately for women (Spirtas *et al*, 1994; Goldberg *et al*, 2006) gave estimates of 75–90% for women.

The ratio of asbestos-related lung cancer to mesothelioma deaths has been estimated in a number of studies and is likely to vary depending on particular exposure circumstances (Albin *et al*, 1999). An analysis based on the overall British population estimated the ratio to be between two-thirds and one (Darnton *et al*, 2006). In the light of an earlier analysis based on the West of Scotland population that estimated the ratio to be somewhat higher (Irvine *et al*, 1993), we judged an overall ratio of 1 : 1 to be a reasonable estimate, and used this rather than our standard method. This takes into account the impact that past levels of exposure to asbestos are having on the current incidence by the direct link to mesothelioma deaths that are still increasing, whereas lung cancer in general is declining because of the reduction in smoking.

A large number of studies report increased lung cancer in asbestos-exposed workers. Steenland *et al* (1996) focussed on larger cohort studies with some estimate of exposure, and derived a combined SMR of 2.00 (95% CI = 1.90–2.11). The review by Goodman *et al* (1999) obtained a meta-SMR of 1.48 (95% CI = 1.44–1.52), although there was a significant heterogeneity between studies.

Exposure circumstances common to laryngeal and lung cancer

Strong inorganic acid mists containing sulphuric acid An increased risk of lung and laryngeal cancer has been suggested in workers exposed to strong inorganic acid; for example, sulphuric acid, in a number of industries, including production of isopropanol and ethanol, steel pickling, battery manufacture and sulphuric acid production, as well as manufacture of soaps and detergents (IARC, 1992).

Soskolne *et al* (1992) conducted a population-based case–control study for laryngeal cancer in Canada, in which work history was collected using questionnaires from which retrospective assessment of exposure to sulphuric acid was carried out. The estimates reported were adjusted for both alcohol and tobacco consumption. A strong association was found overall for laryngeal cancer with exposure to sulphuric acid (odds ratio (OR) = 2.90, 95% CI = 1.62–5.20). An exposure–response relationship was found, and these figures have been used for the AF estimation – high exposure: OR = 4.28 (95% CI = 2.13–8.58); low exposure: OR = 1.91 (95% CI = 0.97–3.78).

In a study of US male workers in pickling operations in the steel industry (Steenland and Beaumont, 1989), the smoking-adjusted SMR for lung cancer for the whole cohort was 1.36 (95% CI = 0.97–1.84), and has been used in the AF estimation for lung cancer for the high-exposed workers. Coggon *et al* (1996) found an RR of 0.98 for lung cancer in a study of lead battery and steel workers exposed to acid mists; an RR of 1.0 has thus been used for the low-exposed group. Many other studies of the relationship between mists containing sulphuric acid and lung cancer have not controlled adequately for smoking and/or other occupational exposures, leading one review to conclude that the evidence of a causal relationship was weak (Sathiakumar *et al*, 1997).

Rubber industry Rubber processes, dusts and fumes may cause exposure to many chemicals, including PAHs, chromium VI compounds, lead and lead compounds, crystalline silica, cadmium and cadmium compounds, cobalt and cobalt compounds, acrylonitrile, styrene, 1,3-butadiene and *n*-nitrosodimethylamine (IARC, 1987). Mortality and cancer morbidity in workers employed in the rubber industry have been investigated in the United Kingdom through two cohorts (Sorahan *et al*, 1989; Straughan and Sorahan, 2000; Dost *et al*, 2007). One cohort (Sorahan *et al*, 1989) followed up male rubber workers from 13 factories during 1946–1985, finding a weak excess mortality from laryngeal cancer (SMR = 1.19, on the basis of 33 observed cases). The second cohort of workers began work at 42 rubber factories in the period 1982–1991; excess mortality from laryngeal cancer was found for men for the period 1983–1998 (SMR = 2.13) (Straughan and Sorahan, 2000) but a much lower estimate in an update from 1983 to 2004 (SMR = 1.03) (Dost *et al*, 2007). As the follow-up for the cohort reported by Sorahan *et al* (1989) was more appropriate for the burden estimation risk exposure period (REP), defined as the period during which exposure occurred that was relevant to the development of cancer in the target year, 2005, an SMR of 1.19 was used for AF estimation for laryngeal cancer. A CI was not provided for this estimate, and therefore we used the Byar's approximation proposed in Breslow and Day (1987) to calculate it: 95% CI = 0.82–1.62. As this study found a deficit for both mortality and cancer incidence for lung cancer, no AF estimation was carried out for this cancer.

Both the UK cohorts were included in a meta-analysis by Alder *et al* (2006) that included studies of the rubber industry from many different countries using several different processes and substances. A meta-SMR of 1.19 (95% CI = 0.88, 1.60) for mortality, similar to that of Sorahan *et al* (1989), and an SIR of 1.39 (95% CI = 0.75, 2.59) for incidence, was estimated for laryngeal cancer. Results for lung cancer were as follows: meta-SMR = 1.05 (95% CI = 0.94, 1.18) for mortality and SIR = 1.12 (95% CI = 0.92, 1.36) for incidence.

Exposure circumstances for lung cancer

Arsenic and arsenical compounds The main occupations with substantial historical exposure levels include hot copper smelting, manufacturing of arsenical pesticides and sheep-dip compounds, fur handling and vineyard working (IARC, 1987; Hayes, 1997). There is a substantial amount of literature linking inhalation exposure to inorganic arsenic and lung cancer. The key studies have been carried out in the United States and involved workers exposed primarily to arsenic trioxide dust in air at copper smelters and mines. Lee-Feldstein (1986) in a study of smelter workers

estimated an SMR of 1.74 for low-exposed groups ($<5\,mg\,m^{-3}$ months; 95% CI = 0.75–3.43) that has been used in the AF estimation for the low-exposure group. For exposures above this level, the SMR was 2.05 (95% CI = 1.43–2.85), and this was used for the high-exposure group.

Beryllium Beryllium exposure occurs mainly in mining and refining, and in the manufacture of ceramics, electronic and aerospace equipment, the majority of studies being carried out in the United States. The overall smoking-adjusted SMR of 1.12 (95% CI = 0.99–1.26) from a study by Ward *et al* (1992) of male workers from seven US beryllium processing facilities in Pennsylvania and Ohio has been used for the high-exposure group (although it should be noted that significant excesses were only seen at two of the seven plants). Because of the absence of sufficient dose–response data, the risk estimate for low exposure was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project where data were available. As this was <1, the RR for low exposure has been set to 1.

Cadmium and cadmium compounds Cadmium is principally used in electroplating, in compounds that serve as stabilisers for plastics, as pigments, in electrodes in batteries and in alloys (Schaller and Angerer, 1992; IARC, 1993). Exposures mainly occur by inhalation. The results of studies investigating the effect of occupational exposure of cadmium are conflicting, and carcinogenicity has not been unequivocally established in human studies. Overall, the results suggest evidence of an increased risk of lung cancer following prolonged inhalation exposure to cadmium (ATSDR, 2008).

Verougstraete *et al* (2003) reviewed seven independent occupational cohorts (three United Kingdom, two Swedish, one United States, one Chinese), totalling to >12 000 workers. From these studies, the SMRs were obtained and the inverse-variance-weighted average SMR of 1.19 (95% CI = 1.09–1.29) was estimated by the research team for the AF estimation for the high-exposed workers. The review also summarised the exposure–response results, and Verougstraete *et al* (2003) found the RR to be 1.0 or <1.0 for low-exposed groups; that is, individuals who are exposed to between 250 and 500 $\mu g\,m^{-3}$ years of cadmium. A RR of 1 has therefore been used for the low-exposure group.

Chromium (hexavalent) compounds Chromium exposure occurs in its production and the production of other alloys, chrome-containing pigments, chrome-plating and welding (of stainless steel) (IARC, 1990). Occupational exposure to hexavalent chromium (CrVI) compounds in chromate production, chromate pigment production and use, as well as chrome plating, has been associated with an increased risk of lung cancer. A comprehensive review and meta-analysis by Cole and Rodu (2005) of 49 epidemiological studies, of various industries (production, pigment manufacture, plating), found an overall meta-SMR of 1.41 (95% CI = 1.35–1.47). In 26 studies that controlled for smoking, the meta-SMR was 1.18 (95% CI = 1.12–1.25) and has been used for the high-exposure group in the AF estimation. However, it has been postulated that the relationship is weak because of the lung's capacity to reduce CrVI to the non-carcinogenic CrIII (de Flora, 2000). Crump *et al* (2003) also concluded that CrVI is a weak carcinogen, estimating that the lifetime additional risk of lung cancer mortality associated with 45 years of occupational exposure to 1 $\mu g\,m^{-3}$ CrVI was 0.002. This is only about 5% of the minimum exposure (1.0 1 $\mu g\,m^{-3}$ years) that consistently was associated with an increased lung cancer risk. This corresponds to an RR of about 1.0, which has been used for the low-exposure group.

