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 frequency. In the United Kingdom in the 1990s, laryngeal cancer (IARC, 2004; Altieri et al., 2005; Pelucchi et al., 2005; McElvenny 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 ~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
| 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**  |                    |                                      |                                                             |          |
| 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 | CAREX |          |
| Beryllium                     | Extraction and processing; aircraft, aerospace, electronics and nuclear industries; jewelers | 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 & chlorophenox herbicides; waste incineration; PCB production; pulp and paper bleaching | Lung limited | LFS, COE |          |
| Environmental tobacco smoke   | Lung sufficient | 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 | Small numbers exposed |          |
| Nickel compounds              | Nickel miners; metal fabrication; grinding; electroplating, and welding | Lung sufficient | CAREX | Clydach refinery only |
| 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  | Pickling operations; steel industry; petrochemical industry; phosphate acid fertilizer manufacturing | Lung limited | CAREX |
|    containing sulphuric acid | Larynx sufficient |                              | |
| Talc containing asbestiform fibres | Manufacture of pottery, paper, paint and cosmetics | Lung sufficient | Included with asbestos |
| Exposure circumstances       | Lung sufficient    |                                   |                              |
| 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) | Radon; silica   | Lung sufficient | Small numbers exposed |
|    with exposure to radon     |                                                                 |                              | |
| 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**

| Agent/Group | Exposure circumstances | Evidence of carcinogenicity in humans | Source of data for estimation of numbers ever exposed over REP | Comments |
|-------------|------------------------|---------------------------------------|-------------------------------------------------------------|----------|
| z-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 | CAREX | Included with dioxins |
| PAHs:                         | Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics | Lung limited | CAREX | Included with dioxins |
| Dibenz(a,j)anthracene         |                   |                                      |                                                               |          |
| Cyclopenta(c,d)pyrene,       |                   |                                      |                                                               |          |
| Dibenzo(a,j)pyrene            |                   |                                      |                                                               |          |
| Exposure circumstances       |                   |                                      |                                                               |          |
| Art glass, glass containers and pressed ware (manufacture) | Lead arsenic; antimony oxides; silica; asbestos; other metal oxides; PAHs | Lung limited | CAREX | Included with arsenic, asbestos, silica, PAHs |
| Hairdressers and barbers      | Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols | Lung limited | CAREX | Included with ETS |
| Isopropyl alcohol manufacture, strong acid process | Disopropyl sulphate | Lung limited | CAREX | Included with strong acids |
| Rubber industry               |                   |                                      |                                                               |          |
| Welders*                      |                   |                                      |                                                               |          |

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. *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, haematitic mining and 2-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 asbestos fibre (included with asbestos); epichlorhydrin (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, serpentinite (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
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 estimate for lung cancer for the high-exposed workers. Coggon et al (1994) 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 (Sathishkumar 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.
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 chrome production, chrome 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 suggested that the relationship between smoking and lung cancer is increased for those who are exposed to chromium, and a meta-analysis by Verougstraete et al. (2003) found an overall meta-SMR of 1.12 (95% CI = 1.00–1.04). For the AF estimation, the industry-wide OR for lung cancer of 1.30 (95% CI 1.00–1.66) was used.

Kurihara and Wada’s (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 for the absence of silicosis (95% CI 0.81–1.15). A systematic review by Pelucchi et al. (2006) found a pooled RR of 1.34 (95% CI 1.25–1.43); 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 (DDE)** 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 Campdemen, 1999). Lipsett and Campdemen reviewed 30 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 (Coggan 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 (B 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 in British radiological workers (Steenland and Boffetta, 2000); US radiological technicians (Rajaraman et al, 2000); nuclear industry workers (Carpenter et al, 1994; Omar et al, 1999); the National Registry for Radiation Workers (Muirhead et al, 1997); and combined analyses 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 a 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 × 20/100)), where x is the mean benzo-a-pyrene (BaP) level (for example, 8-h time-weighted average (TWA)) in μg m^-3 for the exposed. This gives a mean RR of 1.31 (95% CI = 1.16 – 1.48) at 100 μg 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 μg m^-3, with 50% of the samples below 0.01 μg m^-3, 90% below 0.75 μg m^-3 and 95% below 2.0 μg 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), < 0.1 (midpoint 0.05), 0.1–1 (midpoint 0.5), 1–10 (midpoint 5), > 10 (midpoint 10). The RR = 1.3 (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 μg 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-p-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; 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, 1991; Lambur et al, 2001; Creme 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 foundling** Potential exposures in the iron and steel foundry industry include silica, cobalt, airborne PAHs, chrome 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 MRR for lung cancer ranged from 1.2 to 4.2, with an inverse-variance-weighted average of 0.99 (95% CI = 0.91–1.08) (Burns, 2005). However, an RR of ≤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). Ambrose 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 goods, 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 stewards 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% (95% CI = 8.3–20.7).

