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Occupational cancer in Britain

Haematopoietic malignancies: leukaemia, multiple myeloma, non-Hodgkins lymphoma

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OVERVIEW OF LYMPHOHAEMATOPOIETIC MALIGNANCIES

Leukaemia

The major types of leukaemias included in this burden estimation are acute myeloid leukaemia (AML), chronic lymphoid leukaemia (CLL), chronic myeloid leukaemia (CML) and acute lymphoid (ALL) leukaemia. It should be noted that, in the more recent WHO classification of haematopoietic malignancies, both ALL and CLL are classified within non-Hodgkin's lymphomas (NHLs) and in particular in B-cell neoplasms (Jaffe *et al*, 2001). In 2004, the UK age-standardised incidence rates for leukaemia overall for men and women were 13.5 and 9.5 per 100,000, respectively, and have fluctuated around these levels since the 1970s (Swerdlow *et al*, 2001). One-year relative survival from all leukaemias was around 60%, and 5-year survival was around 38% for patients diagnosed between 1996 and 1999 in England and Wales. Survival from leukaemia has steadily increased since the 1980s, and more so in men, but rates differ between the subtypes of leukaemia (Rachet *et al*, 2008c). Non-occupational causes of leukaemia are viruses (e.g., Epstein – Barr virus; Dalgleish, 1991) and smoking, which has been particularly associated with acute leukaemias (Linet *et al*, 2006).

Multiple myeloma

Multiple myeloma (MM) is a disease of the elderly, being virtually unknown in childhood and very uncommon in young adults (LRF, 2006a); it develops from antibody-secreting plasma cells in the bone marrow. Between 1995 and 2005, there was an average of over 3500 new registrations each year in England, Wales and Scotland, and an average of 3180 deaths (HSE, 2012b), with the temporal pattern for mortality being similar to that of incidence (Swerdlow *et al*, 2001). The 5-year relative survival rate for MM has significantly improved between 1986 – 1990 and 1996 – 1999 (Rachet *et al*, 2008a), but with little improvement in 10-year survival rates. Obesity (Alexander *et al*, 2007) and dietary intake of meats and fats have been suggested as risk factors for MM, as have prior medical conditions or treatments (de Roos *et al*, 2006).

Non-Hodgkin's lymphoma

Non-Hodgkin's lymphoma is a mixture of different pathologies of varying aetiology (Zinzani, 2005), most arising in the central lymph nodes (70 – 80%) and the remaining in the extra-nodal tissue (Grulich and Vajdic, 2005). In the United Kingdom, there are over 8500 new registrations of NHL annually (Cartwright *et al*, 2005; LRF, 2006b). The number of deaths from NHL in Great Britain has been consistently around 4400 per year over the past 7 years. Trends in mortality approximately follow those in incidence, with rates significantly increasing in older age groups (Swerdlow *et al*, 2001). In Britain, the age-standardised incidence rate increased by 6% between 1995 and 2004 (ONS, 2006). The 5-year relative survival rate for NHL in England and Wales was around 46% for patients diagnosed in the late 1980s (Rachet *et al*, 2008b), and has improved by about 4% every 5 years since. Certain viral infections, including the Epstein-Barr virus and HIV (AIDS) virus, are known risk factors for NHL (Grulich and Vajdic, 2005), and *Helicobacter pylori* infection is strongly associated with MALT lymphoma of the stomach (Farinha and Gascoyne, 2005). Obesity is associated with an increased risk of NHL (Larsson and Wolk, 2007), and a correlation between the incidence of NHL and ambient solar ultraviolet radiation has been suggested (McMichael and Giles, 1996). Non-ionising radiation (IR; e.g., from mobile phones) may increase the risk of developing NHL (Karipidis *et al*, 2007).