Cobalt Occupational exposure to cobalt occurs predominantly during refining of cobalt, in the production of alloys, and in the manufacture and maintenance of hard-metal tools and the use of diamond-cobalt tools (IARC, 2006).

Studies have been undertaken in various French industries. A nested case–control study in a French hard-metal industry cohort covering 10 facilities found a significantly increased risk of lung cancer associated with simultaneous exposure to cobalt and tungsten carbide (OR = 1.93, 95% CI = 1.03–3.62) (Moulin *et al*, 1998). The OR increased with cumulative exposure and with duration of exposure, and adjustment for smoking did not alter the OR estimates. This increased risk was confirmed in a further study of the largest production site, particularly to those exposed to unsintered hard-metal dust (SMR = 2.02, 95% CI = 1.32, 2.96) (Wild *et al*, 2000). For the AF estimation, the industry-wide OR of 1.93 from Moulin *et al* (1998) has been used for the high-exposure group. For the lower-exposure group, their overall SMR for lung cancer of 1.30 (95% CI 1.00–1.66) was used.

Crystalline silica Exposure to respirable crystalline silica occurs in the following industries: masonry and stonework, concrete and gypsum, pottery, foundries, diatomaceous earth mining, brick making, mining and construction. Increased risk for lung cancer has not been detected in all industrial circumstances and may depend on inherent characteristics of the crystalline silica or on external factors affecting its biological activity or distribution of its polymorphs (IARC, 1997). There have been a number of reviews of the association between lung cancer and exposure to crystalline silica, and these have been summarised in the relevant HSE technical report (HSE, 2012b). Steenland *et al* (1996) estimated a combined RR of 1.33 (95% CI 1.21–1.45) for lung cancer from 13 cohort/case–control studies. An average SMR of 1.2 (95% CI 1.1–1.3) was found for lung cancer in a pooled exposure–response analysis (Steenland *et al*, 2001). Categorical analysis of cumulative exposure resulted in a monotonic trend with ORs. The OR for the second quintile of cumulative exposure (between 0.4 and 2.0 $mg\,m^{-3}$ year) was 1.0 (95% CI = 0.85–1.30). A meta-analysis by Kurihara and Wada (2004) estimated an overall pooled RR of 1.32 (95% CI 1.24–1.41) for lung cancer, with an RR of 2.37 in the presence of silicosis (95% CI 1.98–2.84), and an RR of 0.96 in the absence of silicosis (95% CI 0.81–1.15). A systematic review by Pelucchi *et al* (2006b) estimated a pooled RR for cohort studies of 1.34 (95% CI 1.25–1.45); from case–control studies the pooled RR was 1.41 (95% CI 1.18–1.67) and for proportionate mortality ratio (PMR) studies it was 1.24 (95% CI 1.05–1.47). Results for studies where silicosis status was known and unknown were similar to those found by Kurihara and Wada (2004). For the AF estimation, Kurihara and Wada's overall estimate (which was for men) has been used for the high-exposed group; the low-exposed group is assumed to have an RR of 1.0 following the study of Steenland *et al* (2001).

Diesel engine exhaust (DEE) Diesel engine exhaust is a complex mixture of substances characterised by PAHs surrounding an elemental carbon core. The gas phase includes carbon monoxide and nitrogen oxides, but it is the particulate phase of DEE that appears to be implicated as the lung carcinogen. There have been two major reviews evaluating the association between DEE exposure and lung cancer risk (Bhatia *et al*, 1998; Lipsett and Campleman, 1999). Lipsett and Campleman (1999) reviewed 30 studies; 12 studies (20 risk estimates) had adjusted for smoking and showed little evidence of heterogeneity, giving a pooled smoking-adjusted RR of 1.47 (95% CI = 1.29–1.67). This has been used for the high-exposure group in the AF estimation. For the low-exposure group, we have used a RR of 1.1 (95% CI = 0.7–1.8) from a large United Kingdom-based death-certificate study (Coggon *et al*, 1984).

Since these reviews, new studies have been published with varying results, the majority showing an excess risk and are summarised in the relevant HSE technical report (2001b).

ETS Many epidemiological studies and reviews have established that ETS is a cause of serious disease in adults and children (SCOTH, 1998, 2004). ETS exposure has been particularly prevalent

in the wholesale and retail trade, restaurants and hotels, construction and financing, insurance, real estate and business services.

Zhong *et al* (2000) carried out a comprehensive meta-analysis of 35 case–control and five cohort studies providing quantitative estimates of the association between lung cancer and exposure to ETS. The risk estimates used for the AF estimation from this study were for non-smokers exposed to ETS at work: RR = 1.15 (95% CI = 1.04–1.28) for women and RR = 1.29 (95% CI = 0.93–1.78) for men. These results are similar to a pooled analysis of two large case–control studies (Brennan *et al*, 2004) and another meta-analysis (Boffetta, 2002). Because of the absence of sufficient dose–response data, the risk estimate for low exposure was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project where data were available. As this was <1, the RR for low exposure has been set to 1.

Ionising radiation (IR) Ionising radiation is a well-established cause of cancer but has only occasionally been associated with lung cancer. The relative risks for occupational exposure to IR were obtained from UNSCEAR (2008), using models of excess relative risk per unit of radiation dose (see HSE, 2012b for details). Using this method, an RR estimate of 1.005 for men and 1.021 for women exposed to IR (with an estimated average lifetime dose of 15.3 mSv) was obtained.

However, several studies have not shown an increased risk of lung cancer: physicians in the British Radiological Society (Berrington *et al*, 2001); US radiological technicians (Rajaraman *et al*, 2006); nuclear industry workers (Carpenter *et al*, 1994; Omar *et al*, 1999); the National Registry for Radiation Workers (Muirhead *et al*, 1999); and combined analysis of UK, USA and Canadian studies (Cardis *et al*, 1995).

Lead Almost all of the information regarding lead exposure and cancer is derived from studies of lead battery and smelter workers and involves exposure to inorganic lead. Several reviews have been published on this topic (Landrigan *et al*, 2000; Silbergeld *et al*, 2000; Steenland and Boffetta, 2000).

Two meta-analyses have been undertaken, both showing an increased risk (Fu and Boffetta, 1995; Steenland and Boffetta, 2000). The most recent reviewed eight industry studies, mostly of smelter and battery workers, and obtained an RR of 1.30 (95% CI = 1.15–1.46). Excluding one study with the highest RR where confounding with arsenic was thought to have occurred gave a combined RR of 1.14 (95% CI = 1.04–1.73); this has been used for the higher-exposed workers in the AF estimation. Because of the absence of sufficient dose–response data, the risk estimate for low exposure was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project where data were available. As this was <1, the RR for low exposure has been set to 1.

Mineral oils (untreated and mildly treated) Mineral oils are used in a variety of occupational settings and applications, and those in which inhalation exposure occurs include metalworking, print press operations and cotton and jute spinning. The evidence for an increased risk of lung cancer in exposed workers is not conclusive; for example, studies of metalworkers have generally shown negative results (Calvert *et al*, 1998; NIOSH, 1998), whereas increases have been observed in the majority of studies of workers in the printing industry (Tolbert, 1997). From the studies of print workers in a review by Tolbert, an inverse-variance-weighted combined estimate RR = 1.58 (95% CI = 1.3–1.9) for lung cancer was calculated by the research team and has been used for the AF estimation for printers. Similarly, a weighted average across the case–control and population-based studies from Tolbert's review excluding studies of the printing and newspaper industry gave an overall risk for lung cancer of 1.08 (95% CI = 1.04–1.11), which has been used for industry sectors with high exposure to metalworking fluids. Because of the absence of sufficient dose–response data, the risk estimate for low exposure was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project where data were available. As this was <1, the RR for low exposure has been set to 1.

Nickel and nickel salts Exposure to nickel and nickel salts occurs in the production and welding of stainless steel and non-ferrous alloys, in electroplating and the manufacture of batteries, as well as in nickel mining and refining (IARC, 1990).

Seilkop and Oller (2003) reviewed 25 epidemiological studies of workers employed in the production and use of nickel. The most consistent evidence of an increased risk for lung cancer occurred in nickel refining, particularly those with high exposures in the past because of, now obsolete, operations. In all other workplaces, including mining and smelting, nickel alloy and stainless steel production and stainless steel welding exposures were lower, with generally correspondingly low risks of lung cancer; although some studies of these industries found an increase in lung cancer, these were attributed to other concomitant exposures including PAHs and asbestos. In Britain, the most recent update by Sorahan and Williams (2005) of the Clydach refinery workforce gave an SMR for lung cancer of 1.39 (95% CI = 0.92–2.01); this has been used for the AF estimation and applied to the Clydach refinery population only. Seilkop and Oller (2003) extrapolated the lung cancer risk in 'high-risk' cohorts to low-exposure cohorts. The weighted average of 1.03 (95% CI = 0.97–1.10) was used for all exposed workers apart from the nickel refiners at Clydach. Industry sectors with low or negligible exposure have been assumed to have no excess risk of lung cancer (RR = 1).

