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Occupational cancer in Britain

Remaining cancer sites: brain, bone, soft tissue sarcoma and thyroid

Terry Brown[3], Charlotte Young[2] and Lesley Rushton[*,1] with the British Occupational Cancer Burden Study Group

[3]Institute of Environment and Health, Cranfield Health, Cranfield University, Cranfield MK43 0AL, UK; [2]Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire SK17 9JN, UK; [1]Department of Epidemiology and Biostatistics, School of Public Health and MRC-HPA Centre for Environment and Health, Imperial College London, St Mary's Campus, Norfolk Place, London W2 3PG, UK

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OVERVIEW OF CANCERS

This paper reviews the four cancer sites: brain, bone, sarcoma and thyroid, which do not fit readily into the organ-specific groups defined for the other papers in this supplement. Ionising radiation is a cause of cancers of both the bone and thyroid, and thus this exposure will be considered together in the relevant section.

Brain and central nervous system (CNS) cancers

Primary brain and CNS cancers are rare. Over the past 10 years in Britain, brain cancers have accounted for about 1.8% of male and 1.4% of female cancers, being 20 – 50% more common in men than women. Other cancers of the CNS have accounted for an additional 0.3% of all male and female cancers. The most common types of primary brain tumours are gliomas, meningiomas and astrocytomas (Kleihues and Cavanee, 2000).

Age-specific incidence and mortality rates in both sexes have shown upward trends in all age groups (Preston-Martin *et al*, 2006) since the 1970s and the 1950s, respectively (Quinn *et al*, 2005). There have been few positive findings in searching for environmental causal factors for brain cancer, probably because they comprise a heterogeneous group of cancers with different aetiologies. The nature and magnitude of the risk factors for primary brain tumours are not clear (Wrensch *et al*, 2002), and the definition and classification of these tumours often differ between studies. Retrospective assessment of exposure along with undefined latency periods for induction of these cancers has led to imprecise risk estimates. Despite these limitations, exposure to inorganic lead, non-arsenical insecticides and work in petroleum refining have been identified as relevant occupational risk factors for brain cancer.

Survival from brain cancer is low; 1-year relative survival for patients diagnosed during 1996 – 1999 was reported as 30.4% in men and 28.8% in women, and has shown little change over the years (Rachet *et al*, 2008). Five-year survival was reported as 11.6% in men and 14% in women, with that for men showing a significant improvement since 1986 – 1990.

Bone cancer

Cancers that arise in the bone or articular cartilage account for ~0.5% of all malignant neoplasms in humans (Miller *et al*, 2006). In Britain, over recent years, the number of cancers registered has been relatively stable, whereas the number of people who died from the condition steadily increased between 1995 and 2004. There are three main types of bone cancer: osteosarcoma (the most common), chondrosarcoma and Ewing's sarcoma. Osteosarcoma peaks in adolescence (around 17 years) and later in life (around 80 years), whereas chondrosarcoma is rare in childhood and rates rise with advancing age (peaking between 70 and 80 years of age). Ewing's sarcoma has a similar age distribution to osteosarcoma for early years, but the condition is rare over 35 years of age.

Survival rates have improved over the past 35 years, being consistently higher in females (Cancer Research UK, 2007a), and cancer treatment is usually successful (two out of three people cured) if the disease has not spread to other parts of the body. Five-year survival rates generally vary between 10% and 90% depending on the type, grade and stage of disease, as well as age at diagnosis. The main exposure that induces bone cancer is ionising radiation, with the exception of Ewing's sarcoma (Miller *et al*, 2006). Occupational exposure to radium has been associated with osteosarcoma, and osteosarcoma and chondrosarcoma have both been linked with exposure to plutonium. Other non-occupational risk factors for bone cancer include high-dose therapeutic radiation, predisposing genetic factors and Paget's disease.

Soft-tissue sarcoma (STS)

Soft-tissue sarcoma arises in fibrous tissue, fat, muscle, blood and lymph vessels and cartilage, each with potentially distinct aetiologies (Berwick, 2006; Toro *et al*, 2006). In GB, there are ~1200 new cases diagnosed and 660 STS-related deaths each year (Swerdlow *et al*, 2001). In addition, about 90 men and women are diagnosed with Kaposi's sarcoma, of which there are about eight

*Correspondence: Dr L Rushton; E-mail: l.rushton@imperial.ac.uk
See Appendix for the members of the British Occupational Cancer Burden Study Group.

deaths each year. There have been substantial increases in the incidence of STS among adults (with the exception of an unchanged rate in young women), which may largely be because of changes in reporting and coding (Swerdlow *et al*, 2001). For STS, overall the 5-year survival rate is between 50 and 60% (Storm and Hat, 1998), with a wide variation depending on anatomical site and tumour histology (Weitz *et al*, 2003; Mendenhall *et al*, 2005). The aetiology of STS is difficult to study because of the relatively low incidence and inherent misclassification of histology (Berwick, 2006), with the different histological subtypes often grouped together masking more in-depth analysis. Occupational risk factors may not be uniform across these subtypes (Hoppin *et al*, 1999).