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 leukaemia, MM and NHL are summarised in Table 1. Other occupational circumstances classified by IARC

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

Table 1 Occupational agents, groups of agents, mixtures and exposure circumstances classified by the IARC Monographs, Vols 1–77 (IARC, 1972–2001), into Groups 1 and 2A, which targets the lymphohaematopoietic system and for which burden has been estimated

Agents, mixture, circumstance	Main industry, use	Evidence of carcinogenicity in humans	Source of data for estimation of numbers ever exposed over REP	Comments
Group 1: Carcinogenic to humans				
Agents, groups of agents				
Benzene	Production; boot and shoe industry; chemical, pharmaceutical and rubber industries; printing; petrol additive	Leukaemia *sufficient*	CAREX	Estimated for acute lymphocytic and acute monocytic leukaemia
Ionising radiation	Radiologists, technologists, nuclear workers; aircraft crews; underground miners	Leukaemia *sufficient*	CIDI LFS British Airways Stewards and Stewardesses Association	Excluding CLL
Ethylene oxide	Production; chemical industry; sterilising agent (hospitals, spice fumigation)	Leukaemia *sufficient*	CAREX	
Formaldehyde	Production; pathologists; medical laboratory technicians; plastics, textile and plywood industries	Leukaemia *sufficient*	CAREX	
TCDD	Production; use of chlorophenols and chlorophenoxy herbicides; waste incineration; PCB production; pulp and paper bleaching	NHL *limited*	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	Leukaemia *limited* NHL *limited* Multiple myeloma *limited*	LFS	
1,3-Butadiene	Chemical and rubber industries	Leukaemia *limited*	CAREX	
Tetrachloroethylene	Production; dry cleaning; metal degreasing	NHL *limited*	CAREX	
Trichloroethylene	Production; dry cleaning; metal degreasing	NHL *limited*	CAREX	
Exposure circumstances				
Hairdressers and barbers	Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols	NHL *limited*	LFS	

Abbreviations: CAREX = CARcinogen EXposure database; CIDI = central index of dose information; CLL = chronic lymphoid leukaemia; IARC = International Agency for Research on Cancer; LFS = Labour Force Survey; PCB = polychlorinated biphenyl; REP = risk exposure period; TCDD = 2,3,7,8-tetrachlorodibenzo-*para*-dioxin.

as definite carcinogens for leukaemia that have been considered within the estimate for benzene are boot and shoe manufacture and repair, petroleum refining and work in the rubber industry.

Choice of studies providing risk estimates for leukaemia, MM and NHL

A detailed review of occupational risk factor studies for leukaemia, MM and NHL is provided in the relevant Health and Safety Executive (HSE) technical reports (HSE, 2012a, b, c).

Occupational exposures common to leukaemia, MM and NHL

Non-arsenical insecticides A large number of epidemiological studies have examined cancer risk among farmers and other agricultural workers exposed to non-arsenical insecticides or pesticides in general. These found increased risks for leukaemia (including specific sub-types), MM and NHL (Descatha *et al*, 2005; de Roos *et al*, 2006; Linet *et al*, 2006; Alexander *et al*, 2007). The US Agricultural Health Study, a large study of pesticide users, has observed excesses in mortality and incidence (Alavanja *et al*, 2005; Blair *et al*, 2005), but some of the exposure circumstances are not observed in GB. For the present study, risk estimates were obtained for the following groups of workers and are summarised in Table 2.

Farmers and agricultural workers Two large meta-analyses of farmers exposed to non-arsenical insecticides were undertaken by Khuder *et al* (1998) and Acquavella *et al* (1998), the former including 33 studies and the latter 28 studies; only 16 studies were included in both meta-analyses. The risk estimates of Acquavella *et al* (1998) were used for the present study because the overall relative risks (RRs) were in agreement with a previous analysis by Blair *et al* (1992) and were more applicable to farmers and other workers in GB.

Manufacture of pesticides A meta-analysis by Jones *et al* (2009) that included studies from around the world of crop protection product manufacturing workers was used, and the risk estimate for this group was applied to workers employed in pesticide manufacturing.

Table 2 Summary of risk estimates used for different groups and malignancies related to exposure to non-arsenical pesticides

	Farmers and other workers	Crop protection manufacturers	Flour and grain industry
Leukaemia	1.10 (1.02–1.18)	1.08 (0.81–1.44)	1.07 (0.75–1.47)
NHL	1.03 (0.96–1.12)	1.98 (1.45–2.69)	1.00 (0.64–1.48)
Myeloma	1.09 (0.99–1.19)	1.26 (0.89–1.77)	1.01 (0.50–1.81)

Abbreviation: HHL = Non-Hodgkin's lymphoma.

Flour and grain industry workers A study by Alavanja *et al* (1990) of US Grain Millers using pesticides to control insect infestation was used.