PAHs Exposure to PAHs occurs in a number of industries and occupations including the use of coke ovens, coal gas production, aluminium smelting, carbon anode plants, asphalt use, tar distillation, occupation as a chimney sweep, in thermoelectric power and carbon black industries. Several reviews have concluded that an increased risk for lung cancer owing to PAH exposure is present in many industries and occupations (Boffetta *et al*, 1997; Armstrong *et al*, 2004; Bosetti *et al*, 2007).

The risk estimate used in the AF estimation is an adaptation of the unit relative risk (URR) estimate for all the industrial cohorts from the Armstrong *et al* (2004) meta-analysis, adjusted for smoking. A 20-year exposed working lifetime is assumed and the RR is given by ((URR) to the power of $(x \times 20/100)$), where x is the mean benzo-a-pyrene (BaP) level (for example, 8-h time-weighted average (TWA)) in $\mu g\,m^{-3}$ for the exposed. This gives a mean RR of 1.31 (95% CI = 1.16–1.48) at 100 $\mu g\,m^{-3}$ BaP-years. Unwin *et al* (2006), using airborne monitoring of PAHs, provide the 8-h TWA levels of BaP in a range of workplaces. Levels ranged from <0.01 to 6.21 $\mu g\,m^{-3}$, with 50% of the samples below 0.01 $\mu g\,m^{-3}$, 90% below 0.75 $\mu g/m^3$ and 95% below 2.0 $\mu g\,m^{-3}$. For the present study, the above calculation was used to derive an RR estimate at the midpoint of each of these exposure categories: <0.01 (midpoint 0.005), RR = 1; 0.01–<0.75 (midpoint 0.38), RR = 1.02; 0.75–<2.0 (midpoint 1.375), RR = 1.08; 2.0+ (midpoint 4.105), RR = 1.25. The low exposed were assumed to have an RR of 1.0, corresponding to <0.01 $\mu g\,m^{-3}$ BaP 8-h TWA.

Radon and its decay products Although little occupational exposure to radioactive radon occurs in GB in underground mining, there are estimated to be large numbers of workers exposed through working in sites located in areas of naturally occurring high radon exposure. Using models developed by the Committee on Health Risks of Exposure to Radon, Biological Effects of Ionizing Radiation (BEIRVI, 1998), it is estimated that ~2000 deaths per year are attributable to exposure to radon (NRPB, 2000). Approximately 93–276 of the 2000 deaths are

estimated to result from radon exposure in the workplace. The AF applicable to both men and women related to exposure to radon was estimated directly from the upper and lower estimates of these attributable numbers by dividing by the total lung cancer deaths in patients aged 25 years and above in 2005 (0.28% – 0.84%). This gave a midpoint value for the overall AF of 0.56% for men and women, which was used to calculate the contribution of radon to the overall lung cancer burden. Total attributable deaths and registrations were allocated between industries in proportion to numbers ever exposed in the REP, with industry AFs based on attributable deaths.

TCDD (2,3,7,8-tetrachlorodibenzo-para-dioxin) Dioxin may be formed during the chlorine bleaching process used by pulp and paper mills, and as a contaminant in the manufacturing process of certain chlorinated organic chemicals, such as phenoxy herbicides.

Pesticide manufacturing: Workers involved in the manufacture of pesticides may be exposed to TCDD-contaminated chemicals, and these studies have been reviewed in the relevant HSE report (HSE, 2012b). Jones *et al* (2009) have carried out a meta-analysis of a large number of studies of pesticide manufacturing from around the world and estimated a meta-SMR of 1.22 (95% CI = 1.05 – 1.41). This has been used for the AF estimation for manufacturers of formulated pesticides.

Agricultural work: Workers in agricultural occupations may be exposed to low levels of dioxins in the spraying of contaminated pesticides by various ground-based techniques: hand-held sprayers and dusters; vehicle-mounted hydraulic sprayers; air sprayers, foggers and powder dusters; and mixing and loading of equipment used for spraying and application of insecticides.

A risk estimate from Kogevinas *et al* (1997) for sprayers from an analysis of a register of workers exposed to dioxin-contaminated phenoxy-acid herbicides and chlorophenols has been used for the AF estimation of workers in agriculture, horticulture, forestry and gardening (SMR = 1.03, 95% CI = 0.78 – 1.34).

Non-pesticide-related exposures: For workers in pulp manufacture, an overall risk estimate for lung cancer of 1.04 (95% CI = 0.96 – 1.13) from an international collaborative study of workers employed in 11 countries has been used (McLean *et al*, 2006).

Sweetman *et al* (2004) and Eduljee and Dyke (1996) identified a number of work sites in the United Kingdom where occupational exposure to dioxins could occur. The sites with possibly the highest exposures, greater than in pesticide production, included metal recycling, ferrous metal production, zinc smelting, cement manufacture, municipal waste incinerators, coal power stations and workers on landfill sites. The overall risk estimate of 1.12 (95% CI = 0.98 – 1.28) from the IARC register of workers study (Kogevinas *et al*, 1997) has been used for these and the remaining industry sectors where exposure may occur.

Hairdressers and barbers Various studies from the United States and Europe, including England and Wales, have shown an excess lung cancer risk in the industry (Alderson, 1980; Pukkala *et al*, 1992; Lamba *et al*, 2001; Czene *et al*, 2003). However, it has been concluded that the increases observed in most studies could be explained by the high rate of smoking within the industry and exposure to ETS among non-smokers, with risks ranging from 1.21 to 1.9. Estimation has thus been considered under ETS.

Tin miners Underground miners, and in Britain notably tin miners in Cornwall, are known to be at a high risk of exposure to radon. In a study of these miners followed up from 1941 to 1986, the SMR for lung cancer shows a consistent relationship with duration of underground exposure, increasing from 0.83 for surface workers to 4.47 for workers with >30 years underground exposure (Hodgson and Jones, 1990). An overall SMR for lung cancer for underground workers of 1.83 (95% CI = 1.48 – 2.28) was estimated for the period of the study, based on 82 lung cancer deaths. However, 166 lung cancer deaths were recorded between 1951 and 1999 in this cohort, of which 91 occurred from 1986 to 1999. Adding another 13 person years at risk (PYAR) to the study (1987 – 1999) (i.e., as 13×2509 multiplied by the population lung cancer rate to estimate the expected number of lung cancer deaths up to 1999) gives an approximate overall RR of 2.54 (95% CI = 2.18 – 2.96) for lung cancer, which was the RR used for the burden estimation.

Iron and steel founding Potential exposures in the iron and steel foundry industry include silica, cobalt, airborne PAHs, chromium and nickel, phenol, formaldehyde, isocyanates and various amines. Cohort studies have identified RRs ranging from 1.5 to 2.5, PMR studies show risks ranging from 1.5 to 1.8, whereas higher risks were observed in some case – control studies (IARC, 1984, 1987). PAHs and silica have been suggested as main exposures associated with an increased risk in iron foundries, whereas PAHs, silica, chromium and nickel are implicated in steel foundries (Austin *et al*, 1997).

A UK study of steel foundry workers found an SMR of 1.46 (95% CI = 1.34 – 1.58) for lung cancer (Sorahan *et al*, 1994). Smoking data were not available, but the SMRs for other smoking-related cancers were not increased. This result is similar to the results of other European studies (Hansen, 1997; Rodriguez *et al*, 2000; Adzersen *et al*, 2003) and has been used for the AF estimation.

Painters Many chemicals are used in paint products such as pigments, extenders, binders, solvents and additives. Painters are commonly exposed by inhalation to solvents and other volatile paint components; inhalation of less volatile and non-volatile compounds is common during spray painting (IARC, 1989). Studies of painters consistently show an excess of lung cancer of about 40% (IARC, 1989), and the evidence indicates that the excess cannot be explained by smoking alone. A meta-analysis of studies of workers exposed to paints, over a 30-year period, by Chen and Seaton (1998) was used to obtain the risk estimate. The overall combined SMR among painters for lung cancer was 1.29 (95% CI = 1.19 – 1.40), and the combined SMR for lung cancer among painters from occupational cohort studies (excluding national surveys) was 1.21 (95% CI = 1.12 – 1.31), although the confounding effects of smoking and alcohol could not be entirely excluded. This latter estimate has been used for the AF applicable to lung cancer and employment as a painter.

Non-arsenical insecticides (occupational exposure in spraying and application) Workers exposed to non-arsenical insecticides in pesticide manufacture and in agriculture will also potentially be exposed to TCDD, and therefore the burden estimate for non-arsenical insecticides has been included in the estimate for TCDD. However, grain millers are also potentially exposed to non-arsenical insecticides. A review of the literature on cancer incidence and mortality among pesticide manufacturers and applicators found that the SMR/SIR for lung cancer ranged from 0.4 to 3.2, with an inverse-variance-weighted average of 0.99 (95% CI = 0.91 – 1.08) (Burns, 2005). However, an RR of $\leqslant 1$ will result in an AF of 0, and therefore an estimate was not calculated for grain millers.