Thyroid cancer

This cancer is relatively uncommon but is the most common malignancy of the endocrine system (Ron and Schneider, 2006) and is more common in women (2.1% of cancers in women) than in men (0.7% of cancers in men) (Parkin *et al*, 2001). In Britain, the numbers of registered cancers have steadily increased, although the number of deaths has been steady over recent years. There are four main types of thyroid cancer: papillary, follicular, anaplastic and medullary, these being either well differentiated (papillary, follicular and medullar) or poorly differentiated (i.e., anaplastic). Papillary thyroid cancer is the most common, accounting for about 60% of diagnosed cases (Cancer Research UK, 2007b). Thyroid cancer survival rates have improved over the past 35 years, with rates being consistently higher in women. Survival rates generally depend on tumour histology, stage and age at diagnosis. Anaplastic thyroid cancer has the lowest (10–20%) 5-year survival rates, and papillary thyroid cancer has the best 5-year survival rate ($\sim$100%) if diagnosed early.

Radiation is one of the main risk factors clearly associated with thyroid cancer (Ron and Schneider, 2006), and these risks are particularly evident in those exposed during childhood. Well-differentiated papillary cancer is the principal cell type induced by radiation, but an increase in follicular and anaplastic carcinomas may occur as the population ages. Other non-occupational risk factors for thyroid cancer include a history of benign thyroid diseases, a family history of thyroid cancer and dietary factors, especially iodine deficiency.

METHODS

Occupational risk factors

Group 1 and 2A human carcinogens The agents that the International Agency for Research on Cancer (IARC) has classified as either definite (Group 1) or probable (Group 2A) human carcinogens for brain, bone, STS and thyroid cancer are summarised in Table 1.

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 target the brain, bone, soft-tissue sarcoma or thyroid and for which burden has been estimated

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in human	Source of data for estimation of numbers ever exposed over REP	Comments
Group 1: Carcinogenic to humans				
Agents, groups of agents				
Ionising radiation	Radiologists, technologists, nuclear workers, radium-dial painters, underground miners, plutonium workers, cleanup workers following nuclear accidents and aircraft crew	Bone *sufficient* Thyroid *sufficient*	CIDI LFS (male travel and flight attendants) British Airways Stewards & Stewardesses Union (1956–1995)	
2,3,7,8-tetrachlorodibenzo-*para*-dioxin (TCDD)	Production; use of chlorophenols and chlorophenoxy herbicides; waste incineration; PCB production; pulp and paper bleaching	STS *sufficient*	LFS	
Group 2A: Probably carcinogenic to humans				
Agents, groups of agents				
Non-arsenical insecticides	Production; pest control and agricultural workers; flour and grain mill workers	Brain *limited*	LFS	
Epichlorohydrin	Production and use of resins, glycerine and propylene-based rubbers; used as a solvent	Brain *inadequate*	CAREX	
Inorganic lead	Lead battery industry, demolition industry, scrap industry, smelting, refining, alloying and casting, glass making	Brain *limited*	CAREX	Industry sectors categorised as highly exposed were: metal ore mining, manufacture of industrial and other chemical products, iron and steel basic industries, non-ferrous metal basic industries, manufacture of electrical machinery, apparatus, appliances and construction
Exposure circumstances				
Petroleum refining	PAHs	Brain	UK Petroleum Industry Records	

Abbreviations: CAREX = CARcinogen EXposure Database; CIDI = Central Index of Dose Information; CoE = Census of Employment; LFS = Labour Force Survey; REP = risk exposure period.

Choice of studies providing risk estimates for brain, bone, soft-tissue sarcoma and thyroid cancer

Detailed reviews of occupational risk factor studies identified for cancers of the brain, bone and thyroid, as well as STS, are provided in the relevant Health and Safety Executive (HSE) technical reports (Health and Safety Executive (HSE), 2012a, b, c).

Occupational exposures considered for brain cancer

The exposures/occupational circumstances that have been classified as Group 1/2A, where there is strong or suggestive evidence for brain cancer carcinogenicity, are as follows: non-arsenical insecticides, epichlorohydrin, inorganic lead and petroleum refining (Siemiatycki *et al*, 2004). Other exposures that have been proposed as relevant agents but which were not considered here because of insufficient evidence include vinyl chloride, formaldehyde, radiation and electromagnetic fields (mobile phones), and work in the rubber industry, fire-fighting and laboratory scientists (Wrensch *et al*, 2002; Preston-Martin *et al*, 2006).