Occupational exposures considered for NHL

TCDD Dioxins or chlorinated dibenzo-*p*-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:

Risk estimates for occupational exposure to TCDD and NHL

Agriculture/horticulture workers: an estimate for NHL was not carried out because non-arsenical insecticides were considered to be the dominant exposure.

Manufacture of pesticides: an overall risk estimate from the meta-analysis by Jones *et al* (2009) (SMR = 1.98, 95% CI = 1.45–2.69) 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 = 0.86, 95% CI = 0.64–1.13) was chosen from an international collaborative study (McLean *et al*, 2006), which included a study from Scotland (Coggon *et al*, 1997).

Other industries: an SMR of 1.4 (95% CI = 0.6–2.7) from a study by Bodner *et al* (2003) was chosen, which reported eight NHL deaths among a cohort of workers involved in chemical production.

Risk estimates for employment as hairdressers and barbers and NHL An increased risk of NHL has been associated with work as a hairdresser, barber or beautician (Teta *et al*, 1984; Boffetta *et al*, 1994; Lamba *et al*, 2001). For the present study, a standardised incidence ratio (SIR) of 1.20 (95% CI = 0.84–1.66) was chosen from the study by Boffetta *et al* (1994), which covered four European countries (Denmark, Sweden, Norway and Finland) and was adjusted for age. The studies by Teta *et al* (1984) and Lamba *et al* (2001) were excluded as they were conducted outside Europe.

Tetrachloroethylene (perchloroethylene) Tetrachloroethylene (PERC) is widely used for dry cleaning fabrics, metal degreasing in the automotive and metalworking industries and in consumer products, e.g., paint strippers, printing inks (IARC, 1995; ATSDR, 1997a). This chemical has consistently been associated with an increased risk of NHL (Fritschi *et al*, 2005).

Risk estimates for occupational exposure to PERC and NHL For the present study, a US study by Ruder *et al* (2001) was chosen to obtain a risk estimate of 1.39 (95% CI = 0.56–2.86), because it involved a large number of dry cleaning and laundry workers with an extended follow-up and good exposure assessment; individuals 'ever exposed' to carbon tetrachloride (the primary solvent used in dry cleaning until the 1950s) were excluded. This risk estimate was used for all workers (not just dry cleaners) with high exposure to PERC. Because of the absence of sufficient dose–response data for low exposure, the risk estimate 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.

Trichloroethylene Trichloroethylene (TCE) is a chlorinated hydrocarbon commonly used as an industrial solvent for vapour or cold degreasing operations: furniture and fixtures, fabricated metal products, electrical equipment and transport equipment (IARC, 1995). It has also been used as a chemical intermediate and component in adhesives, lubricants, paints, varnishes, paint strippers and pesticides (ATSDR, 1997b).

Risk estimates for occupational exposure to TCE and NHL For TCE, the summary risk estimate of 1.29 (95% CI = 1.00–1.66) from the study by Mandel *et al* (2006) was used, as this meta-analysis included recent published studies not considered in previous quantitative and qualitative reviews. 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.

Other occupational exposures considered for leukaemia

Benzene Benzene is a by-product of coke production, a constituent of petrol, and is used extensively in the chemical industry, and previously in shoe and boot manufacturing. Exposure to benzene among motor mechanics and aviation workers has been shown to be high (Capleton and Levy, 2005). There is a complex relationship between exposure to benzene and the risk of developing different types of leukaemia, which is summarised in the HSE technical report (HSE, 2012a) and by Schnatter *et al* (2005). For some types of leukaemia (e.g., AML), the relationship is considered by some researchers to be strong, but for other types such as CLL it is regarded as equivocal. Risk estimates for total leukaemia for the populations studied vary widely from below 1 to about 7 (Savitz and Andrews, 1997). The following risk estimates were selected and used for acute non-lymphocytic leukaemia (ANNL).

Work in industrial chemical manufacturing: the RR of 2.17 (95% CI = 0.9–5.2) from a mortality study of Collins *et al* (2003) of men and women in a US chemical plant exposed to benzene.

Distribution and land transport: the RR estimate of 1.32 (95% CI = 0.49–2.88) for acute non-lymphocytic leukaemia (ANLL) from a cohort mortality study of a large Canadian petroleum company (Lewis *et al*, 2000).