Welders Welders are exposed to a variety of fumes and gases containing a mixture of oxides and salts of metals and other compounds. An early meta-analysis among shipyard, mild steel and stainless steel welders observed an increased lung cancer risk among all types of workers (Moulin, 1997). Ambroise *et al* (2006) updated this study and found an overall meta-RR after partial control for publication bias of 1.26 (95% CI = 1.20 – 1.32); this has been used for the AF estimation.

Estimation of numbers ever exposed

Data sources The data sources, major industry sectors and jobs for estimation of numbers ever exposed over the REP are given in Table 1. Exposure was assigned as high for the following carcinogens and industry sectors.

Arsenic: manufacture of wood product, furniture and glass, and in non-ferrous metal industries and construction.

Asbestos: all manufacturing industry sectors, electricity and gas utilities and land transport.

Beryllium: manufacture of glass, fabricated metal products, machinery, transport equipment and instruments, photographic and optical goods, as well as in the electricity and gas sectors.

Cadmium: manufacture of industrial chemicals and electrical machinery, and non-ferrous metal industries.

Chromium: manufacture of textiles, clothes, leather goods, footwear, wood products, furniture, industrial chemicals, other chemical, rubber, plastic, glass, non-metallic and fabricated metal products, pottery and machinery except electrical, and in iron and steel and non-ferrous metal industries, construction and electricity and gas sectors.

Cobalt: manufacture of textiles, paper, industrial chemicals, other chemical products, pottery, machinery, fabricated metal products, transport equipment and instruments, and in non-ferrous metal industries and construction.

Crystalline silica: mining, manufacture of industrial chemicals, other chemical products, coal and petroleum products, pottery, glass, other non-metallic mineral products, fabricated metal products, machinery except electrical and transport equipment, as well as in petroleum refining, iron and steel industries, electricity and gas sectors and construction.

DEE: mining, construction, land transport and service allied to land transport.

ETS: wholesale and retail trade, hotels and restaurants, all transport sectors, communication, finance and business, public administration and defence, education and research, recreational and cultural services and personal and household services.

Lead (inorganic): metal-ore mining, manufacture of industrial chemicals, chemical products, plastic products and electrical machinery, and in iron and steel and non-ferrous metal industries, as well as in construction.

PAHs: manufacture of industrial chemicals, petroleum products and non-metallic mineral products, and in iron and steel and non-ferrous metal industries.

Strong inorganic acid mists: manufacture of leather and leather products, paper, industrial chemicals, other chemical products, fabricated metal products, machinery and transport equipment, and in iron and steel and non-ferrous metal industries.

Mineral oils: all jobs known to involve exposure to metalworking fluid (i.e., metal workers, machine operators, tool setters and fitters) and print machine workers.

TCDD: the industrial processes operating in the United Kingdom listed by Eduljee and Dyke (1996) were used to identify the relevant occupational groups.

IR: three sources of data were used to obtain numbers exposed >0.1 mSv IR in Britain: numbers exposed >0.1 mSv from the HSE's Central Index of Dose Information in various industries (HSE, 1998); the Labour Force Survey 1979 for aircraft flight deck officers and male travel and flight attendants; information from the British Airways Stewards and Stewardesses Union for female air stewardesses employed since 1958.

Tin miners: the number of tin miners was obtained from the study of Hodgson and Jones (1990).

RESULTS

Because of assumptions made about cancer latency and working age range, only cancers in patients aged 25 years and above in 2005/2004 could be attributable to occupation. A latency period of at least 10 years and up to 50 years has been assumed for all respiratory tract cancers.

Table 1 lists the carcinogens and occupational circumstances for which separate estimates were carried out. Table 2 gives the numbers and proportions of those ever exposed over the REP separately for men, women and overall. The AFs, attributable numbers of deaths and attributable numbers of registrations are given in Table 3 for men, women and overall.

The AF for all exposures combined for laryngeal cancer was 2.61% (95% CI = 0.83–4.32), which equates to 20 (95% CI = 5–101) attributable deaths and 56 (95% CI = 8–101) attributable registrations (Table 3). The estimated total (men and women) AF for all exposures combined for lung cancer was 14.47%

Table 2 Respiratory cancer numbers and proportions ever exposed

Agent	Number of men ever exposed	Number of women ever exposed	Proportion of men ever exposed	Proportion of women ever exposed
Larynx cancer				
Asbestos	350,302	82,336	0.0181	0.0039
Rubber industry	146,089	62,237	0.0075	0.0030
Strong inorganic acid mists	144,265	102,415	0.0074	0.0049
Lung cancer				
Arsenic	92,144	44,705	0.0047	0.0021
Asbestos	350,302	82,336	0.0181	0.0039
Beryllium	40,180	22,142	0.0021	0.0011
Cadmium	130,986	58,839	0.0068	0.0028
Chromium	444,417	243,102	0.0229	0.0116
Cobalt	129,070	64,849	0.0067	0.0031
DEE	1,632,804	425,017	0.0842	0.0202
ETS	758,415	1,524,013	0.0391	0.0726
Inorganic lead	795,404	405,530	0.0410	0.0193
Ionising radiation	252,035	39,420	0.0130	0.0019
Mineral oils	4,770,047	574,012	0.2459	0.0273
Nickel	305,877	165,889	0.0159	0.0079
PAHs	316,278	178,332	0.0163	0.0085
Painters	1,118,813	130,630	0.0577	0.0062
Radon	1,273,684	1,327,973	0.0657	0.0632
Silica	2,525,118	256,311	0.1302	0.0122
Steel foundry workers	54,358	3180	0.0028	0.0002
Strong inorganic acid mists	136,098	96,613	0.0070	0.0046
TCDD	2,436,500	687,514	0.1256	0.0327
Tin miners	416	0	0.00002	0.0000
Welders	545,544	81,434	0.0281	0.0039
Mesothelioma				
Asbestos	350,302	82,336	97.0000	82.5000

Abbreviations: DEE = diesel engine exhaust; ETS = environmental tobacco smoke; TCDD = 2,3,7,8-tetrachlorodibenzo-para-dioxin.

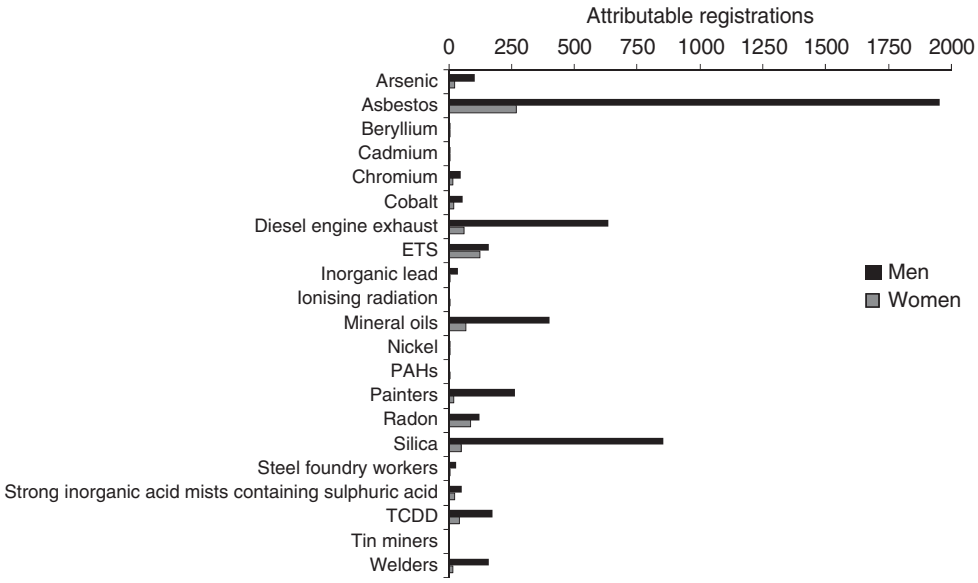

Figure 1 Number of attributable lung cancer registrations in 2004 for men and women by carcinogen or occupational circumstance.

(95% CI = 12.96 – 17.20), which equates to 4745 (95% CI = 4251 – 5643) attributable deaths and 5442 (95% CI = 4877 – 6469) attributable registrations. The estimated total (male and female) AFs for mesothelioma related to occupational exposure was 95.1% (95% CI = 93.0, 96.9), which equates to 1937 (95% CI = 1898 – 1976) attributable deaths and 1937 (95% CI = 1898 – 1976) attributable registrations.

Figure 1 illustrates the attributable registrations for lung cancer for the 21 carcinogens for which estimation was carried out for men and women. Asbestos exposure contributed by far the largest number of lung cancer registrations and was responsible for all the mesothelioma registrations (Table 3). A total of 350 302 men and 82 336 women were estimated to have been exposed to asbestos in the REP (Table 2). The majority of cases occurred in workers in the construction industry; however, the epidemiological studies of asbestos were in other industries, such as insulation work, dock work, asbestos manufacture and use.