Risk estimates for occupational exposure to non-arsenical insecticides and brain cancer A large number of occupational studies have examined cancer risk among workers exposed to non-arsenical insecticides (or pesticides in general), but no studies of UK workers have been published. For the present study, the risk estimate obtained from a meta-analysis of 28 studies of farmers (published through 1994) was selected (for risk to farmers and other workers), and this reported a summary relative risk (RR) of 1.06 (95% confidence interval (CI) = 0.99 – 1.14) (Acquavella *et al*, 1998). This risk estimate was also consistent with a previous analysis (Blair *et al*, 1992). The Acquavella *et al* (1998) estimate was chosen in preference to another meta-analysis that also investigated the association between farming and pesticide exposure and the risk of brain cancer using studies published between 1981 and 1996 (Khuder *et al*, 1998). This obtained a summary RR of 1.30 (95% CI = 1.09 – 1.56), which the authors suggested as evidence for a weak association with pesticide exposure. However, in this meta-analysis, four studies were included in which the risk estimates were greater than three, and one of these studies was from China where exposure circumstances are different from those in GB.

The result of a further meta-analysis of crop protection product manufacturing workers by Jones *et al* (2009), which included studies from around the world, was used for workers employed in pesticide manufacturing (meta-RR = 1.01, 95% CI = 0.75 – 1.36). A review of cohort and case – control studies published before 1995 found equivocal results for risk of brain tumours and exposure to pesticides (Bohnen and Kurland, 1995). In another large US Agricultural Health Study that investigated licensed pesticide applicators, no increase in brain cancer incidence (Alavanja *et al*, 2005) or mortality was observed (Blair *et al*, 2005).

Epichlorohydrin Epichlorohydrin has been used in the production of epoxy resins, synthetic glycerine and elastomers (NCI, 1985), is used to cure propylene-based rubbers, as a solvent for cellulose esters and ethers, and in resins for the paper industry (International Agency for Research on Cancer (IARC), 1999).

Risk estimates for occupational exposure to epichlorohydrin and brain cancer A small nested case – control study of 11 cases observed that routine potential exposure to epichlorohydrin was associated with CNS tumours, but with a large CI (odds ratio = 4.2, 95% CI = 0.7 – 26.0) (Barbone *et al*, 1994). Other cohort studies of epichlorohydrin-exposed workers (mostly carried out in the United States) suggest that the number of people exposed has been small (Enterline *et al*, 1990; Tsai *et al*, 1990, 1996), with only a few deaths from brain cancer/CNS resulting in standardised mortality ratios (SMR) <1.0. As the number of workers exposed to high concentrations of epichlorohydrin was very small, no attributable fraction (AF) was calculated in the current study for exposure to epichlorohydrin.

Inorganic lead In 2004, the IARC reassessed the evidence on the carcinogenicity of lead and reclassified inorganic lead as a probable carcinogen (Group 2A) based on additional limited evidence in humans (International Agency for Research on Cancer (IARC), 2006). Occupational exposure occurs in mining, smelting and refining, storage battery manufacture, welding and steel cutting, as well as printing. High exposure occurs in smelting and refining of the metal, as well as in battery plants (Fu and Boffetta, 1995). Moderate exposure has occurred among welders of metals containing lead, or painted with lead, lead glass workers, lead miners, workers repairing car radiators, printers using lead type and production workers using lead (e.g., producing lead chromate paint). However, it has been noted that exposures have decreased markedly since the 1950s in industrialised countries (Steenland and Boffetta, 2000), and epidemiological studies have mainly concentrated on highly exposed workers in these occupations historically exposed.

Risk estimates for occupational exposure to inorganic lead and brain cancer For the present study, the summary RR of 1.06 (95% CI = 0.80 – 1 40) was taken from the meta-analysis of Steenland and Boffetta (2000) for 'high'-exposure industries and used in the AF calculation. This study included battery and smelter workers and workers monitored for lead exposure from the United States, Italy, Sweden and Finland, although only a small number of cancer cases were observed ($n = 69$). Fu and Boffetta (1995) reviewed 16 cohort studies and 13 case – control studies (nested and population based) relating to lead exposure and cancer risk, but no meta-analysis was performed for brain/CNS cancers.

Risk estimates for employment in petroleum refining and brain cancer All of the studies of petroleum refining industry workers are relatively extensive, and the exposure circumstances of each cohort in the various countries would be expected to be similar because the refining process is relatively standard. For the present study, an SMR of 1.02 (95% CI = 0.83 – 1.25) was obtained from a recent update study by Sorahan (2007). This study had followed up mortality (1951 – 2003) and cancer incidence (1971 – 2003) in a large number of UK workers (28,555 refinery workers and 16,477 distribution workers) over the exposure period of interest.

