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The burden of cancer at work: estimation as the first step to prevention

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ABSTRACT

Objectives: Work-related cancers are largely preventable. The overall aim of this project is to estimate the current burden of cancer in Great Britain attributable to occupational factors, and identify carcinogenic agents, industries and occupations for targeting risk prevention.

Methods: Attributable fractions and numbers were estimated for mortality and incidence for bladder, lung, non-melanoma skin, and sinonasal cancers, leukaemia and mesothelioma for agents and occupations classified as International Agency for Research on Cancer (IARC) Group 1 and 2A carcinogens with "strong" or "suggestive" evidence for carcinogenicity at the specific cancer site in humans. Risk estimates were obtained from published literature and national data sources used for estimating proportions exposed.

Results: In 2004, 78 237 men and 71 666 women died from cancer in Great Britain. Of these, 7317 (4.9%) deaths (men: 6259 (8%); women: 1058 (1.5%)) were estimated to be attributable to work-related carcinogens for the six cancers assessed. Incidence estimates were 13 338 (4.0%) registrations (men: 11 284 (6.7%); women 2054 (1.2%)). Asbestos contributed over half the occupational attributable deaths, followed by silica, diesel engine exhaust, radon, work as a painter, mineral oils in metal workers and in the printing industry, environmental tobacco smoke (non-smokers), work as a welder and dioxins. Occupational exposure to solar radiation, mineral oils and coal tars/pitches contributed 2557, 1867 and 550 skin cancer registrations, respectively. Industries/occupations with large numbers of deaths and/or registrations include construction, metal working, personal and household services, mining (not metals), land transport and services allied to transport, roofing, road repair/construction, printing, farming, the Armed Forces, some other service industry sectors and manufacture of transport equipment, fabricated metal products, machinery, non-ferrous metals and metal products, and chemicals.

Conclusions: Estimates for all but leukaemia are greater than those currently used in UK health and safety strategy planning and contrast with small numbers (200–240 annually) from occupational accidents. Sources of uncertainty in the estimates arise principally from approximate data and methodological issues. On balance, the estimates are likely to be a conservative estimate of the true risk. Long latency means that past high exposures will continue to give substantial numbers in the near future. Although levels of many exposures have reduced, recent measurements of others, such as wood dust and respirable quartz, show continuing high levels.

There is increasing interest in estimating and comparing burdens of disease generally[1] and for cancer.[2 3] Estimates can identify major risk factors and high-risk populations, support decisions on priority actions for risk reduction and provide an understanding of important contributions to health inequalities. Nearly 30 years ago Doll and Peto (1981), in their report to the US Congress, presented a method of estimating the effects of different factors on cancer mortality in the USA[4]; their estimate for occupational factors was 4% of all US cancer deaths with an uncertainty range of 2%–8%. The aim of this project is to produce an updated and detailed estimate of the current burden of occupational cancer in Great Britain (GB) that will help to inform the development and prioritisation of practical measures to reduce the burden in the future, specifically in GB, but also more generally in the developed world. The estimates of current burden of occupational cancer are based on exposure levels from up to 50 years ago when exposure levels may have been much higher than they are at present. Prioritisation for preventive effort requires consideration of ongoing risks and current exposures. The next phase of the project will include predictions of future burden based on current exposure levels.

In this paper the outcomes of the first phase of the project are presented. Estimates have been made of the current burden due to past occupational exposures for six cancers, which are important in terms of both the annual numbers of deaths and cancer registrations they produce and their potential to be caused by exposure to occupational carcinogens. The six are cancer of the bladder; leukaemia; cancer of the lung, mesothelioma; non-melanoma skin cancer (NMSC) and sinonasal cancer. An overview of the methodology developed and the data used is also given.

METHODS

Occupational carcinogens assessed

At two international workshops held as part of the project to discuss the methodology (http://www.hse.gov.uk/research/hsl_pdf/2005/hsl0554.pdf; http://www.hse.gov.uk/research/hsl_pdf/2007/hsl0732.pdf) the participants advised that priority should be given initially to International Agency for Research on Cancer (IARC) Group 1 and 2A occupationally related carcinogens. Agents or occupations in these IARC groups were included that had either "strong" or "suggestive" evidence of carcinogenicity in humans for the specific cancer site, as defined by Siemiatycki et al (2004) and subsequent IARC publications.[5 7] Those with "strong" evidence were defined as "certain" carcinogens for the purposes of this study and those with "suggestive" evidence of carcinogenicity in humans were defined as "uncertain"

carcinogens. In addition there had to be substantial existing exposures in GB and/or cases of cancer still occurring due to past exposures.

Data sources

(i) Cancer mortality and registration data

Estimation was carried out on a cancer by cancer basis for 2004 for mortality and 2003 for cancer incidence, the most recent years for which published data were available at the time of estimation. Deaths for 2005 and cancer registrations for 2004 are now available but total numbers do not differ substantially from those used. Mortality data were obtained from ONS, Mortality Statistics, Series DH2, for England and Wales and the General Register Office for Scotland. Cancer incidence data were obtained from ONS, Cancer Statistics, Registrations, Series MB1 for England, the Scottish Cancer Registry, (http://www.isdscotland.org/isd) and the Welsh Cancer Intelligence and Surveillance Unit (http://www.wales.nhs.uk/sites3/home.cfm?OrgID = 242).