Figure 1 and Table 3 show that silica, DEE, mineral oils, TCDD, ETS, radon and arsenic were also responsible for considerable numbers of cancer registrations (100 and above). A total of 2,525,118 men and 256,311 women were estimated to have been exposed to crystalline silica during the REP (Table 2). In men, >80% of cases were in the construction industry, whereas in women cases occurred in the manufacture of other non-metallic mineral products and pottery, china and earthenware.

Diesel engine exhaust exposure occurred among 1,632,804 men and 425,017 women over the REP. For men, the majority of cases occurred in occupations related to construction and land transport, whereas for women cases occurred in land transport only. A large number of men (4,770,047) and women (574,012) were estimated to have ever been exposed to mineral oils; the majority (25% men, 50% women) worked as machine tool operators.

Dioxin exposure was estimated to have ever occurred among 2,436,500 men and 687,514 women over the REP. The largest numbers occurred for farmers, farmer workers, gardeners and other agricultural workers (68 registrations), with registrations also being high for aluminium processing (15), manufacture of ceramic products (23) and manufacture of steel tubes and wires (27). ETS exposure occurred more among women (1,524,013) than among men (758,415) over the REP. The majority of these occurred in wholesale and retail trade, and restaurants and hotels. An estimated 1,273,684 men and 1,327,973 women were exposed to naturally occurring radon at their workplace during their working lifetime in areas of the country with known high levels of exposure. A total of 92,144 men and 44,705 women were estimated to have been ever exposed to arsenic in the REP. Non-ferrous metal basic industries were the industries in which most cases occurred.

Two occupational circumstances, work as a painter and work as a welder, were evaluated by IARC without attribution to particular exposures encountered within these occupations. They also contribute over 100 cancer registrations (Table 3, Figure 1). An estimated 1,111,813 men and 130,630 women were ever employed as a painter over the REP, the majority of men as painters and decorators, and women in painting assembling and related occupations.

DISCUSSION

The overall AF for laryngeal cancer was estimated to be 2.61%, which is within the range of 1 – 20% given by Steenland *et al* (2003), but well below the figure given by Nurminen and Karjalainen (2001) of 9.1% for Finland. In the present study, the majority of the burden was attributed to strong inorganic acid mists, whereas in the Finnish study it was because of asbestos exposure. There have been a number of studies that have reported the AF for lung cancer owing to occupation. Overall, in this study, the AF was estimated to be about 15% (men: 21.1%; women: 5.3%), with a total of 4748 deaths and 5445 registrations. The figure for men is significantly greater than the 15% given by Doll and Peto (1981), whereas the figure for women is similar. Our estimate is, however, much lower than that obtained in Finland (24%) by Nurminen and Karjalainen (2001) who also included agents for which the epidemiological evidence is not universally accepted; for example, lead and employment as a hairdresser. The present study estimated the AF for asbestos, chromium, ETS, lead, nickel and radon to be significantly lower than those of the Finnish study. In contrast, Boffetta *et al* (2010) estimated the overall AF to be 12.5% for men and 6.5% for women, although their estimates for chromium, nickel, PAHs and ETS were much higher than those obtained by us, the estimate for ETS being almost ten times greater. Other studies have estimated an AF for lung cancer ranging from about 5% to 40% in men and 2% to 4% in women

Table 3 Respiratory cancer burden estimation results for men and women

Agent	AF men (95% CI)	AF women (95% CI)	Attributable deaths men (95% CI)	Attributable deaths women (95% CI)	Attributable registrations men (95% CI)	Attributable registrations women (95% CI)	AF total (95% CI)	Attributable deaths totals (95% CI)	Attributable registrations totals (95% CI)
Larynx cancer									
Asbestos	0.0047 (0.0022–0.0076)	0 (0–0)	3 (1–5)	0	8 (4–13)	0	0.0037 (0.0017–0.0060)	3 (1–5)	8 (4–13)
Rubber industry	0.0014 (0.0000–0.0050)	0.0006 (0.0000–0.0020)	1 (0–3)	0	2 (0–9)	0 (0–1)	0.0012 (0.0000–0.0044)	1 (0–3)	3 (0–10)
Strong inorganic acid mists	0.0229 (0.0083–0.0511)	0.0152 (0.0055–0.0341)	14 (5–31)	2 (1–5)	40 (15–89)	6 (2–12)	0.0213 (0.0077–0.0476)	16 (6–36)	46 (17–102)
Totals[a]	**0.0288 (0.0138–0.0569)**	**0.0157 (0.0060–0.0348)**	**17 (3–50)**	**3 (3–50)**	**50 (3–50)**	**6 (6–50)**	**0.0261 (0.0083–0.0432)**	**20 (5–101)**	**56 (8–101)**
Lung cancer									
Arsenic	0.0048 (0.0023–0.0084)	0.0016 (0.0000–0.0058)	91 (43–161)	22 (0–79)	105 (49–185)	24 (0–89)	0.0034% (0.0013–0.0073)	113 (43–240)	129 (49–274)
Asbestos	0.0892 (0.0835–0.0950)	0.0173 (0.0131–0.0211)	1699 (1590–1810)	238 (180–290)	1956 (1830–2083)	267 (202–326)	0.0591 (0.0540–0.0640)	1937 (1770–2100)	2223 (2032–2409)
Beryllium	0.0002 (0.0000–0.0005)	0.0001 (0.0000–0.0003)	5 (0–10)	2 (0–4)	5 (0–12)	2 (0–4)	0.0002 (0.0000–0.0004)	6 (0–14)	7 (0–16)
Cadmium	0.0003 (0.0001–0.0005)	0.0002 (0.0001–0.0002)	6 (3–9)	2 (1–3)	7 (3–10)	2 (1–4)	0.0002 (0.0001–0.0004)	8 (4–12)	9 (4–14)
Chromium	0.0022 (0.0015–0.0031)	0.0011 (0.0007–0.0016)	43 (28–59)	16 (4–33)	49 (32–68)	18 (12–24)	0.0018 (0.0012–0.0025)	58 (38–81)	67 (44–92)
Cobalt	0.0025 (0.0006–0.0050)	0.0012 (0.0003–0.0024)	47 (12–95)	16 (4–33)	54 (14–110)	18 (5–37)	0.0019 (0.0005–0.0039)	63 (16–128)	73 (18–147)
DEE	0.0290 (0.0143–0.0481)	0.0039 (0.0000–0.0138)	552 (272–917)	53 (0–190)	635 (313–1055)	60 (0–214)	0.0184 (0.0000–0.0337)	605 (272–1107)	695 (313–1269)
ETS	0.0073 (0.0000–0.0195)	0.0081 (0.0020–0.0148)	138 (0–370)	111 (27–203)	159 (0–426)	125 (30–228)	0.0076 (0.0008–0.0175)	249 (27–574)	284 (30–655)
Inorganic lead	0.0016 (0.0000–0.0058)	0.0004 (0.0000–0.0015)	30 (0–110)	5 (0–20)	35 (0–126)	6 (0–22)	0.0011 (0.0000–0.0040)	36 (0–130)	41 (0–149)
Ionising radiation	0.0001	0.0000	1	1	1	1	0.0001	2	2
Mineral oils	0.0183 (0.0063–0.0315)	0.0045 (0.0019–0.0073)	348 (119–600)	61 (27–100)	401 (137–691)	69 (30–113)	0.0125 (0.0044–0.0214)	410 (146–701)	470 (167–804)
Nickel	0.0003 (0.0000–0.0010)	0.0001 (0.0000–0.0005)	6 (0–19)	2 (0–6)	6 (0–22)	2 (0–7)	0.0002 (0.0000–0.0008)	8 (0–25)	9 (0–29)
PAHs	0.00003 (0.00002–0.00004)	0.00001 (0.00001–0.00002)	1 (0–1)	0 (0–0)	1 (0–1)	0 (0–0)	0.00003 (0.00001–0.00003)	1 (0–1)	1 (0–1)
Painters	0.0120 (0.0068–0.0175)	0.0013 (0.0007–0.0019)	228 (130–333)	18 (10–26)	262 (150–384)	20 (11–30)	0.0075 (0.0043–0.0110)	246 (140–360)	282 (161–413)
Radon	0.0056 (0.0028–0.0084)	0.0056 (0.0028–0.0084)	107 (53–160)	77 (39–116)	123 (61–184)	87 (43–130)	0.0056 (0.0028–0.0084)	184 (92–276)	209 (105–314)
Silica	0.0390 (0.0293–0.0493)	0.0033 (0.0024–0.0043)	743 (559–939)	45 (33–59)	856 (643–1081)	51 (37–67)	0.0241 (0.0180–0.0304)	789 (592–998)	907 (680–1147)
Steel foundry workers	0.0013 (0.0010–0.0016)	0.0001 (0.0001–0.0001)	25 (18–31)	1 (1–1)	28 (21–36)	1 (1–1)	0.0008 (0.0006–0.0010)	25 (19–32)	29 (22–37)
Strong inorganic acid mists	0.0024 (0.0000–0.0064)	0.0016 (0.0000–0.0042)	45 (0–123)	21 (0–58)	52 (0–141)	24 (0–66)	0.0020 (0.0000–0.0055)	67 (0–181)	76 (0–207)