Wong and Raabe (2000) conducted a meta-analysis of combined data from studies in the United States, Canada, Australia, Finland, Sweden, Italy and United Kingdom, resulting in a combined database of $>350\,000$ workers. For brain cancer, individual study SMRs ranged from 0.34 to 2.14, and the overall meta-SMR was 1.01 (95% CI = 0.93 – 1.09). The review indicated that the risk for US studies was 1.04 compared with 0.97 for non-US studies.

Occupational exposures common to bone and thyroid cancer

Ionising radiation Key occupational groups exposed to ionising radiation include nuclear industry workers, disaster clean-up workers, radiologists, technologists and military personnel (typically through weapon production and testing). Airline cockpit crews also are occupationally exposed to ionising radiation of cosmic origin. Occupational exposure via inhalation or ingestion occurs in many situations, including underground mining, working with plutonium, reactor fuel manufacture and radium-dial painting (luminising industry).

Risk estimates for occupational exposure to ionising radiation and bone and thyroid cancer By using models for workers exposed to ionising radiation from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 2006) (UNSCEAR, 2008), RR estimates of 1.03 for bone cancer and 1.09 for thyroid cancer, for both men and women, were obtained (the same estimate is used for aircrew) on the basis of an estimated average lifetime dose of 15.3 mSv.

United Kingdom studies of radiation exposure in various jobs show that not all radiation workers are at increased risk for bone cancer, with radiation work registry studies consistently reporting reduced risks for bone cancer and an increased risk for thyroid cancer (with and without a 10-year latency period) (Kendall *et al*, 1992; Muirhead *et al*, 1999). In contrast, studies conducted on nuclear industry workforces show an elevated risk for both bone and thyroid cancer (Carpenter *et al*, 1998; Omar *et al*, 1999).

For example, Muirhead *et al* (1999) undertook a cohort study on 124,743 radiation workers in the United Kingdom with a follow-up through 1992. Two types of analyses were carried out on this cohort. The first was an external analysis producing SMRs and using the general population of England and Wales for reference. The second was an internal analysis to investigate dose–response relationships. Standardised mortality ratios were adjusted for age, calendar year and sex, and then were reported using an unlagged and a lagged analysis (based on a 10-year latency period). An SMR of 0.75 (95% CI = 0.36–1.38, $n = 10$) was obtained for mortality from bone cancer in the unlagged analysis and an SMR of 0.52 (95% CI = 0.14–1.34, $n = 4$) for the lagged analysis. However, risk for thyroid cancer was elevated in both the unlagged (SMR = 1.52, 95% CI = 0.79–2.66, $n = 12$) and lagged (SMR = 1.80, 95% CI = 0.90–3.21, $n = 11$) analyses. The internal analysis provided a nonsignificant negative dose trend for bone cancer ($P = 0.28$) from 4 deaths, and a non-significant positive trend associated with thyroid cancer ($P = 0.31$) from 11 deaths.

In another study, follow-up was conducted from 1946 to 1988 for mortality from bone and thyroid cancer in 75,006 employees of three United Kingdom Nuclear Industry Workforces (Carpenter *et al*, 1998). Data on external radiation dose were obtained for $n = 40\,761$ workers, and individuals not monitored for exposure to any radionuclide were used as reference in the analysis. Four deaths from bone cancer were observed in the reference group (SMR = 0.83), but for those monitored for radionuclide exposure elevated SMRs of 1.81 ($n = 1$), 1.00 ($n = 2$) and 1.42 ($n = 2$) were observed for tritium, plutonium and others sources, respectively. Rate ratios were elevated but not significantly (tritium: RR = 1.31, 95% CI = 0.05–14.71, plutonium: RR = 1.01, 95% CI = 0.12–7.35 and other: RR = 2.07, 95% CI = 0.21–18.61). In this study, there were no thyroid deaths among the tritium and other radionuclide subgroups, and only one observed death in the plutonium subgroup (SMR = 0.85). A significantly elevated SMR of 2.69 ($n = 7$, $P < 0.05$) for thyroid cancer was observed in the reference group, resulting in a significantly lowered rate ratio (RR = 0.15, 95% CI = 0.01–0.89) for the group monitored for plutonium.

Occupational exposures considered for soft-tissue sarcoma

TCDD Dioxins or chlorinated dibenzo-*para*-dioxins are structurally similar to chlorinated hydrocarbons (the most toxic form being dioxins) and are by-products of industrial processes (e.g., coke production, manufacture of non-ferrous metals, lime) (Eduljee and Dyke, 1996) and combustion (e.g., burning biomass, coal, oil), and may be released at metal and waste recycling sites (Sweetman *et al*, 2004). For TCDD, the following risk estimates were used for specific occupational groups.