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                      | 0.0181                        | 0.0039                          |

Abbreviations: DEE = diesel engine exhaust; ETS = environmental tobacco smoke; TCDD = 2,3,7,8-tetrachlorodibenzo-p-dioxin.
(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 252,017 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)                                  | 0.0037           | 3                                   | (1 – 5)                                  |
| Rubber industry              | 0.0014          | (0.0000 – 0.0050) | 0.0006                           | (0.0000 – 0.0020)                 | 1                                      | (0 – 3)                                  | 0.0012           | 1                                   | (0 – 3)                                  |
| Strong inorganic acid mists  | 0.0229          | (0.0083 – 0.0511) | 0.0152                           | (0.0055 – 0.0341)                 | 14                                     | (5 – 31)                                 | 0.0213           | 16                                  | (6 – 36)                                 |
| **Totals**                   | 0.0288          | (0.0138 – 0.0569) | 0.0157                           | (0.0060 – 0.0348)                 | 17                                     | (3 – 50)                                 | 0.0261           | 20                                  | (5 – 101)                               |
| **Lung cancer**              |                 |                   |                                  |                                   |                                        |                                          |                  |                                     |                                          |
| Arsenic                      | 0.0048          | (0.0023 – 0.0084) | 0.0016                           | (0.0000 – 0.0058)                 | 91                                     | (43 – 161)                                | 0.0034           | 0.0261                              | (0.0013 – 0.0072)                                 |
| Asbestos                     | 0.0892          | (0.0835 – 0.0950) | 0.0173                           | (0.0131 – 0.0211)                 | 1699                                   | (1590 – 1810)                             | 0.0591           | 19.37                               | (0.0540 – 0.0640)                                 |
| Beryllium                    | 0.0002          | (0.0000 – 0.0005) | 0.0001                           | (0.0000 – 0.0003)                 | 5                                      | (0 – 10)                                 | 0.0002           | 6                                   | (0 – 14)                                 |
| Cadmium                      | 0.0003          | (0.0001 – 0.0005) | 0.0002                           | (0.0001 – 0.0002)                 | 6                                      | (3 – 9)                                  | 0.0002           | 8                                   | (4 – 12)                                 |
| Chromium                     | 0.0022          | (0.0015 – 0.0031) | 0.0011                           | (0.0007 – 0.0016)                 | 43                                     | (28 – 59)                                 | 0.0018           | 58                                  | (0.0012 – 0.0025)                                 |
| Cobalt                       | 0.0025          | (0.0006 – 0.0050) | 0.0012                           | (0.0003 – 0.0024)                 | 47                                     | (12 – 95)                                 | 0.0019           | 63                                  | (0.0005 – 0.0039)                                 |
| DEE                          | 0.0290          | (0.0143 – 0.0481) | 0.0039                           | (0.0000 – 0.00138)                | 552                                    | (272 – 917)                               | 0.0184           | 605                                 | (0.0000 – 0.00337)                                 |
| ETS                          | 0.0073          | (0.0000 – 0.0195) | 0.0081                           | (0.0020 – 0.0148)                 | 138                                    | (27 – 203)                                | 0.0076           | 249                                 | (0.0008 – 0.0175)                                 |
| Inorganic lead               | 0.0016          | (0.0000 – 0.0058) | 0.0004                           | (0.0000 – 0.0015)                 | 30                                     | (0 – 110)                                 | 0.0011           | 36                                  | (0.0000 – 0.0040)                                 |
| 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 – 660)                               | 0.0125           | 410                                 | (0.0044 – 0.0214)                                 |
| Nickel                       | 0.0003          | (0.0000 – 0.0010) | 0.0001                           | (0.0000 – 0.0005)                 | 6                                      | (0 – 19)                                  | 0.0002           | 8                                   | (0.0000 – 0.0008)                                 |
| PAHs                         | 0.0003          | (0.0002 – 0.0004) | 0.0001                           | (0.0000 – 0.0002)                 | 1                                      | (0 – 1)                                  | 0.0003           | 1                                   | (0 – 1)                                  |
| Painters                     | 0.0120          | (0.0068 – 0.0175) | 0.0013                           | (0.0007 – 0.0019)                 | 228                                    | (130 – 333)                               | 0.0075           | 246                                 | (0.0043 – 0.0110)                                 |
| Radon                        | 0.0056          | (0.0028 – 0.0084) | 0.0056                           | (0.0028 – 0.0084)                 | 107                                    | (53 – 160)                                | 0.0056           | 184                                 | (0.0028 – 0.0084)                                 |
| Silica                       | 0.0390          | (0.0293 – 0.0493) | 0.0333                           | (0.0244 – 0.0403)                 | 743                                     | (559 – 939)                                | 0.0241           | 789                                 | (0.0180 – 0.0304)                                 |
| Steel foundry workers        | 0.0013          | (0.0001 – 0.0016) | 0.0001                           | (0.0001 – 0.0001)                 | 25                                     | (18 – 31)                                 | 0.0008           | 25                                  | (0.0006 – 0.0010)                                 |
| Strong inorganic acid mists  | 0.0024          | (0.0000 – 0.0064) | 0.0016                           | (0.0000 – 0.0042)                 | 45                                     | (0 – 123)                                 | 0.0020           | 67                                  | (0.0000 – 0.0055)                                 |
(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 workplaces (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 overview 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 (2003) Cancer mortality in male hairdressers. J Epidemiol Commun Health 57: 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) A 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 Commun Health 34: 182 – 185