(ii) Risk estimates

Standard search criteria were used to identify key studies, meta-analyses or pooled studies, taking into account relevance to GB, large sample size, effective control for confounders, adequate exposure assessment, and clear case definition. Where only a narrative review was available giving a range of risk estimates from several relevant studies a combined estimate of the relative risks (RRs) was calculated based on a random- (for heterogeneous RRs) or fixed- (for homogeneous RRs) effects model. If no meta-analysis, pooled study or narrative review were available a single key study was selected using the criteria above. Dose-response risk estimates were generally not available, nor were proportions of those exposed at different levels of exposure over time available for the working population in GB. In our study separate risk estimates were generally extracted relating to an overall "higher" level and an overall "lower" level. For one or two specific agents it was possible to extract risk estimates for three levels of exposure or for specific exposure scenarios (see table 2 footnotes). Where no estimate could be identified for very low/background/environmental levels of exposure, an RR of one was arbitrarily assigned.

(iii) Exposed population estimates

If the relative risks were extracted from an industry-based study population, for example a cohort study, a national (external) data source was used for estimating the proportion of the population exposed. If the relative risks were extracted from a population-based study, for example a case-control study of cancer registry cases, an estimate of the proportion of cases exposed was also obtained from the study, although such studies were rarely available for GB. The national data sources used were the CARcinogen EXposure (CAREX) database,[8] and for exposures not covered by CAREX, the annual Labour Force Survey (LFS) (http://www.statistics.gov.uk/) and the Census of Employment (CoE) (https://www.nomisweb.co.uk/). Data from CAREX are not differentiated by sex; 1991 Census data by industry and occupation were used to estimate the relative proportions of men and women exposed (http://cdu.mimas.ac.uk). The industry categories listed in CAREX were allocated to "higher" and "lower" exposure categories assuming the distributions of levels of exposure and risks associated with these broadly matched those of the studies from which RRs were extracted.

Statistical analysis

The attributable fraction (AF), that is the proportion of cases that would not have occurred in the absence of exposure, has been estimated. There are two principal methods for estimating the AF, both of which depend on knowledge of the risk of the disease due to the exposure of interest and the proportion of the population exposed.[9]

To estimate the AFs for each cancer/occupational carcinogen Levin's equation[10] was used if risk estimates came from an industry-based study, review or meta-analysis together with estimates of the proportion of the population exposed from independent sources of data. Miettinen's equation was used if risk estimates and proportion of cases exposed came from a population-based study.[11] The equations used are given in the Statistical Appendix. The AFs were applied to total numbers of cancer-specific deaths (2004) and cancer registrations (2003) to give attributable numbers. Where AFs were only available for mortality these were used for estimation of attributable registrations and vice versa. Similarly if separate AFs for women could not be estimated those for men or for men and women combined were used.

To take account of cancer latency a "relevant exposure period" (REP) was defined as the period during which exposure occurred that was relevant to the development of the cancer in the target year 2004. For solid tumours a latency of at least 10 years and at most 50 years was assumed giving an REP of 1955–1994. For haematopoietic neoplasms 0–20 years latency was assumed giving an REP of 1985–2004. The proportion of the GB population exposed to the occupational carcinogens of concern over the REP was estimated taking into account changes in numbers employed in the primary and manufacturing industry and service sectors in GB over the REP. Figures from the LFS show, for example, that the numbers of men employed in primary and manufacturing industry were 40% higher in the 1970s than they were in the early 1990s, whereas the numbers employed in the service industries were 10% lower. Adjustment for employment turnover over the period for grouped main industry sectors was also carried out using LFS data on the distribution of length of time with current employer (in excess of 1 year) by length of employment. This gave the numbers ever employed for at least 1 year during the REP allowing for normal life expectancy to 2004 (see Statistical Appendix equation 3). The adjustment factors for changing employment levels and percentage annual turnovers used are shown in the table in the Statistical Appendix.

The AF for mesothelioma was derived directly from several studies of UK mesothelioma cases that suggest that between 85% and 90% of male mesothelioma cases are due to occupational exposure[12 13] (Darnton, personal communication). Studies in which results were reported separately for females in the UK (Darnton, personal communication) and elsewhere[14 15] gave estimates of 20%–30%. For the estimate of the AF due to the "Established plus Uncertain carcinogens", cases described as due to paraoccupational (eg, exposure from living near an asbestos factory or handling clothes contaminated due to occupational exposure) or environmental exposure to asbestos are also included.

A recent analysis of lung cancer mortality for the whole of GB between 1980 and 2000 by occupational group in relation to indices of asbestos exposure and smoking habits suggested that the ratio of asbestos-related lung cancer to mesothelioma deaths is between two-thirds and one.[16] A ratio of 1:1, mesothelioma to

lung cancer deaths has been used for the estimation of numbers of lung cancers attributable to asbestos.

For lung cancer associated with radon exposure from natural sources, estimates of rates of lung cancer due to exposure to radon in domestic buildings were applied to estimates of the time employees spend in workplaces where radon exposure occurs.

AFs for all the relevant carcinogenic agents and occupational circumstances were combined into a single estimate of AF for each separate cancer. AFs in general cannot be summed directly if there is a possibility that workers will have been exposed to more than one occupational carcinogen during their working lifetimes in the relevant exposure period. Where data allowed, the exposed numbers were therefore partitioned between overlapping exposures, for example by excluding steel foundry workers from the CAREX estimates of numbers exposed to other lung carcinogens. Alternatively, where exposure to more than one carcinogen associated with the same cancer site occurred, an AF was estimated only for the "dominant" carcinogen with the highest risk estimate. The method of combining the AFs was then determined by whether there was residual exposure to multiple carcinogens. If so, it was assumed that the exposures were independent of one another and that their joint carcinogenic effects were multiplicative. Such multiple/overlapping exposures were assigned to exposure sets that were judged to be non-overlapping with other exposure sets and single exposure scenarios. The AFs within exposure sets were multiplied using equation 5 in the Statistical Appendix. The combined AFs for each non-overlapping exposure set were then summed, together with non-overlapping single exposures.