Agriculture/horticulture workers: A summary risk estimate SMR of 1.03 (95% CI = 0.90–1.17) was obtained from a meta-analysis by Acquavella *et al* (1998) to calculate the AF for horticultural, agriculture/fishing, pest control workers, as well as for similar occupations.

Manufacture of pesticides: An overall risk estimate from a meta-analysis by Jones *et al* (2009) (SMR = 1.13, 95% CI = 0.75–1.70) was used because the number of workers specifically involved in the manufacture of phenoxy herbicide pesticides in GB could not be identified.

Pulp manufacture: The risk estimate (SMR = 1.13, 95% CI = 0.59–1.98) was chosen from an international collaborative study (McLean *et al*, 2006), which included a study from Scotland (Coggon *et al*, 1997).

Other industries: For industries in which levels of exposure were not monitored, a risk estimate of 2.03 (95% CI = 0.75–4.43) was taken from the IARC register of workers exposed to phenoxy-acid herbicides and chlorophenols contaminated with dioxins (especially TCDD) and furans (Kogevinas *et al*, 1997). This study included 21,000 workers and found six deaths from STS among exposed workers.

Estimation of numbers ever exposed

The data sources, major industry sectors and jobs for estimation of numbers ever exposed over the risk exposure period (REP), defined as the period during which exposure occurred that was relevant to the development of the cancer in the target year 2005, are given in Table 1. The occupations with likely exposure to non-arsenical insecticides are linked with agriculture and horticulture, gardening, forestry, pest control, as well as with the manufacture of these products. The Labour Force Survey gives a number of job titles that fit these occupations, giving an estimated total of 25,563 workers (20,792 men and 4771 women) involved in their use and 4153 workers (2835 men and 1318 women) involved in their production. For inorganic lead exposure, the CArcinogen EXposure database, CAREX, estimated that a total of 249,412 workers were exposed in the period 1990–1993 in a variety of industries (Kauppinen *et al*, 1998). According to HSE statistics, in the same period just $<27,000$ individuals were under surveillance for lead exposure (in workplaces where exposure was at least 50% of the Occupational Exposure Limit (OEL) or workers who had a blood lead level above the action limit); by 2006/2007 this had decreased by almost 70%.

Data from the LFS and Census of Employment (CoE) provided conflicting figures of the number of people employed in the petroleum industry. A study by Sorahan (2007) estimated that 28,555 refinery workers were first employed between 1946 and 1974; however, not all UK refineries were included in this study. The petroleum industry was therefore contacted to obtain numbers of the workers employed in petroleum refining in 1981, the year for which a point estimate was required; numbers were estimated as 36,500 (32,602 men and 3898 women, assuming a similar split as indicated by CoE data in same year). These figures were used to calculate the AF.

RESULTS

Owing to assumptions made about cancer latency and working age range, only cancers in ages 25 years and above in 2005/2004 could be attributable to occupation. In the present study, a latency period of at least 10 years and up to 50 years has been assumed for bone, brain and thyroid cancers; a latency period of between 0 and 20 years has been assumed for STS. Attributable fractions have been calculated as follows: brain cancer – ionising radiation, non-arsenical pesticides, inorganic lead, petroleum refining; bone and thyroid cancer – ionising radiation; STS – TCDD. Table 2 provides a summary of the attributable deaths and registrations in GB for

Table 2 Cancer burden estimation results for brain, bone, soft-tissue sarcoma and thyroid cancers

Agent	Number of men ever exposed	Number of women ever exposed	Proportion of men ever exposed	Proportion of women ever exposed	AF men (95% CI)	AF women (95% CI)	Attributable deaths (men) (95% CI)	Attributable deaths (women) (95% CI)	Attributable registrations (men) (95% CI)	Attributable registrations (women) (95% CI)
Brain cancer										
Inorganic lead	809,058	413,029	0.0417	0.0197	0.0007 (0.0000–0.0049)	0.0002 (0.0000–0.0012)	1 (0–9)	0 (0–2)	2 (0–11)	0 (0–2)
Non-arsenical insecticides	1,444,111	288,832	0.0744	0.0138	0.0044 (0.0012–0.0077)	0.0008 (0.0002–0.0014)	8 (2–15)	1 (0–2)	10 (3–18)	1 (0–2)
Petroleum refining	117,471	22,434	0.0061	0.0011	0.0001 (0.0000–0.0015)	0.0000 (0.0000–0.0003)	0 (0–3)	0	0 (0–3)	0
Totals[a]					**0.0052 (0.0006–0.0012)**	**0.0010 (0.0000–0.0023)**	**10 (1–20)**	**1 (0–3)**	**12 (1–25)**	**2 (0–4)**
Bone cancer										
Ionising radiation	252,035	39,420	0.0130	0.0019	0.0004	0.0001	0	0	0	0
Soft-tissue sarcoma										
TCDD	2,084,061	649,435	0.0906	0.0281	0.0338 (0.0000–0.1137)	0.0106 (0.0000–0.0376)	11 (0–36)	3 (0–9)	22 (0–75)	4 (0–15)
Thyroid cancer										
Ionising radiation	252,035	39,420	0.0130	0.0019	0.0012	0.0002	0	0	0	0