Amespy Stott JA, Calvert J, Melia P, Small McHale P, Backhouse CR, Bhatia R, Lopipero P, Smith AH (1998) Diesel exhaust exposure and lung cancer. Epidemiology 9: 84 – 91

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

Bofetta 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

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

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

Bosetti C, Bofetta P, La Vecchia C (2007) Occupational exposures to polycyclic aromatic hydrocarbons. Cancer Causes Control 18: 444 – 472

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

Brennan P, Bufler PA, Reynolds P, Wu AH, Wichmann HE, Agudo A, Preshagen G, Jockel KH, Benhamou S, Greenberg RS, Merletti F, Winck C, Fontham ETH, Kreuzer M, Darby S, Forastiere F, Simonato L, Bofetta 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

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British Journal of Cancer (2012) 107(51), 556 – 570
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 J, Pellet A, Bozec C, Deguerry J, 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 Prot* 19: 3 – 26

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

NPK (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 site of British Nuclear Fuels. *Br J Cancer* 79: 1288 – 1301

Pelucchi C, Gallus S, 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, Pirolato G, Coggia 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) *Health Risks of Radon*. Oxford University Press: Oxford

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

Quinn CJ, 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: 540 – 542

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: 535 – 537

Rafferty MA, Fenton JE, Jones AS (2001) The history, aetiology and epidemiology of laryngeal carcinoma. *Clin Otolaryngol* 26(4): 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 – 1993: the NHLBI lung health study. *Am J Epidemiol* 164: 835 – 846

Rake C, Gilham C, Hatch J, Darnton A, Hodgson J, Peto J (2009) Occupational, domestic and environmental mesothelioma 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

Sathiyakumar 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 Toxicol* 27: 233 – 251

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

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

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

Seccom Project

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

Solomon DI, occupational factors in Finland. *Scand J Work Environ Health* 18(4): 225 – 232

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

Steinland K, Beaumont J (1989) Further follow-up and adjustment for smoking in a study of lung cancer and acid mists. *Am J Ind Med* 17: 347 – 354

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

Steinland 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

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

Steinland K, Mannette J, Boffetta P, Stayer L, Attfield MD, Chen J, Dosemeci M, de Klerk NH, Inhibo 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

Straugham 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, Dary 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

Ververgaertse V, Lison D, Hotz P (2003) Cadmium, lung and prostate cancer: a systematic review of recent epidemiological data. *J Tox Environ Health* 66: 227 – 256

Virta 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: 685 – 904

Wight R, Paleri V, Arulendran 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. *Occip 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

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Appendix

British Occupational Cancer Burden Study Group

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