Other exposures considered low: for those industry groups where benzene exposure occurred at low levels, i.e., likely to be below 1 p.p.m., including refinery and oil distribution workers (Runion, 1988; Schnatter *et al*, 2005), an overall RR of 1.11 (95% CI = 0.3–2.83) was selected from a study by Bloemen *et al* (2004).

1,3-Butadiene 1,3-butadiene is used in the production of synthetic rubbers, synthetic elastomers, carpets, paper coatings, paints and vehicle parts.

Risk estimates for occupational exposure to 1,3-butadiene and leukaemia The highest risk estimate (adjusted for exposure to styrene and dimethyldithiocarbamate) of 2.30 (95% CI = 0.6–8.3)

from a study of workers at eight styrene–butadiene plants in the United States and Canada (Delzell *et al*, 2001) was selected for the highly exposed workers based on a precautionary approach. A risk estimate of 1.30 (95% CI = 0.4–4.3) from the same study was selected for low-exposure groups. All of the exposed workers were assumed to be men. This cohort has consistently been shown to be at an increased risk (Sathiakumar *et al*, 1998; Delzell *et al*, 2001), and the most recent assessment of this cohort gave an SMR of 1.41 (95% CI = 1.05–1.86); however, no relationship with duration of employment was reported, and all the leukaemia deaths occurred in men first employed before 1950.

Ethylene oxide/ethylene dioxide Ethylene oxide (EO) is used widely as a sterilising agent, disinfectant, pesticide, and as an intermediary in the synthesis of ethylene glycol (anti-freeze) and other products. Exposure occurs in hospitals, as well as in chemical and pharmaceutical manufacture.

Risk estimates for occupational exposure to EO/ethylene dioxide and leukaemia For the present study, risk estimates for high exposure groups were selected from a study of workers exposed to EO in Britain (Coggon *et al*, 2004), and in which the leukaemia deaths occurred in a subset of subjects with the greatest potential for exposure to EO: a risk estimate of 1.08 (95% CI = 0.03–6.02) was obtained for high exposure among medical workers (males and females); and an estimate of 2.29 (95% CI = 0.62–5.86) was obtained for high exposure in chemical manufacture. For the low-exposure groups (male and female), a RR of 1.0 was assigned based on the meta-SMR of 0.95 (95% CI = 0.64–1.35) in Teta *et al* (1999). In general, studies of EO exposure and leukaemia have been of varying size and quality.

Formaldehyde Formaldehyde is used mainly in the production of phenolics, urea, melamine and polyacetal resins, and as an intermediary in industrial chemical manufacture. These have wide uses as adhesives and binders for wood products, pulp and paper manufacture, in synthetic vitreous fibre industries, for the production of plastics and coatings and in textile finishing. High formaldehyde exposure occupations include textile operations and wood product manufacture/processing (with coexposure to wood dust); short-term high-exposure episodes have been reported for embalmers, pathologists and paper industry workers.

Risk estimates for occupational exposure to formaldehyde and leukaemia For the present study, risk estimates were chosen from a meta-analysis of 18 epidemiological studies of workers exposed to formaldehyde (Collins and Lineker, 2004). For embalmers, a meta-RR (mRR) = 1.6 (95% CI = 1.2–2.0) for leukaemia, was used for health and veterinary service employees, as well as for research scientists. For pathologists and anatomists, an mRR of 1.4 (95% CI = 1.0–1.9) from this same study was chosen. For those industrial workers reported to have high cumulative exposures to formaldehyde, an mRR of 1.2 (95% CI = 0.8–1.8) was taken from the study by Collins and Lineker (2004). For the low 'background' exposure groups (men and women), the risk estimate was assigned an RR of 1.0. Other studies of industrial workers exposed to formaldehyde report a positive association between exposure and leukaemia risk (Hauptmann *et al*, 2003; Pinkerton *et al*, 2004), whereas one British study did not find any positive association even for those exposed at high levels for long periods (Coggon *et al*, 2003).

Ionising radiation Ionising radiation is an established cause of leukaemia, although it appears to have no effect on the risk of CLL (Higginson *et al*, 1992).

Risk estimates for occupational exposure to IR and leukaemia For the present study, the RRs for occupational exposure to IR were obtained from UNSCEAR (2008), using models of excess RR (HSE, 2012a) with an RR estimate of 1.027 (for an estimated average lifetime dose of 11.5 mSv) and a separate RR estimate of 1.036 for male and female aircrew (with an estimated average lifetime dose of 15.3 mSv).