An overall AF for occupation for the six cancers assessed so far was estimated by summing the attributable numbers for the six cancers and dividing by the total number of cancers in GB (table 1).

Although it is relatively straightforward to estimate a confidence interval for AFs of single carcinogenic agents,[9] the methodology for estimating confidence intervals for AFs estimated from more than one risk estimate for multiple exposure levels and for combinations of AFs is more complex, for example requiring Monte Carlo methods. The methodology for this is currently under development and confidence limits are not presented.

Separate technical reports for each cancer giving full details of data and calculations, and a report expanding on the statistical methodology are accessible at http://www.hse.gov.uk/research/rrhtm/rr595.htm.

RESULTS

The overall occupational AFs for the six cancers investigated so far are summarised in table 1. Six per cent (n = 4693) of cancer deaths in 2004 in men and 1.0% (n = 701) in women in GB have been estimated to be due to occupation for carcinogens with strong human evidence of carcinogenicity, our "established" carcinogens. These estimates were 4.9% (7317 deaths) in total, 8.0% for men (6259 deaths) and 1.5% for women (1058 deaths), for carcinogens with strong or suggestive evidence of carcinogenicity in humans, our "established plus uncertain" carcinogens.

The combined AFs for registrations are 6.7% (n = 11 284) for men in 2003 and 1.2% (n = 2054) for women based on established and uncertain carcinogens. These are lower than that for deaths because of the very large numbers for NMSC.

Table 2 gives the number of deaths for each cancer attributable to each of the agents and occupations considered (so far) for established and uncertain carcinogens together. The studies that were used for the risk estimates for each agent or occupation and the type of study are also given in table 2. Overall, asbestos exposure contributes the largest number of deaths (mesothelioma and lung cancer), followed by exposure to silica (lung), diesel engine exhaust (DEE) (lung, bladder), radon exposure from natural exposure in workplaces (lung), occupation as a painter (lung, bladder), mineral oils in metal workers (bladder, sinonasal, NMSC), environmental tobacco smoke (ETS) in non-smokers (lung), mineral oils in printers (lung), occupation as a welder (lung) and exposure to dioxins (lung).

For the six cancers, exposures in the construction industry are estimated to produce over half of GB's occupational attributable cancer deaths in men (n = 3219). Workers in this industry are exposed to 17 of the carcinogens considered so far (13 resulting in at least one death), shown in fig 1 for men, who account for an estimated 99% of the construction workforce in the REPs for these cancers.

There are 44 deaths for NMSC attributable to occupational exposure to mineral oils, polycyclic aromatic hydrocarbons (PAHs) and solar radiation. However, estimated numbers of registrations for NMSC associated with mineral oils are 1745 males (M), 122 females (F), with PAHs; mainly coal tars and pitches are 547 M (544 in construction), 3 F; and with solar radiation are 1824 M (805 in construction), 733 F.

Table 3 gives for each cancer, numbers of deaths (registrations for NMSC) within industry sectors or jobs for which there were at least 50 estimated attributable cancers; the exposures concerned are listed, with those contributing most (at least 10 cancers in men plus women) being shown in bold. Painters and welders are assumed to be exposed to many different carcinogens. The importance of single exposures within some industry sectors is also highlighted, for example PAHs in coal tar and pitches in roofing and road repair and construction, metal working fluids in the metal industries, mineral oils and printing inks in the printing industry. In addition to the construction industry table 3 shows that multiple exposures potentially occur in several other industries, including the manufacture of industrial chemicals (18, notably asbestos) and other chemical products (16, also notably asbestos), manufacture of transport equipment (15, particularly asbestos, chromium, cobalt, silica, radon and solar radiation), electricity, gas and steam (15, notably asbestos and solar radiation), non-ferrous metal basic industries (14, notably arsenic), the manufacture of fabricated metal products (14, notably cobalt, chromium and silica), the manufacture of machinery except electrical (13, notably silica, chromium, cobalt and radon), services allied to transport (13, notably DEE and solar radiation), and printing, publishing and allied industries (12, notably solar radiation). More than 10 different exposures were also found in sanitary and similar services (14, notably solar radiation and asbestos), personal and household services (11, notably asbestos, diesel engine exhaust, ETS and radon), and land transport (11, notably DEE, asbestos and solar radiation).

Table 3 also highlights the range of industry sectors where particular substances are occurring and contributing to the burden of occupational cancer. These sectors are not always those where substantial historical exposures have occurred. For example, the main occupations with substantial historical exposure to inorganic arsenic include hot copper smelting, manufacturing of arsenical pesticides and sheep-dip compounds, fur handlers and vineyard workers and some miners.[63 64] In GB the majority of exposure occurs in the non-ferrous metal basic industry and the manufacture of wood and wood and cork products (44 and 31 lung cancer deaths, respectively).