Abbreviations: AF = attributable fraction; CI = confidence interval; 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 AF, deaths and registrations for each agent. The difference is especially notable where the constituent AFs are large.

2005 and 2004, and shows the separate estimates for men and women, respectively.

For all exposure scenarios combined, the overall estimated AF fraction for brain cancer was 0.35% (95% CI = 0.03–0.72%), giving in total (male and female) 11 (95% CI = 1–23) attributable deaths and 14 (95% CI = 1–28) attributable registrations. On the basis of the UNSCEAR methodology for exposure to ionising radiation, the overall estimated AF for bone cancer was 0.02%, and for thyroid cancer the AF was 0.05%. These estimates of risk resulted in no attributable deaths or registrations for bone cancer, and only one estimated thyroid cancer registration attributable to occupational exposure. For STS, the overall AF was 2.27% (95% CI = 0.00–7.73%), giving in total 13 (95% CI = 0–45) attributable deaths and 27 (95% CI = 0–90) attributable registrations.

Exposures affecting brain cancer

For non-arsenical insecticides, a total of 1,444,111 men and 288,832 women were estimated as 'ever' exposed during the REP. The overall estimated total AF (for men and women) was 0.29% (95% CI = 0.08–0.51%), which resulted in 9 (95% CI = 2–17) attributable deaths and 11 (95% CI = 3–20) attributable registrations.

An estimated 809,058 men and 413,029 women were 'ever exposed' during the REP to inorganic lead. The overall estimated total AF (for men and women) was 0.05% (95% CI = 0.00–0.34%), with two (95% CI = 0–11) attributable deaths and two (95% CI = 0–13) attributable registrations.

For work in the petroleum industry, there were an estimated 117,481 men and 22,434 women 'ever employed' during the REP. The overall estimated total AF (for men and women) was 0.01% (95% CI = 0.00–0.10%), which resulted in no attributable deaths or registrations.

Exposures affecting soft-tissue sarcoma

An estimated 838,863 men and 272,873 women were assessed as 'ever exposed' to TCDD during the REP. For STS, the total AF from exposure to TCDD was 2.27% (95% CI = 0.00–7.73%), with 13 (95% CI = 0–45) attributable deaths and 27 (95% CI = 0–90) attributable registrations. Men involved in the iron and steel industry had the largest number of attributable registrations and deaths (seven and three, respectively, for STS).

DISCUSSION

Owing to the rarity of bone cancer, all the studies reviewed reported relatively small number (typically fewer than six cases) of attributable cancer deaths or registrations, and this limits the reliability of the estimates obtained. Although studies in the United States and China have suggested that occupational exposure to ionising radiation increases the risk for both bone and thyroid cancer, this has not been observed in large cohort studies in the United Kingdom, which reported no risk for bone cancer and only an elevated risk for thyroid cancer. In addition, radiation has been shown to be associated with STS in radium-dial painters, although this occupation has ceased to exist since many decades (Polednak *et al*, 1978).

The total AF for brain cancer for men and women of 0.35 is significantly lower than the estimates obtained by Nurminen and Karjalainen (2001) of 10.6 and 1.3 for men and women, respectively, and also lower than the 2000 worldwide estimate given by Parkin *et al* (2001) of 2.1% of deaths and 1.8% of registrations. Nurminen and Karjalainen (2001) also estimated that 0.6% of bone cancers were due to occupational exposures compared with the 0.02% estimate obtained in this study. These authors did not provide an estimate for thyroid cancer. In contrast, Parkin *et al* (2001) estimated that 0.4% of thyroid cancer deaths and 1.2% of registrations were due to occupational exposures, which is comparable to the 0.05% reported in this study.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Acquavella J, Olsen G, Cole P, Ireland B, Kaneene J, Schuman S, Holden L (1998) Cancer among farmers: a meta-analysis. *Ann Epidemiol* **8:** 64–74