A large number of studies with varying risk estimates have been carried out of workers (in nuclear power stations and defence work and workers included in the National Registry for Radiation Workers) in the United Kingdom exposed to IR. A meta-analysis of UK and US studies showed a significantly increased RR for leukaemia of 1.8 for workers who received a cumulative dose of 10–50 mSv (Wilkinson and Dreyer, 1991). For European airline pilots and flight engineers exposed to IR of cosmic origin, a range of risk factors from 0.51 to 1.39 have been reported for all leukaemias and sub-types (Irvine and Davies, 1999; Blettner *et al*, 2003; Langner *et al*, 2004). A combined study of UK, Canadian and US cohorts found a mortality risk for all leukaemias (excluding CLL) with an excess RR of 2.18 per Sv (95% CI = 0.1–5.7) (Cardis *et al*, 1995). An update including a further 12 countries found similar results (Cardis *et al*, 2005).

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.

Three sources of data were used to obtain numbers exposed above 0.1 mSv IR in Britain: numbers exposed in 1995 above 0.1 mSv from the HSE's Central Index of Dose Information in various industries (HSE, 1998); the 1991 Labour Force Survey for aircraft flight deck officers and male travel and flight attendants; information from the British Airways Stewards and Stewardesses Union for female air stewardesses.

High exposures to formaldehyde were assumed for textile and glass manufacture, education, research, health, and household and personal services. The industrial processes operating in the United Kingdom listed by Eduljee and Dyke (1996) were used as the basis for identifying the relevant occupational groups exposed to TCDD. High exposure to 1,3-butadiene was assumed for the manufacture of rubber. Workers involved in the manufacture of machinery, personal and household services and manufacture of fabricated metal products were classified as high exposure to tetrachloroethylene. High exposures to TCE were assumed for manufacture of clothes, manufacture of fabricated metal products, machinery and transport equipment, as well as personal and household services.

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. In the present study, a latency period of between 0 and 20 years has been assumed for all the haematopoietic malignancies. Estimation has been carried out for all leukaemias together, except for benzene where attributable numbers have been calculated by applying the estimated AF to estimated numbers of AML, acute promyelocytic leukaemia, acute myelomonocytic leukaemia, and acute monocytic leukaemia and IR where CLL has been excluded. Attributable fractions have been calculated for the following: leukaemia and exposure to 1,3-butadiene, benzene, EO, formaldehyde, IR and non-arsenical insecticides; NHL and exposure to non-arsenical insecticides, TCDD (dioxins), tetrachloroethylene, TCE, and work as a hairdresser and barber; and MM and exposure to non-arsenical insecticides. Table 3 provides a summary of the attributable deaths and registrations in GB for 2005 and 2004 and shows the separate estimates for men and women, respectively.

For all exposure scenarios the combined AFs, deaths and registrations (male and female) for each type of malignancy were as follows. For leukaemia the AF was 0.74% (95% CI = 0.00–3.86%), giving in total 23 (95% CI = 5–120) attributable deaths and 38 (95% CI = 8–198) registrations. For MM the AF was 0.30% (95% CI = 0.00–0.64%), giving in total 6 (95% CI = 0–12) attributable deaths and 10 (95% CI = 0–21) registrations. For NHL the AF was 1.74% (95% CI = 0.03–5.35%), giving in total 57 (95% CI = 1–176) attributable deaths and 140 (95% CI = 3–430) registrations.

Exposures affecting leukaemia, MM and NHL

An estimated 1 159 288 men and 348 966 women were assessed as 'ever exposed' to non-arsenical insecticides during the REP. The total AF for leukaemia and exposure to non-arsenical insecticides was 0.38% (95% CI = 0.09–0.68%), with 12 (95% CI = 3–21) attributable deaths and 19 (95% CI = 5–35) attributable registrations. For NHL, the total AF from exposure to non-arsenical insecticides was 0.38% (95% CI = 0.19–0.58%), with 13 (95% CI = 7–21) attributable deaths and 33 (95% CI = 16–50) attributable registrations. For MM, the total AF from exposure to non-arsenical insecticides was 0.30% (95% CI = 0.00–0.64%), with 6 (95% CI = 0–12) attributable deaths and 10 (95% CI = 0–21) attributable registrations.