Table 1 Estimated attributable fractions, deaths and registrations by cancer site in 2004 (2003 for registrations)

	Attributable fraction (%)			Attributable numbers: Deaths		Attributable numbers: Registrations	
Cancer site	Male	Female	Total	Male	Female	Male	Female
(a) Established carcinogens only (IARC Group 1, strong human evidence)							
Bladder	1.3	0.6	1.0	40	10	89	17
Leukaemia	0.3	0.5	0.2	4	5	5	6
Lung	16.5	4.5	11.6	3137	599	3509	680
Mesothelioma	85–90	20–30	74–80	1450	75	1450†	75†
NMSC	11.8	3.0	8.4	38	6	3992	855
Sinonasal	34.1	10.8	23.4	24	6	74	18
Total							
Based on deaths	6.0	1.0	3.6	4693	701		
Based on registrations	5.4	1.0	3.2			9120	1652
(b) Established + uncertain carcinogens (IARC Group 1 and 2A, strong + suggestive human evidence)							
Bladder	11.6	2.0	8.3	362	32	816	57
Leukaemia	2.7	0.8	1.7	58	11	93	15
Lung	21.6	5.5	15.0	4106	728	4594	826
Mesothelioma	98*	90*	97*	1650	270	1650†	270†
NMSC	11.8	3.0	8.4	38	6	3992	855
Sinonasal	64.3	18.4	43.3	45	11	140	31
Total:							
Based on deaths	8.0	1.5	4.9	6259	1058		
Based on registrations	6.7	1.2	4.0			11 284	2054
Total cancers in GB				78 237	71 666	167 506	164 586

*includes cases described as due to paraoccupational or environmental exposure to asbestos.

†Taken as equal to attributable deaths for this short-survival cancer.

Mid-points of ranges used when estimating attributable numbers and combining results for mesothelioma with the other cancers.

GB, Great Britain; IARC, International Agency for Research on Cancer; NMSC, non-melanoma skin cancer.

Although potential asbestos exposure occurred in large numbers of workers (over 65 000 in the REP) in the mining industry (excluding coal mining) giving 305 deaths each from lung cancer and mesothelioma in men, the industry with the greatest potential for asbestos exposure was the construction industry, occurring for example in asbestos removal or stripping, giving 1012 deaths each from lung cancer and mesothelioma in men. In personal and household services, 362 deaths each from lung cancer and mesothelioma occurred (221 each of these in women). Other industry groups where asbestos exposure contributed to fairly large numbers of deaths in men for both lung cancer and mesothelioma were work in land transport[45] and manufacture of transport equipment.[39]

Other substances occurring across several industry sectors that contributed substantially to the burden of cancer are listed below.

Diesel engine exhaust

In addition to 21 male bladder cancer deaths and a total of 268 lung cancer deaths attributed to exposure to DEE in the land transport industry where over 600 000 workers were estimated to be potentially exposed over the REP, an additional half a million workers were exposed to DEE over the REP in the construction industry giving 20 male bladder cancer deaths and 238 male lung cancer deaths.

ETS (non-smokers)

Significant numbers of workers were exposed to ETS in the wholesale and retail trade, restaurants and hotels, construction, and financing, insurance, real estate and business services giving 104, 35 and 29 lung cancer deaths, respectively.

Radon

There are now very few workers in metal ore mining in the UK exposed to radioactive radon and its progeny. High levels of radon in the workplace occur in similar areas to those of concern in residential dwellings in the UK such as Cornwall, Devon Northamptonshire and parts of Derbyshire, Somerset, Wales, Grampian and the Highlands of Scotland. Approximately 2000 lung cancer deaths a year have been estimated to be due to radon exposure of which between about 90 and 275 are attributable to exposure occurring in the workplace.[55] Although any workplace in the affected areas is potentially at risk of exposure, the large numbers of workers employed in the wholesale and retail trade, restaurants and hotels, and in finance, insurance, real estate and business services gave relatively high estimated numbers of lung cancer deaths — 75 and 47, respectively.

Silica

In GB the majority of workers exposed to silica work in the construction industry, manufacture of other non-metallic mineral products and manufacture of pottery, china and earthenware giving an estimated 667, 28 and 25 deaths of men in these industries, respectively.

Solar radiation

The risk for NMSC caused by occupational exposure to solar radiation is difficult to estimate because everyone is exposed to sunlight to a greater or lesser degree depending on residential location and leisure time activities. Risk estimates from a US-based case-control study of 6565 cases of NMSC were used that estimated separate risks for work that combined indoor and outdoor work, outdoor work by non-farmers and farming.[58]