Alavanja MCR, Sandler DP, Lynch CF, Knott C, Lubin JH, Tarone R, Thomas K, Dosemeci M, Barker J, Hoppin JA, Blair A (2005) Cancer incidence in the Agricultural Health Study. *Scand J Work Environ Health* **31:** 39–45

Barbone F, Delzell E, Austin H, Cole P (1994) Exposure to epichlorohydrin and central nervous system neoplasms at a resin and dye manufacturing plant. *Arch Environ Health* **49:** 355–359

Berwick M (2006) Soft tissue sarcoma. In *Cancer Epidemiology and Prevention*, Schottenfeld D, Fraumeni Jr JF (eds), pp 959–974. Oxford University Press: Oxford

Blair A, Sandler DP, Tarone R, Lubin JH, Thomas K, Hoppin JA, Samanic C, Coble J, Kamel F, Knott C, Dosemeci M, Zahm SH, Lynch CF, Rothman N, Alavanja MCR (2005) Mortality among participants in the Agricultural Health Study. *Ann Epidemiol* **15:** 279–285

Blair A, Zahm SH, Pearce N, Heineman EF, Fraumeni Jr JF (1992) Clues to cancer etiology from studies of farmers. *Scand J Work Environ Health* **18:** 209–215

Bohnen NI, Kurland LT (1995) Brain tumor and exposure to pesticides in humans: a review of the epidemiologic data. *J Neurol Sci* **132:** 110–121

Cancer Research UK (2007a) Last update, UK bone and connective tissue cancer statistics. Available at http://info.cancerresearchuk.org/cancerstats/types/bone/?a = 544 [June, 2008]

Cancer Research UK (2007b) Last update, UK thyroid cancer statistics. Available at http://info.cancerresearchuk.org/cancerstats/types/thyroid/?a = 5441 (June, 2008)

Carpenter LM, Higgins CD, Douglas AJ, Maconochie NE, Omar RZ, Fraser P, Beral V, Smith PG (1998) Cancer mortality in relation to monitoring for radionuclide exposure in three UK nuclear industry workforces. *Br J Cancer* **78:** 1224–1232

Coggon D, Wield G, Pannett B, Campbell L, Boffeta P (1997) Mortality in employees of a Scottish paper mill. *Am J Ind Med* **32:** 535–539

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

Enterline PE, Henderson VL, Marsh GM (1990) Mortality of workers potential exposed to epichlorohydrin. *Br J Ind Med* **47:** 269–276

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

Hoppin JA, Tolbert PE, Flanders WD, Zhang RH, Daniels DS, Ragsdale BD, Brann EA (1999) Occupational risk factors for sarcoma subtypes. *Epidemiology* **10:** 300–306

Health and Safety Executive (HSE) (2012a) The burden of occupational cancer in Great Britain: Technical Report: Brain cancer. Health and Safety Executive: http://www.hse.gov.uk/cancer/

Health and Safety Executive (HSE) (2012b) The burden of occupational cancer in Great Britain: Technical Report: Bone and Thyroid Cancer. Health and Safety Executive: http://www.hse.gov.uk/cancer/

Health and Safety Executive (HSE) (2012c) The burden of occupational cancer in Great Britain – Technical Report: Soft tissue sarcoma. Health and Safety Executive: http://www.hse.gov.uk/cancer/

International Agency for Research on Cancer (IARC) (1999) *IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans: Re-Evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide*, Vol. 71. International Agency for Research on Cancer: Lyon

International Agency for Research on Cancer (IARC) (2006) *IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans: Inorganic and Organic Lead Compounds*, Vol. 87. International Agency for Research on Cancer: Lyon

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

Kauppinen T, Toikkanen J, Pedersen D, Young R, Kogevinas M, Ahrens W, Boffetta P, Hansen J, Kromhout H, Blasco JM, Mirabelli D, de la Orden-Rivera V, Plato N, Pannett B, Savela, Veulemans H, Vincent R (1998) *Occupational Exposure to Carcinogens in the European Union in 1990–93*. Finnish Institute of Occupational Health: Helsinki

Kendall GM, Muirhead CR, Maggibbon CR, Macgibbon BH, O'hagen JA, Conquest AJ, Goodill AA, Buland BK, Fell TP, Jackson DA, Webb MA (1992) Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers. *Br Med J* **304**(6821)**:** 220–225

Khuder SA, Mutgi AB, Schaub EA (1998) Meta-analyses of brain cancer and farming. *Am J Ind Med* **34:** 252–260

Kleihues P, Cavanee WK (2000) *World Health Organization Classification of Tumours: Pathology and Genetics of Tumors of the Nervous System*. IARC Press: Lyon, France

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

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

Mendenhall WM, Zlotecki RA, Hochwald SN, Hemming AWGSR, Cancer WG (2005) Retroperitoneal soft tissue sarcoma. *Cancer* **104:** 669–675

Miller RW, Boice JD Jr B, Curtis RE (2006) Bone cancer. In *Cancer Epidemiology and Prevention*, Vol. 48, Schottenfeld D, Fraumeni JF (eds) 3rd edn, pp 946–958. Oxford University Press: Oxford

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

NCI (1985) Monograph on human exposure to chemicals in the workplace: Epichlorohydrin. Technical Report No. 84631.