Exposures affecting ANLL

An estimated 342 236 men and 704 474 women were assessed as 'ever exposed' to benzene during the REP. For ANLL and exposure to benzene, the total AF was 0.25% (95% CI = 0.00–4.65%), with 4 (95% CI = 0–78) attributable deaths and 7 (95% CI = 0–128) registrations.

Exposures affecting leukaemia

An estimated 5468 men and 2817 women were assessed as 'ever exposed' to 1,3-butadiene. For leukaemia and exposure to 1,3-butadiene, the total AF was 0.01% (95% CI = 0.00–0.06%), with 0 (95% CI = 0–2) attributable deaths and 0 (95% CI = 0–3) registrations.

An estimated 5310 men and 4429 women were assessed as 'ever exposed' to EO. For leukaemia and exposure to EO, the total AF was 0.01% (95% CI = 0.00–0.21), with 0 (95% CI = 0–7) attributable deaths and 1 (95% CI = 0–11) registrations.

An estimated 186 617 men and 83 078 women were assessed as 'ever exposed' to formaldehyde. For leukaemia and exposure to formaldehyde, the total AF was 0.20% (95% CI = 0.05–0.48%), with 6 (95% CI = 2–15) attributable deaths and 10 (95% CI = 3–25) registrations.

Table 3 Lymphohaematopoietic malignancies: burden estimation results

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)
Leukaemia										
Benzene	342,236	704,474	0.0149	0.0305	0.0019 (0.0000–0.0033)	0.0034 (0.0000–0.0068)	2 (0–33)	2 (0–45)	3 (0–59)	3 (0–68)
1,3-Butadiene	5,468	2,817	0.0002	0.000	0.0001 (0.0000–0.0008)	0.0000 (0.0000–0.0004)	0 (0–2)	0	0 (0–3)	0 (0–1)
Ethylene oxide	5,310	4,429	0.0002	0.0002	0.0002 (0.0000–0.0019)	0.0000 (0.0000–0.0026)	0 (0–4)	0 (0–3)	1 (0–6)	0 (0–5)
Formaldehyde	186,617	83,078	0.0081	0.0036	0.0024 (0.0006–0.0060)	0.0012 (0.0004–0.0027)	5 (1–12)	1 (0–3)	8 (2–20)	2 (1–5)
Ionising radiation	149,974	33,770	0.0065	0.0015	0.0002	0.0001	0	0	1	0
Non-arsenical insecticides	1,159,288	348,966	0.0504	0.0151	0.0050 (0.0012–0.0091)	0.0015 (0.0004–0.0027)	10 (2–18)	2 (0–3)	17 (4–30)	3 (1–5)
Totals[a]					**0.0088 (0.0020–0.0353)**	**0.0048 (0.0008–0.0447)**	**18 (4–71)**	**5 (1–49)**	**30 (7–118)**	**9 (1–80)**
Multiple myeloma										
Non-arsenical insecticides	1,159,288	348,966	0.0504	0.0151	0.0045 (0.0000–0.0097)	0.0014 (0.0000–0.0029)	5 (0–10)	1 (0–2)	8 (0–18)	2 (0–3)
Non-Hodgkin's lymphoma										
Hairdressers and barbers	45,726	404,672	0.0020	0.0175	0.0004 (0.0000–0.0014)	0.0035 (0.0000–0.0012)	1 (0–3)	4 (0–15)	2 (0–6)	12 (0–41)
Non-arsenical insecticides	1,159,288	348,966	0.0504	0.0151	0.0056 (0.0027–0.0086)	0.0018 (0.0009–0.0027)	11 (5–17)	2 (1–3)	27 (13–41)	6 (3–9)
TCDD	838,863	272,873	0.0036	0.0118	0.013 (0.0000–0.059)	0.0040 (0.0000–0.0019)	25 (0–118)	5 (0–24)	61 (0–281)	14 (0–65)
Tetrachloro-ethylene	249,421	123,004	0.0108	0.0053	0.0025 (0.0000–0.0135)	0.0016 (0.0000–0.0085)	5 (0–27)	2 (0–11)	12 (0–64)	5 (0–30)
Trichloroethylene	24,728	26,444	0.0011	0.0011	0.0003 (0.0000–0.0007)	0.0003 (0.0000–0.0007)	1 (0–1)	0 (0–1)	1 (0–3)	1 (0–2)
Totals[a]					**0.0021 (0.0000–0.0069)**	**0.0011 (0.0009–0.0029)**	**43 (0–138)**	**14 (1–37)**	**102 (0–328)**	**39 (3–101)**

Abbreviations: AF = attributable fraction; TCDD = 2,3,7,8-tetrachlorodibenzo-*para*-dioxin. [a]Totals are the product sums and are not therefore equal to the sums of the separate estimates of attributable fraction, deaths and registrations for each agent. The difference is especially notable where the constituent AFs are large.