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Table 2 Continued

Exposure‡	Reference (numbers 16–62 in the reference list)§	Type of study	Cancer site													
			Bladder		Leukaemia		Lung		Mesothelioma		NMSC		Sinonasal		Total	
			M	F	M	F	M	F	M	F	M	F	M	F	M	F
Ionising radiation	Blettner *et al* (2003)[38]	Multi-national occupation group cohort			1	1									1	1
Lead	Steenland & Boffetta (2000)[39]	Meta-analysis					38‡‡‡	7‡‡‡							38	7
Leather dust§§§§	Fu *et al* (1996)[40]	English shoe-manufacturing workers cohort											5	6	5	6
Mineral oils (metalworkers)	Tolbert (1997)[41]**	Review¶¶¶	243‡‡‡	13‡‡‡							17‡‡‡	1‡‡‡	20‡‡‡	2‡‡‡	279	16
	Eisen *et al* (2001)[42]‡‡	US automobile industry cohort														
	Roush *et al* (1980)[43]††	US case-control study														
Mineral oils (printers)	Leon *et al* (1994)[44]	Industry cohorts¶¶¶					195	40							195	40
Nickel	Sorohan & Williams (2005)[45]¶	Clydach refinery cohort					6***,‡‡‡	2‡‡‡					3***,‡‡‡	1‡‡‡	8	3
	Seilkop & Oller (2003)[46]¶	Review of industry studies														
	Grimsrud & Peto (2006)[47]††	Clydach refinery cohort														
Non-arsenical pesticides	Acquavella (1998)[48]	Meta-analysis of industry cohorts			15	3									15	3
Painters (occupation)	Chen & Seaton (1998)[49]¶	Meta-analysis of cohort studies	32	2			244	17							277	19
	Bosetti *et al* (2005)[50]**	Quantitative review of industry-based studies														
PAHs (general)	Armstrong *et al* (2004)[51]¶	Meta-analysis of industry cohorts****	18‡‡‡	0‡‡‡			6	0							23	0
	Unwin *et al* (2006)[52]¶	Narrative review of industry cohorts¶¶¶														
	Boffetta *et al* (1997)[53]**															
PAHs (coal tars and pitches)	Partanen & Boffetta (1994)[54]	Meta-analysis of cohort studies in asphalt workers									5	0			5	0
Radon	NRPB (2000)[55]	Attributable domestic death rates applied to employees time at work					185	185							185	185
Silica	Kurihara & Wada (2004)[56]	Meta-analysis					797	53							797	53
	Steenland *et al* (2001)[57]	Cohort pool														
Solar radiation	Freedman *et al* (2002)[58]	US death certificate-based case-control study									17†††	5†††			17	5
Steel foundry workers	Sorahan *et al*. (1994)[59]	UK industry cohort					25	1							25	1
Textile dust††††	Luce *et al* (2002)[60]	Pool of population-/hospital-based case-control studies¶¶¶											1	2	1	2

Continued

Table 2 Continued

Exposure‡	Reference (numbers 16–62 in the reference list)§	Type of study	Cancer site: Bladder M	Bladder F	Leukaemia M	Leukaemia F	Lung M	Lung F	Mesothelioma M	Mesothelioma F	NMSC M	NMSC F	Sinonasal M	Sinonasal F	Total M	Total F
Welders (occupation)††††	Ambroise *et al* (2006)[61]	Meta-analysis					139	13							139	13
Wood dust	Demers *et al* (1995)[62]	Pool of population-based case-control studies											21***	0***	21	0
Established exposures only†			40	10	4	5	3137	599	1450	75	38	6	24	6	4692	701
Established plus uncertain exposures†			362	32	58	11	4106	728	1650	270	38	6	45	11	6259	1058

*Totals do not always sum across rows due to rounding error.
†Numbers for the separate exposures do not sum to the combined exposure totals due to allowance made for overlapping exposures.
‡Estimates have not been made for some IARC Group 1 and 2A carcinogens. Reasons include: relevant exposures had ceased in GB by 1950 (rubber industry/for bladder cancer); very small or unknown numbers of workers exposed (BCME and CME, αCT&BC, epichlorohydrin, haematite mining, 1,3-butadiene,ethylene oxide in men); no relative risk (RR) estimates were available (4,4′methyl bis(2-chloroaniline) and styrene-7,8-oxide for bladder cancer, benzo[a]pyrene, benzo[a]anthracene & dibenz[a,h]anthracene for NMSC, isopropanol manufacture, strong acid process for sinonasal cancer); workers were also exposed to another dominant carcinogen (boot and shoe manufacture and repair included under benzene for leukaemia, and under exposure to aromatic amines before 1962 for bladder cancer, rubber industry exposure included under exposure to chromium, cadmium, silica and PAHs for lung cancer).
§Where two references are given, the first was used for a "higher" exposure risk estimate and the second for a "lower/background" exposure risk estimate, unless otherwise stated.
¶Lung cancer.
**Bladder cancer.
††Sinonasal cancer.
‡‡Non-melanoma skin cancer.
§§Leukaemia.
¶¶Mesothelioma.
***Based on three exposure levels.
†††Based on separate exposure scenario categories.
‡‡‡RR for background exposure level was set to 1, giving AF = 0.
§§§RRs from incidence studies used. For all other estimates RRs from mortality studies or meta-analyses combining mortality and incidence studies were used.
¶¶¶Inverse variance weighted average RR estimated by study team using RRs given in the reference.
****A unit relative risk estimate was used to derive exposure level-specific RRs.
††††Exposure classified as IARC 2B; included in the "uncertain" group. For cobalt, estimated lung cancer deaths were based on total numbers exposed to cobalt, with or without exposure to tungsten carbide. Cobalt with tungsten carbide is classified as IARC 2A.
‡‡‡‡Low exposed RR estimated by the study team as $1+(RR_{high}-1)/2$.
§§§§Boot and shoe manufacture and repair.
αCT&BC, α-chlorinated toluenes & benzoyl chloride; BCME, bis(chloromethyl)ether; CMF, chloromethyl methyl ether; IARC, International Agency for Research on Cancer; NMSC, non-melanoma skin cancer; PAH, polycyclic aromatic hydrocarbon; RR, relative risk.