Nurminen M, Karjalainen A (2001) Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. *Scand J Work Environ Health* **27**(3)**:** 161–213

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**(7–8)**:** 1288–1301

Parkin DM, Bray FI, Devesa SS (2001) Cancer burden in the year 2000. The global picture. *Eur J Cancer* **37:** S4–S66

Polednak AP, Stehney F, Rowland RE (1978) Mortality among women first employed before 1930 in the US radium dial-painting industry: a group ascertained from employment lists. *Am J Epidemiol* **107:** 179–195

Preston-Martin S, Munir R, Chakrabarti I (2006) Nervous system. In *Cancer Epidemiology and Prevention*, Schottenfeld D, Fraumeni JFJ (eds), pp 1176–1195. Oxford University Press: Oxford

Quinn M, WH, Cooper N, Rowan S (eds) (2005) *Cancer Atlas of the United Kingdom and Ireland 1991–2000: Studies on Medical and Population Subjects No. 68*. Palgrave Macmillan

Rachet B, Mitry E, Quinn MJ, Cooper N, Coleman MP (2008) Survival from brain tumours in England and Wales up to 2001. *Br J Cancer* **99:** S98–S101

Ron E, Schneider AB (2006) Thyroid cancer. In *Cancer Epidemiology and Prevention*, Schottenfeld D, Fraumeni JF (eds) 3rd edn, pp 975–994. Oxford University Press: Oxford

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

Sorahan T (2007) Mortality of UK oil refinery and petroleum distribution workers, 1951–2003. *Occup Med* **57:** 177–185

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

Storm H, Hat EWG (1998) Survival of adult patients with cancer of soft tissues or bone in Europe. *Eur J Cancer* **34:** 2212–2217

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

Swerdlow AJ, dos Santos Silva I, Doll R (2001) *Cancer Incidence and Mortality in England and Wales: Trends and Risk Factors*. Oxford University Press: New York

Toro JR, Travis LB, Wu HJ, Zhu K, Fletcher CDM, Devesa SS (2006) Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978–2001: an analysis of 26 758 cases. *Int J Cancer* **119:** 2922–2930

Tsai SP, Cowles SR, Tackett DL, Barclay MT, Ross CE (1990) Morbidity prevalence study of workers with potential exposure to epichlorohydrin. *Br J Ind Med* **47:** 392–399

Tsai SP, Gilstrap EL, Ross CE (1996) Mortality study of employees with potential exposure to epichlorohydrin: a 10-year update. *Occup Environ Med* **53:** 299–304

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) (2008) Effects of ionising radiation: UNSCEAR 2006, Volume 1, Report to the General Assembly, United Nations Scientific Committee on the Effects of Atomic Radiation, Annex A.
Weitz J, Anonescu CR, Brennan MF (2003) Localized extremity soft tissue sarcoma: improved knowledge with unchanged survival over time. *J Clin Oncol* **21:** 2719–2725
Wong O, Raabe GK (2000) A critical review of cancer epidemiology in the petroleum industry, with a meta-analysis of a combined database of more than 350 000 workers. *Regul Toxicol Pharmacol* **32:** 78–98
Wrensch M, Minn Y, Chew T, Bondy M, Berger MS (2002) Epidemiology of primary brain tumours: current concepts and review of the literature. *Neurooncology* **4:** 278–299

Appendix

British Occupational Cancer Burden Study Group

Lesley Rushton (PI)*[,1], Sanjeev Bagga[3], Ruth Bevan[3], Terry Brown[3], John W Cherrie[4], Gareth S Evans[2], Lea Fortunato[1], Phillip Holmes[3], Sally J Hutchings[1], Rebecca Slack[5], Martie Van Tongeren[4] and Charlotte Young[2].

[1]Department of Epidemiology and Biostatistics, School of Public Health and MRC-HPA Centre for Environment and Health, Imperial College London, St Mary's Campus, Norfolk Place, London W2 3PG, UK; [2]Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire SK17 9JN, UK; [3]Institute of Environment and Health, Cranfield Health, Cranfield University, Cranfield MK43 0AL, UK; [4]Institute of Occupational Medicine, Research Avenue North, Riccarton, Edinburgh EH14 4AP, UK; [5]School of Geography, University of Leeds, Leeds LS2 9JT, UK.