Table 3 (*Continued*)

Agent	AF men (95% CI)	AF women (95% CI)	Attributable deaths men (95% CI)	Attributable deaths women (95% CI)	Attributable registrations men (95% CI)	Attributable registrations women (95% CI)	AF total (95% CI)	Attributable deaths totals (95% CI)	Attributable registrations totals (95% CI)
TCDD	0.0080 (0.0000–0.0212)	0.0026 (0.0000–0.0060)	152 (0–405)	36 (0–83)	175 (0–466)	40 (0–93)	0.0057 (0.0000–0.0149)	187 (0–488)	215 (0–559)
Tin miners	0.0030 (0.0020–0.0050)	0.0000 (0.0000–0.0000)	1 (0–1)	0 (0–0)	1 (0–1)	0 (0–0)	0.0000 (0.0000–0.0000)	1 (0–1)	1 (0–1)
Welders	0.0073 (0.0056–0.0090)	0.0010 (0.0008–0.0012)	138 (107–171)	14 (11–17)	159 (123–197)	16 (12–19)	0.0046 (0.0036–0.0057)	152 (118–188)	175 (135–216)
Totals[a]	**0.2111 (0.1921–0.2466)**	**0.0527 (0.0431–0.0688)**	**4020 (3659–4696)**	**725 (592–946)**	**4627 (4212–5406)**	**815 (666–1063)**	**0.1447 (0.1296–0.1720)**	**4745 (4251–5643)**	**5442 (4877–6469)**
Mesothelioma									
Asbestos	0.9700 (0.9600–0.9800)	0.8250 (0.7500–0.9000)	1699 (1681–1717	238 (216–260)	1699 (1681–1717)	238 (216–260)	0.9509 (0.9303–0.09687)	1937 (1898–1976)	1937 (1898–1976)

Abbreviations: AF = attributable fraction; DEE = diesel engine exhaust; ETS = environmental tobacco smoke; PAHs = polycyclic aromatic hydrocarbons; TCDD = 2,3,7,8-tetrachlorodibenzo-para-dioxin. [a]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.

(Vineis and Simonato, 1991; Steenland *et al*, 1996, 2003; Dreyer *et al*, 1997; Imbernon, 2003; Driscoll *et al*, 2004, 2005).

During 2009, the IARC reviewed recent evidence for all Group 1 carcinogens. In addition to lung cancer, ETS has now been classified as a Group 2A carcinogen for laryngeal cancer (Secretan *et al*, 2009). Although legislation in Britain has now banned smoking in all work places (as well as in public places), thus reducing ETS exposure, exposure in the past will continue to cause work-related lung and laryngeal cancer for some time in the future.

In addition, a number of other substances, not yet classified as Group 1 or 2A carcinogens, may be associated with respiratory cancers. For example, our overviews indicated associations with laryngeal cancer for occupational exposures to metalworking fluids, especially straight oil (Tolbert, 1997; Calvert *et al*, 1998) and wood dust (Ward *et al*, 1997).

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Adzersen K, Becker N, Steindorf K, Frentzelbeyme R (2003) Cancer mortality in a cohort of male German iron foundry workers. *Am J Ind Med* **43:** 295–305

Albin M, Magnani C, Krstev S, Rapiti E, Shefer I (1999) Asbestos and cancer: an overview of current trends in Europe. *Environ Health Perspect* **107:** 289–298

Alder N, Fenty J, Warren F, Sutton AJ, Rushton L, Jones DR, Abrams KR (2006) Meta-analysis of mortality and cancer incidence among workers in the synthetic rubber-producing industry. *Am J Epidemiol* **164:** 405–420

Alderson MR (1980) Cancer mortality in male hairdressers. *J Epidemiol Comm Health* **34:** 182–185

Altieri A, Garavello W, Bosetti C, Gallus S, La Vecchia C (2005) Alcohol consumption and risk of laryngeal cancer. *Oral Oncol* **41**(10)**:** 956–965

Ambroise D, Wild P, Moulin JJ (2006) Update of a meta-analysis on lung cancer and welding. *Scand J Work Environ Health* **32:** 22–31

Armstrong B, Hutchinson E, Unwin J, Fletcher T (2004) Lung cancer risk after exposure to polycyclic aromatic hycrocarbons: a review and meta-analysis. *Environ Health Perspect* **112:** 970–978

ATSDR (2008) Toxicological profile for cadmium. 1–512, Agency for Toxic Substances and Disease Registry (ATSDR), US Department of Health and Human Services, Public Health Service: http://www.atsdr.cdc.gov/toxprofiles/tp5.pdf

Austin H, Delzell E, Lally C, Rotimi C, Oestenstad K (1997) A case-control study of lung cancer at a foundry and two engine plants. *Am J Ind Med* **31:** 414–421

BEIR VI (1998) *Effects of Exposure to Radon*. National Academy Press: Washington.

Berrington A, Darby SC, Weiss HA, Doll R (2001) 100 years of observation on British radiologists: mortality from cancer and other causes 1897–1997. *Br J Radiol* **74:** 507–519

Bhatia R, Lopipero P, Smith AH (1998) Diesel exhaust exposure and lung cancer. *Epidemiology* **9:** 84–91

Boffetta P (2002) Involuntary smoking and lung cancer. *Scand J Work Environ Health* **28:** 30–40

Boffetta P, Autier P, Boniol M, Boyle P, Hill C, Aurengo A, Masse R, de The G, Valleron A-J, Monier R, Tubiana M (2010) An estimate of cancers attributable to occupational exposures in France. *J Occup Environ Med* **52**(4)**:** 399–406

Boffetta P, Jourenkova N, Gustavsson P (1997) Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. *Cancer Causes Control* **8:** 444–472

Boffetta P, Trichopoulos D (2002) Cancer of the lung, larynx, and pleura. In *Textbook of Cancer Epidemiology*, Adami HO, Hunter D, Trichopoulos S (eds), pp 248–280. Oxford University Press: Oxford

Bosetti C, Boffetta P, La Vecchia C (2007) Occupational exposures to polycyclic aromatic hydrocarbons, and respiratory and urinary tract cancers: a quantitative review to 2005. *Ann Oncol* **18:** 431–446

Brennan P, Buffler PA, Reynolds P, Wu AH, Wichmann HE, Agudo A, Pershagen G, Jockel KH, Benhamou S, Greenberg RS, Merletti F, Winck C, Fontham ETH, Kreuzer M, Darby S, Forastiere F, Simonato L, Boffetta P (2004) Secondhand smoke exposure in adulthood and risk of lung cancer among never smokers: a pooled analysis of two large studies. *Int J Cancer* **109:** 125–131

Breslow NE, Day NE (1987) *Statistical Methods in Cancer Research, Vol. 2, The Design and Analysis of Cohort Studies (IARC Scientific Publications No. 82)*. IARC: Lyon

Browne K, Gee JB (2000) Asbestos exposure and laryngeal cancer. *Ann Occup Hyg* **44**(4)**:** 239–250

Burns CJ (2005) Cancer among pesticide manufacturers and applicators. *Scand J Work Environ Health* **31:** 9–17

Calvert GM, Ward E, Schnorr TM, Fine LJ (1998) Cancer risks among workers exposed to metalworking fluids: a systematic review. *Am J Ind Med* **33:** 282 – 292

Cardis E, Gilbert ES, Carpenter L (1995) Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. *Rad Res* **142:** 117 – 132

Carpenter LM, Higgins CD, Douglas AJ, Fraser D, Beral V, Smith PG (1994) Combined analysis of mortality in three United Kingdom nuclear industry workforces, 1946 – 1988. *Rad Res* **138:** 224 – 238

Chen R, Seaton A (1998) A meta-analysis of painting exposure and cancer mortality. *Cancer Detect Prev* **22:** 533 – 539

Coggon D, Pannett B, Acheson ED (1984) Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. *J Natl Cancer Inst* **72:** 61 – 65

Coggon D, Pannett B, Wield G (1996) Upper aerodigestive cancer in battery manufacturers and steel workers exposed to mineral acid mists. *Occup Environ Med* **53:** 445 – 449

Cole P, Rodu B (2005) Epidemiologic studies of chrome and cancer mortality: a series of meta-analyses. *Reg Tox Pharm* **43:** 225 – 231

CRUK (2011) http://info.cancerresearchuk.org/cancerstats/types/Mesothelioma

Crump C, Crump KS, Hack E, Luippold RS, Mundt KA, Liebig E, Panko J, Paustenbach D, Proctor D (2003) Dose-response and risk assessment of airborne hexavalent chromium and lung cancer mortality. *Risk Anal* **23:** 1147 – 1163