Original article

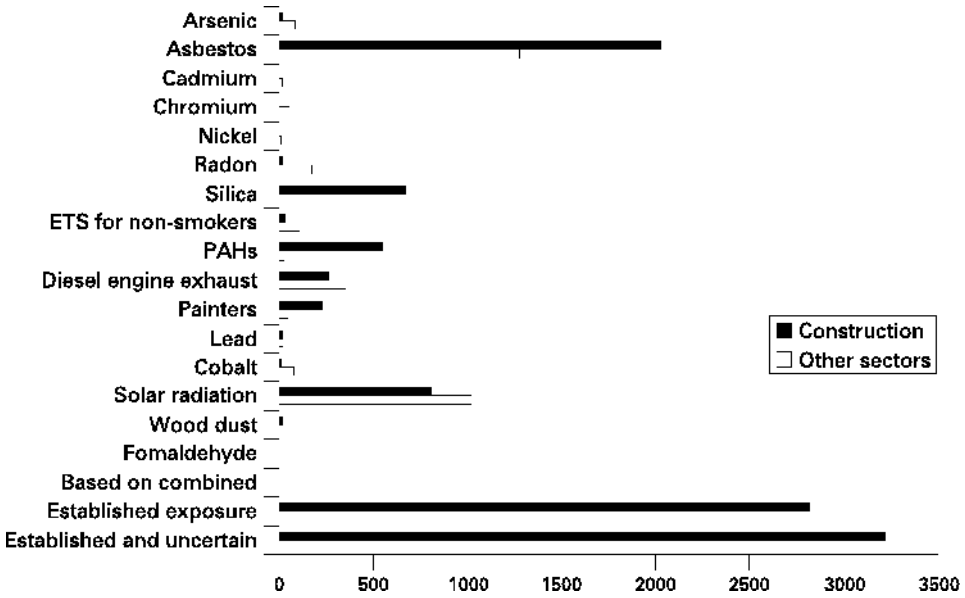

Figure 1 Lung cancer deaths for men in 2004 attributable to work in the construction industry. ETS, environmental tobacco smoke; PAH, polycyclic aromatic hydrocarbon.

Large numbers of registrations were estimated for the construction industry (860), public administration and defence (armed forces) (232), wholesale and retail trade, restaurants and hotels (168), land transport (166), manufacture of transport equipment (154), agriculture and hunting (143) and communication (132).

A table giving industry sectors and occupations with at least 10 attributable deaths and/or registrations for each of the six cancer sites assessed so far (50 registrations for NMSC) by occupational exposure is given in a supplementary table online.

DISCUSSION

All occupational cancers are potentially avoidable. Our estimate of the current burden in 2004 of six cancers due to past occupational exposures of 8% for men and 1.5% for women translates to over 7300 cancer deaths in GB. This is in contrast to the 223 deaths due to occupational injuries that occurred that year (http://www.hse.gov.uk/statistics/overall/fatl0506.pdf). Burden estimates from other studies range between 3% and 10%.[65–72] With the exception of leukaemia, all our updated estimates are greater than those of Doll and Peto (1981).[4] The steep rise in asbestos-related deaths from lung cancer and mesothelioma since 1981 has made a major contribution to the increase.[16 73]

Our methodology and the data available in GB have allowed a more detailed investigation of the carcinogenic agents, occupational circumstances and industry sectors than has been possible in other burden estimation studies. We have also addressed the potential to be exposed to several carcinogens concurrently and the impact on total burden.

The results must be considered taking account of several uncertainties and limitations. These are discussed below and the potential impact on the estimates is indicated in table 4.

Agents classified by IARC as Group 1 and 2A carcinogens were assessed. Other substances such as IARC Group 2B carcinogens, many of which may be treated as if they were human carcinogens in regulatory settings have not yet been evaluated; our estimates could thus be too low.

Uncertainty or bias may have been introduced in the choice of the study for obtaining data for the risk estimates, for example if the exposures in the source study did not reflect those experienced in GB or distributions of confounders differed between the source population and GB. A major gap in available information was a lack of separate risk estimates for women and/or cancer incidence. The use of risk estimates derived from studies of men for women and mortality risk estimates for incidence may have biased the AFs. Epidemiological studies of occupational groups often result in a "healthy worker effect", that is a reduced overall risk estimate compared to the general population. This together with potential misclassification of exposure in epidemiological studies could lead to an underestimation of the true effect and thus an underestimation of the burden.

Most of the risk estimates from the published literature were related to some estimate of cumulative exposure. In assigning "higher" and "lower" categories to the CAREX industry groups implicit assumptions were made regarding the similarity of durations and intensities of exposure between the source and target (national) populations. National data are not generally available on the proportions of those exposed at different levels of exposure.

Where no risk estimate could be identified for very low/background/environmental levels of exposure, a risk estimate of one was arbitrarily assigned to the "lower" group, giving a zero attributable burden. This implies an assumption that a threshold existed in the dose relationship between exposure and effect contrary to usual risk assessment guidelines for carcinogens; this may have contributed to underestimation of the burden; a large number of people exposed at low levels associated with a low risk of disease may contribute more to the burden than a small number exposed at high levels associated with a high risk.

In most occupational epidemiological studies very short-term workers, for example those employed for less than 1 year, are excluded. Our turnover factor was thus calculated excluding workers with less than 1 year's employment. Inclusion of these would have increased the numbers ever exposed considerably. For example, for the construction industry, the annual turnover would increase from 13% excluding workers with under 1 year of employment to 22% when they are included. The overall effect of including these short-term workers would be to increase the AFs and attributable numbers. However, when these short-term workers are excluded the turnover factor

Table 3 Industry sectors and occupations with an estimate of a total of at least 50 attributable deaths (registrations for NMSC) by cancer site and occupational exposure