An estimated 149,974 men and 33,770 women were assessed as 'ever exposed' to IR during the REP. For the total leukaemias (excluding CLL) and exposure to IR, the total AF was 0.02%, with no attributable deaths and only one registration.

Exposures affecting NHL

An estimated 838,863 men and 272,873 women were assessed as 'ever exposed' to TCDD during the REP. For NHL, the total AF from exposure to TCDD was 0.86% (95% CI = 0.00 – 4.00%), with 31 (95% CI = 0 – 142) attributable deaths and 74 (95% CI = 0 – 346) attributable registrations. Men involved in the iron and steel industry had the largest number of attributable registrations and deaths (19 and 8, respectively, for NHL).

An estimated 45,726 men and 404,672 women were assessed as 'ever employed' as a hairdresser or barber during the REP. For the NHL and employment as a hairdresser, the total AF was 0.19% (95% CI = 0.00 – 0.63%), with 5 (95% CI = 0 – 18) attributable deaths and 14 (95% CI = 0 – 48) registrations.

An estimated 249,421 men and 123,004 women were assessed as 'ever exposed' to tetrachloroethylene during the REP. For NHL and exposure to tetrachloroethylene, the total AF was 0.20% (95% CI = 0.00 – 1.12%), with 7 (95% CI = 0 – 38) attributable deaths and 17 (95% CI = 0 – 94) registrations. Individuals involved in personal and household services, which includes dry cleaning, had the largest number of attributable registrations and deaths, for both men (9 and 4, respectively) and women (4 and 2, respectively).

An estimated 24,728 men and 26,444 women were assessed as 'ever exposed' to TCE during the REP. For NHL and exposure to TCE, the total AF was 0.03% (95% CI = 0.00 – 0.07), with 1 (95% CI = 0 – 2) death and 3 (95% CI = 0 – 6) registrations.

DISCUSSION

The results for leukaemia update those previously published (HSE, 2007). Because of the availability of more recent data, the overall estimates have increased from 0.2% to 0.74% (0.3% to 0.88% for men, and 0.05% to 0.48% for women). However, the revised overall estimate is at the lower end of the range given by Steenland *et al* (2003) of an AF estimate ranging from 0.8 to 2.0. It is also significantly lower than the AF estimate of 10.9 reported by Nurminen and Karjalainen (2001) for Finland; the AF estimate of 4.1 for workers in France (Boffetta *et al*, 2010); and the global estimate of 3% reported by Driscoll. It should be noted that in the Global Burden study the risk estimates for leukaemia were 2.0 for low exposures and 4.0 for high exposures, with countries such as the United Kingdom assumed to have 90% of the exposed workforce at the 'low level' and 10% at the high level of exposure (Driscoll *et al*, 2005). Exposure levels, which could give risk estimates of this size, are unlikely to have existed in Britain in the REP of concern in this study.

For NHL, the overall AF estimate was 1.74, with 57 deaths and 140 registrations. This is a third of the figure of 4.7 given by Nurminen and Karjalainen (2001) for Finland, who also gave figures of 13.5% for men and 3.1% for women, compared with 0.9% and 0.5% in this study. Classification changes agreed in a recent re-evaluation of chemical agents by IARC (Baan *et al*, 2009) mean that our estimates for all of these malignancies are likely to be underestimated. Benzene was classified as a probable carcinogen (2A) for chronic lymphocytic leukaemia, MM and NHL; EO was classified as probable carcinogen for NHL, MM and CLL; and work in the rubber industry was classified as a definite carcinogen for lymphomas overall (Baan *et al*, 2009).

Conflict of interest

The authors declare no conflict of interest.

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Appendix

British Occupational Cancer Burden Study Group

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