Czene K, Tiikkaja S, Hemminki K (2003) Cancer risks in hairdressers: assessment of carcinogenicity of hair dyes and gels. *Int J Cancer* **105:** 108 – 112

Darnton AJ, McElvenny DM, Hodgson JT (2006) Estimating the number of asbestos-related lung cancer deaths in Great Britain from 1980 to 2000. *Ann Occup Hyg* **50:** 29 – 38

de Flora S (2000) Threshold mechanisms and site specificity in chromium (VI) carcinogenesis. *Carcinogenesis* **21:** 533 – 541

Doll R, Peto R (1981) *The Causes of Cancer*. Oxford University Press: Oxford

Dost A, Straughan JK, Sorahan T (2007) A cohort mortality and cancer incidence survey of recent entrants (1982 – 91) to the UK rubber industry: findings for 1983 – 2004. *Occup Med* **57:** 186 – 190

Dreyer L, Andersen A, Pukkala E (1997) Occupation. *Acta Pathol Microbiol Immunol Scand* **105**(suppl 76)**:** 68 – 79

Driscoll T, Nelson DI, Steenland K, Leigh J, Concha-Barrientos M, Fingerhut M, Pruss-Ustun A (2005) The global burden of disease due to occupational carcinogens. *Am J Ind Med* **48:** 419 – 431

Driscoll T, Steenland K, Pruss-Ustun A, Nelson DI, Leigh J (2004) *Occupational Carcinogens: Assessing the Environmental Burden of Disease at National and Local Levels*. World Health Organization: Geneva

Eduljee GH, Dyke P (1996) An updated inventory of potential PCDD and PCDF emission sources in the UK. *Sci Total Environ* **177:** 303 – 321

Fu H, Boffetta P (1995) Cancer and occupational exposure to inorganic lead compounds: a meta-analysis of published data. *Occup Environ Med* **52:** 73 – 81

Goldberg M, Imbernon E, Rolland P, Gilg Soit Ilg A, Saves M, de Quillacq A, Frenay C, Chamming S, Arveux P, Boutin C, Launot G, Pairon J, Astoul P, Galateau-Salle F, Brochard P (2006) The French National Mesothelioma Surveillance Program. *Occup Environ Med* **63:** 390 – 395

Goodman M, Morgan RW, Ray RM, Malloy CD, Zhao K (1999) Cancer in asbestos-exposed occupational cohorts: a meta-analysis. *Cancer Causes Control* **10:** 453 – 465

Griffiths H, Molony NC (2003) Does asbestos cause laryngeal cancer? *Clin Otolaryngol* **28**(3)**:** 177 – 182

Hansen ES (1997) A cohort mortality study of foundry workers. *Am J Ind Med* **32:** 223 – 233

Hayes RB (1997) The carcinogenicity of metals in humans. *Cancer Causes Control* **8:** 371 – 385

Hodgson JT, Jones RD (1990) Mortality of a cohort of tin miners 1941 – 86. *Br J Ind Med* **47:** 665 – 676

Howel D, Arblaster L, Swinburne L, Schweiger M, Renvoize E, Hatton P (1997) Routes of asbestos exposure and the development of mesothelioma in an English region. *Occup Environ Med* **54:** 403 – 409

HSE (1998) Occupational Exposure to Ionising Radiation 1990 – 1996. Analysis of doses reported to the Health and Safety Executive's Central Index of Dose Information.

HSE (2010) Mesothelioma: overall scale including trends. Health and Safety Executive: http://www.hse.gov.uk/statistics/causdis/mesothelioma/scale.htm

HSE (2012a) The burden of occupational cancer in Great Britain – technical report: cancer of the larynx. Health and Safety Executive: http://www.hse.gov.uk/cancer/

HSE (2012b) The burden of occupational cancer in Great Britain – technical report: lung cancer. Health and Safety Executive: http://www.hse.gov.uk/cancer/

HSE (2012c) The burden of occupational cancer in Great Britain – technical report: mesothelioma. Health and Safety Executive: http://www.hse.gov.uk/cancer/

IARC (1984) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Polynuclear Aromatic Hydrocarbons, Part 3: Industrial Exposures in Aluminium Production, Coal Gasification, Coke Production, and Iron and Steel Founding*, Vol. 34. International Agency for Research on Cancer: Lyon

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42*, Vol. 7. International Agency for Research on Cancer: Lyon

IARC (1989) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Some Organic Solvents, Resin Monomers and Related Compounds, Pigments and Occupational Exposures in Paint Manufacture and Painting*, Vol. 47. International Agency for Research on Cancer: Lyon

IARC (1990) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Chromium, Nickel and Welding*, Vol. 49. International Agency for Research on Cancer: Lyon

IARC (1992) *IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans: Occupational Exposures to Mists and Vapours from Strong Inorganic Acids; and Other Industrial Chemicals*, Vol. 54. International Agency for Research on Cancer: Lyon

IARC (1993) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry*, Vol. 58. International Agency for Research on Cancer: Lyon

IARC (1997) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Silica, Some Silicates, Coal Dust and Para- Aramid Fibrils*, Vol. 68. International Agency for Research on Cancer: Lyon

IARC (2004) *IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans: Tobacco Smoke and Involuntary Smoking*, Vol. 83. International Agency for Research on Cancer: Lyon

IARC (2006) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Cobalt in Hard Metals and Cobalt Sulfate, Gallium Arsenide, Indium Phospide and Vanadium Pentoxide*, Vol. 86. International Agency for Research on Cancer: Lyon

Imbernon E (2003) *Estimation du nombre de cas de certains cancers attribuables a' des facteurs professionnels en France*. Institut de Veille Sanitaire: Paris

IPCS (1998) *Chrysotile Asbestos. Environmental Health Criteria 203*. World Health Organization: Geneva

Irvine HDV, Lamont DW, Hole DJ, Gillis CR (1993) Asbestos and lung cancer in Glasgow and the west of Scotland. *Br Med J* **306:** 1503 – 1506

Jones DR, Sutton AJ, Abrams KR, Fenty J, Warren F, Rushton L (2009) Systematic review and meta-analysis of mortality in crop protection product manufacturing workers. *Occup Environ Med* **66:** 7 – 15

Kogevinas M, Becher H, Benn T (1997) Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: an expanded and updated international cohort study. *Am J Epidemiol* **145:** 1061 – 1075

Kurihara N, Wada O (2004) Silicosis and smoking strongly increase lung cancer risk in silica-exposed workers. *Ind Health* **42:** 303 – 314

Lamba AB, Ward MH, Weeks JL, Dosemeci M (2001) Cancer mortality patterns among hairdressers and barbers in 24 US States, 1984 to 1995. *J Occup Environ Med* **43:** 250 – 258

Landrigan PJ, Boffetta P, Apostoli P (2000) The reproductive toxicity and carcinogenicity of lead: a critical review. *Am J Ind Med* **38:** 231 – 243

Lee-Feldstein A (1986) Cumulative exposure to arsenic and its relationship to respiratory cancer among copper smelter employees. *J Occup Environ Med* **28:** 296 – 302

Lipsett M, Campleman S (1999) Occupational exposure to diesel exhaust and lung cancer: a meta-analysis. *Am J Pub Health* **89:** 1009 – 1017

McElvenny D, Darnton A, Price M, Hodgson J (2005) Mesothelioma mortality in Great Britain from 1968 to 2001. *Occup Med* **55:** 79 – 87

McLean D, Pearce N, Langseth H, Jappinen P, Szadkowska-Stanczyk I, Persson B, Wild P, Kishi R, Lynge E, Henneberger P, Sala M, Teschke K, Kauppinen T, Colin D, Kogevinas M, Boffetta P (2006) Cancer mortality in workers exposed to organochlorine compounds in the pulp and paper

industry: an international collaborative study. *Environ Health Perspect* **114:** 1007 – 1012

Moulin JJ (1997) A meta-analysis of epidemiologic studies of lung cancer in welders. *Scand J Work Environ Health* **23:** 104 – 113

Moulin JJ, Wild P, Romazini S, Lasfargues G, Peltier A, Bozec C, Deguerry P, Pellet F, Perdrix A (1998) Lung cancer risk in hard-metal workers. *Am J Epidemiol* **148:** 241 – 248

Muirhead CR, Goodhil AA, Haylock RGE, Vokes J, Little MP, Jackson DA, O'Hagan JA, Thomas JM, Kendall GM, Silk TJ, Bingham D, Berridge GLC (1999) Occupational radiation exposure and mortality: second analysis of the National registry for Radiation Workers. *J Radiol Protect* **19:** 3 – 26

NIOSH (1998) *Occupational Exposure to Metalworking Fluids*. DHHS (NIOSH) Publication No. 98-102

NRPB (2000) *Health Risks of Radon*. National Radiological Protection Board: Chilton

Nurminen M, Karjalainen A (2001) Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. *Scand J Work Environ Health* **27:** 161 – 213