	Attributable deaths (registrations for NMSC)														
	Bladder		Leukaemia		Lung		Mesothelioma		NMSC		Sinonasal		Total*		
Industry/job categories	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Exposures
Construction including:	47	0	0	0	2132	10	1012		1336	58	15	0	4543	69	Ar, Asb, Ch, Co, DEE, ETS, Pb, PAH, R, Si, Sr, W, Ca, N, Fo, PAHc, "painting"
Roofers, glaziers, road surfacers, concreters, roadman, paviours, kerb layers and their foremen					544					3			544	3	PAHc
Painters & decorators	27	0			201	2			228	2	"painting"Metal workers		243	13	1745 122 20
	2	2008			137	MWF									
Personal and household services	0	0	1	0	170	240	141	221	6	7			317	468	Asb,Ca,Bz,DEE,ETS,PAH, R, Sr, Ch, Pb, Fo
Mining (not metals)	2	1			347	15	305		20	11			674	27	Asb, DEE, PAH, Si, Sr
Land transport	21	2	0	0	288	30	45		77	89			431	121	Asb, Bz, DEE, ETS, PAH, R, Sr, Ch, Pb, Si, W
Wholesale and retail trade and restaurants and hotels			0	0	100	110	26		78	90			204	200	Asb, Bz, DEE, ETS, PAH, R, Sr, Pb
Printers and printing machine minders and their foremen					195	40							195	40	mineral oils + printing ink
Printing, publishing and allied industries					7	3			58	32			65	35	Ca, Co, DEE, Pb, PAH, R, Sr, Ch, ETS, Ni, Si, W
Farming, horticulture, gardening, forestry and related			15	3	110	11			114	29			239	43	D, NAP, Sr, R, ETS
Manufacture of transport equipment	3				71	11	39		100	54	1		214	65	Ar, Asb, Be, Ch, Co, DEE, N, PAH, R, Si, Sr, Ca, ETS, Pb, W
Public administration and defence (Armed Forces)					19	22			215	17			234	39	R, ETS, PAH, DEE, Sr, Pb
Services allied to transport	2	0	0	0	26	6			61	71			89	77	Bz, Co, DEE, ETS, Pb, PAH, R, Sr, Ca, Ch, N, Si, W
Welders					139	13							139	13	''Welding fumes"
Financing, insurance, real estate and business services					27	25			46	53			73	78	R, ETS, Sr
Communication					7	6			61	71			68	77	DEE, ETS, R, Sr, Pb
Manufacture of fabricated metal products, except machinery and equipment	2		0	0	61	21			16	9	1	1	80	31	Be, Ca, Co, Ch, Fo, DEE, Pb, N, PAH, R, Si, Sr, ETS, W
Sanitary and similar services			0	0	9	13	5	8	30	35			44	56	Ar, Asb, Bz, Co, DEE, ETS, PAH, R, Sr, Ca, Ch, Pb, Si, W
Electricity, gas and steam	2				16	3	7		33	18			58	21	Ar, Asb, Be, Ch, Co, DEE, PAH, R, Si, Sr, Ca, ETS, Pb, N, W
	1		0	0	57	20							58	20	Be, Ca, Ch, Co, DEE, PAH, R, Si, Fo, ETS, Pb, N, W
	1		0	0	53	15			6	3	0	0	60	18	Ar, Bz, Ca, Ch, Co, DEE, Pb, N, PAH, R, Si, Sr, Fo, W
Manufacture of machinery except electrical			0	0	4 1	6	2 3		6 4	6	Ar, Bz, EO,		1–3B, Asb, Ch, Co, DEE, Pb, R, Si, Fo, Ca, ETS, N, W		
Non-ferrous metal basic industries															
Manufacture of other chemical products	5	0			44	15							49	15	''Spray painting"
Coach and other spray painters and painting assembling and related occupations					7	8			24	28			31	36	Ar, ETS, R, Sr
Recreational and cultural services	0	0	0	0	36	5	22						58	5	Ar, AA, Asb, Bz, Fo, 1–3B, Ca, Ch, Co, DEE, Pb, PAH, R, Si, Be, ETS, N, W
Manufacture of industrial chemicals															

Table 3 gives for each cancer, numbers of deaths (registrations for NMSC) within industry sectors or jobs for which there were at least 50 estimated attributable cancers; the exposures concerned are listed, with those contributing most (at least 10 cancers in men plus women) being shown in bold. *Totals are for lung, bladder, leukaemia, mesothelioma and nasal cancers plus attributable registrations for NMSC. 0 = .0.5; blank cell = cancer not represented.

AA, aromatic amine (bladder); Ar, arsenic (lung); Asb, asbestos (lung, mesothelioma); Be, beryllium (lung); Bz, benzene (leukaemia); Ca, cadmium (lung); Ch, chromium IV (lung, sinonasal); Co, cobalt (lung); D, dioxins (lung); DEE, diesel engine exhaust (lung, bladder); EO, ethylene oxide (leukaemia); ETS, environmental tobacco smoke (lung); F, female; Fo, formaldehyde (sinonasal, leukaemia); M, male; MWF, metal working fluids (bladder, NMSC, sinonasal); N, nickel (lung, sinonasal); NAP, non-arsenical pesticide (leukaemia); NMSC, non-melanoma skin cancer; PAH, polycyclic aromatic hydrocarbon (lung, bladder); PAHc, coal tar and pitch (NMSC); Pb, lead (lung); R, radon (lung); Si, silica (lung); Sr, solar radiation (NMSC); W, wood dust (Sinonasal); 1–3B 1–3 butadiene (leukaemia).

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estimates are similar to those used in the Global Burden of Disease project.[66]

There was a general lack of information on the latency of the cancers, particularly in relation to specific occupational exposures. The assumptions made in the study have influenced the numbers ever exposed giving high estimates in some cases. In particular a uniform distribution of cancer induction between the maximum and minimum latency was assumed, although reality may be a distribution that peaks in the early 1970s and tails off towards more recent periods.