Olshan A (2006) Cancer of the larynx. In *Cancer Epidemiology and Prevention* Schottenfeld D, Fraumeni J (eds), 3rd ed, pp 627 – 637. Oxford University Press: New York

Omar RZ, Barber JA, Smith PG (1999) Cancer mortality and morbidity among plutonium workers at the Sellafield plant of British Nuclear Fuels. *Br J Cancer* **79:** 1288 – 1301

Pelucchi C, Gallus S, Garavello W, Bosetti C, La Vecchia C (2006a) Cancer risk associated with alcohol and tobacco use: focus on upper aero-digestive tract and liver. *Alcohol Research & Health. J Natl Inst Alcohol Abuse Alcoholism* **29**(3)**:** 193 – 198

Pelucchi C, Pira E, Piolatto G, Coggiola M, Carta P, La Vecchia C (2006b) Occupational silica exposure and lung cancer risk: a review of epidemiological studies 1996 – 2005. *Ann Oncol* **17:** 1039 – 1050

Peto R, Lopez AD, Boreham J, Heath C, Thun M (1994) *Mortality from Tobacco in Developed Countries, 1950 – 2000*. Oxford University Press: Oxford

Pukkala E, Noksokoivisto P, Roponen P (1992) Changing cancer risk pattern among Finnish hairdressers. *Int Arch Occup Environ Health* **64:** 39 – 42

Quinn M, Wood H, Cooper N, Rowan S (eds) (2005) Cancer Atlas of the United Kingdom and Ireland 1991 – 2000. In *Series on Medical and Population Subjects No. 68*. Office for National Statistics: London

Rachet B, Quinn MJ, Cooper N, Coleman MP (2008a) Survival from cancer of the lung in England and Wales up to 2001. *Br J Cancer* **99:** S40 – S42

Rachet B, Quinn MJ, Cooper N, Coleman MP (2008b) Survival from cancer of the larynx in England and Wales up to 2001. *Br J Cancer* **99:** S35 – S37

Rafferty MA, Fenton JE, Jones AS (2001) The history, aetiology and epidemiology of laryngeal carcinoma. *Clin Otolaryngol* **26**(6)**:** 442 – 446

Rajaraman P, Sigurdson AJ, Doody MM, Freedman DM, Hauptman M, Ron E, Alexander BH, Linet MS (2006) Lung cancer risk among US radiologic technologists, 1983 – 1998. *Int J Cancer* **119:** 2481 – 2486

Rake C, Gilham C, Hatch J, Darnton A, Hodgson J, Peto J (2009) Occupational, domestic and environmental mesotheliomia risks in the British population: a case-control study. *Br J Cancer* **100**(7)**:** 1175 – 1183

Rodriguez V, Tardon A, Kogevinas M, Prieto CS, Cueto A, Garcia M, Menendez IA, Zaplana J (2000) Lung cancer risk in iron and steel foundry workers: a nested case control study in Asturias, Spain. *Am J Ind Med* **38:** 644 – 650

Sathiakumar N, Delzell E, Amoateng-Adjepong Y, Larson R, Cole P (1997) Epidemiologic evidence on the relationship between mists containing sulfuric acid and respiratory tract cancer. *Crit Rev Tox* **27:** 233 – 251

Schaller KH, Angerer J (1992) Biological monitoring in the occupational setting—relationship to cadmium exposure. *IARC Sci Publ* **118:** 53 – 63

SCOTH (1998) *Report of the Scientific Committee on Tobacco and Health*. Stational Office: London

SCOTH (2004) Scientific Committee on Tobacco and Health (SCOTH): Secondhand Smoke: Review of Evidence Since 1998, Update of Evidence on Health Effects of Secondhand Smoke.

Secretan B, Straif K, Baan R, Gross Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V, WHO International Agency for Research on Cancer Monograph Working Group (2009) A review of human carcinogens – Part E: tobacco, areca nut, alcohol, cola smoke and salted fish. *Lancet* **10:** 1033 – 1034

Seilkop SK, Oller AR (2003) Respiratory cancer risks associated with low-level nickel exposure: an integrated assessment based on animal, epidemiological, and mechanistic data. *Reg Tox Pharm* **37:** 173 – 190

Siemiatycki J, Richardson L, Straif K, Latreille B, Lakhani R, Campbell S, Rousseau MC, Boffetta P (2004) Listing occupational carcinogens. *Environ Health Perspect* **112:** 1447 – 1459

Silbergeld EK, Waalkes M, Rice JM (2000) Lead as a carcinogen: experimental evidence and mechanisms of action. *Am J Ind Med* **38:** 316 – 323

Sorahan T, Faux AM, Cooke MA (1994) Mortality among a cohort of United Kingdom steel foundry workers with special reference to cancers of the stomach and lung, 1946 – 90. *Occup Environ Med* **51:** 316 – 322

Sorahan T, Parkes HG, Veys CA, Waterhouse JA, Straughan JK, Nutt A (1989) Mortality in the British rubber industry 1946 – 85. *Br J Ind Med* **46:** 1 – 10

Sorahan T, Williams SP (2005) Mortality of workers at a nickel carbonyl refinery, 1958 – 2000. *Occup Environ Med* **62:** 80 – 85

Soskolne CL, Jhangri GS, Siemiatycki J, Lakhani R, Dewar R., Burch JD, Howe GR, Miller AB (1992) Occupational exposure to sulfuric acid in southern Ontario, Canada, in association with laryngeal cancer. *Scand J Work Environ Health* **18**(4)**:** 225 – 232

Spirtas R, Heineman E, Bernstien L, Beebe G, Keehn R, Stark A, Harlow B, Benichou J (1994) Malignant mesothelioma: attributable risk of asbestos exposure. *Occup Environ Med* **51:** 804 – 811

Steenland K, Beaumont J (1989) Further follow-up and adjustment for smoking in a study of lung cancer and acid mists. *Am J Ind Med* **16:** 347 – 354

Steenland K, Boffetta P (2000) Lead and cancer in humans: where are we now? *Am J Ind Med* **38:** 295 – 299

Steenland K, Burnett C, Lalich N, Ward E, Hurrell J (2003) Dying for work: the magnitude of US mortality from selected causes of death associated with occupation. *Am J Ind Med* **43:** 461 – 482

Steenland K, Loomis D, Chy C, Simonsen N (1996) Review of occupational lung carcinogens. *Am J Ind Med* **29:** 474 – 490

Steenland K, Mannetje A, Boffeta P, Stayner L, Attfield MD, Chen J, Dosemeci M, de Klerk NH, hnizdo E, Koskela RS, Checkoway H (2001) Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: an IARC multicentre study. *Cancer Causes Control* **12:** 773 – 784

Straughan JK, Sorahan T (2000) Cohort mortality and cancer incidence survey of recent entrants (1982 – 91) to the United Kingdom rubber industry: preliminary findings. *Occup Environ Med* **57:** 574 – 576

Sweetman A, Keen C, Healy J, Ball E, Davy C (2004) Occupational exposure to dioxins at UK worksites. *Ann Occup Hyg* **48:** 425 – 437

Tolbert PE (1997) Oils and cancer. *Cancer Causes Control* **8:** 386 – 405

UNSCEAR (2008) *Effects of Ionizing Radiation*. United Nations Scientific Committee on the Effects of Atomic Radiation. UNSCEAR 2006

Unwin J, Cocker J, Scobbie E, Chambers H (2006) An assessment of occupational exposure to polycyclic aromatic hydrocarbons in the UK. *Ann Occup Hyg* **50:** 395 – 403

Verougstraete V, Lison D, Hotz P (2003) Cadmium, lung and prostate cancer: a systematic review of recent epidemiological data. *J Tox Environ Health* **6:** 227 – 256

Vineis P, Simonato L (1991) Proportion of lung and bladder cancers in males resulting from occupation: a systematic approach. *Arch Environ Health* **46:** 6 – 15

Ward EM, Burnett CA, Ruder A, Davis-King K (1997) Industries and cancer. *Cancer Causes Control* **8**(3)**:** 356 – 370

Ward E, Okun A, Ruder A, Fingerhut M, Steenland K (1992) A mortality study of workers at seven beryllium processing plants. *Am J Ind Med* **22:** 885 – 904

Wight R, Paleri V, Arullendran P (2003) Current theories for the development of nonsmoking and nondrinking laryngeal carcinoma. *Curr Opin Otolaryngol Head Neck Surg* **11**(2)**:** 73 – 77

Wild P, Perdrix A, Romazini S, Moulin JJ, Pellet F (2000) Lung cancer mortality in a site producing hard metals. *Occup Environ Med* **57:** 568 – 573

Yates D, Corrin B, Stidolph P, Browne K (1997) Malignant mesothelioma in south east England: clinicopathological experience of 282 cases. *Thorax* **52:** 507 – 512

Zhong L, Goldberg M, Parent ME, Hanley JA (2000) Exposure to environmental tobacco smoke and the risk of lung cancer: a meta-analysis. *Lung Cancer* **27:** 3 – 18

Appendix

British Occupational Cancer Burden Study Group

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