In combining the AFs for different risk factors, multiple exposures and other non-occupational risk factors were considered. Cancer is a multifactorial and multistage disease that may not be due to any single sufficient cause but rather a sequence of "hits" over a life course. For example, smoking alone may not be sufficient to cause lung cancer and those who get it are likely to have been exposed to several lung carcinogens and possess other characteristics such as some form of inherited susceptibility. The mathematical implication of this is that the sum of attributable fractions for several exposures may be greater than 100%, with the amount exceeding 100% being partly due to synergistic interactions among the risk factors.[74] We have avoided this problem of "double counting" of the interactions to some extent by partitioning exposed worker populations between overlapping carcinogenic exposures before estimating AFs. In other cases where overlap remains we have assumed risks are multiplicative, so that the combined AF incorporates the interaction between exposures.

Many past exposures will have been at much higher levels than those existing today. However, trends vary depending on the substance and source of data. For example, analyses of exposure measurement data held in the National Exposure Database (NEDB) and from Health and Safety Executive (HSE) inspection surveys and other surveys showed downward trends of 11% per year for toluene between 1985 and 2002 based on inspection surveys but follow-up surveys of eight companies using toluene-containing compounds show an average decrease of only 1% per year in toluene concentrations.[75] Although respirable dust exposure in the quarry industry declined by 6% each year from 1984 to 2003 there was no clear change in exposure over time for respirable quartz exposure.

Other exposures have all but disappeared due to the decline of the industry or the substitution of hazardous substances by other non-carcinogenic agents. Other carcinogens such as naturally occurring radon could also easily be eliminated from workplaces. However, the long latency of some cancers means that numbers of deaths and registrations due to past high exposures will continue to be substantial in the near future (particularly asbestos-related cancers).

For some carcinogenic agents exposures remain high. For example, recent wood dust measurements have shown continuing high exposures.[76] Although some hazards, such as certain solvents in paints, may have been removed from occupations with multiple exposures, the potential for exposure to other hazards remains, for example, silica exposure in the construction industry, in which the number of employees is increasing. Studies in the Dutch construction industry suggested that over half of the full-shift respirable quartz dust measurements were above the Dutch Occupational Exposure Limit with exposure being highly variable from day to day and between jobs and tasks.[77] In addition there will be considerable numbers of workers exposed at low levels and risk to some carcinogens that may contribute substantially to both high AFs and numbers.

Future work will address estimation of the current burden due to occupational exposures for the remaining cancers, the use

Table 4 Uncertainties and limitations of the methodology and their potential impact on the estimate of the burden of disease due to occupation

Source of uncertainty	Potential impact on burden estimate
Exclusion of IARC Group 2B and unknown carcinogens	Q
Inappropriate choice of source study for risk estimate	IQ
Imprecision in source risk estimate	IQ
Source risk estimate from study of highly exposed workers applied to lower exposed target population	I
Risk estimate biased down by healthy worker effect, exposure misclassification in both study and reference population	Q
Use of RR = 1 for very low/background/environmental levels of exposure where no value available from literature	Q
Inaccurate risk-exposure period	IQ
Unknown proportion exposed at different levels of exposure	IQ
Effect of unmeasured confounders	IQ
Use of Levin's formula when RR adjusted for confounders	Q

IARC, International Agency for Research on Cancer; RR, relative risk.

Main messages

- Overall, 4.9% (8% men, 1.5% women) of all cancer deaths in Great Britain in 2004 were attributable to work-related carcinogens (based on the assessment of six cancers and International Agency for Research on Cancer Group 1 and 2A carcinogens with strong or suggestive human evidence).
- Asbestos contributed over half the occupational attributable deaths, followed by silica, diesel engine exhaust, radon, work as a painter, mineral oils in metal workers and in the printing industry, environmental tobacco smoke (non-smokers), work as a welder and dioxins.
- Occupational exposure to solar radiation, mineral oils and coal tars/pitches contributed large numbers of skin cancer registrations.
- Industries/occupations with large numbers of cancer deaths and registrations include construction, metal working, mining, land transport, roofing and road repair/construction, printing, farming, some service industry sectors in particular personal and household services and wholesale and retail trades, restaurants and hotels and manufacture of machinery, transport equipment, non-ferrous metals and metal products, and chemicals.

Policy implications

- Estimates for all but leukaemia are greater than those currently used in UK health and safety strategy planning and contrast with small numbers from occupational accidents.
- Carcinogenic agents, occupations and industrial areas are highlighted for prioritisation of risk reduction strategies.
- Past high exposures will continue to give substantial numbers in the near future and, although levels of many exposures have reduced, recent measurements of others show continuing high levels which must be addressed.

of other measures such as years of life lost and Disability-Adjusted Life Years, together with development of appropriate methodology for predicting future estimates of the occupational cancers due to more recent exposures and for exploring the sensitivity of the estimates to sources of uncertainty and bias.

In summary, this project is the first to quantify in detail the burden of cancer due to occupation specifically for GB. An up-to-date estimation of the current burden of six cancers due to past occupational exposures has been carried out using a robust and transparent methodology. On balance the estimates are likely to be conservative estimates of the true burden. The results highlight specific carcinogenic agents and the occupational circumstances and industrial areas where exposures to these agents occur, and should facilitate prioritisation of risk reduction strategies.

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STATISTICAL APPENDIX

Formulae used in the estimation of attributable fraction

1. Levin's equation

$AF = Pr(E)*(RR-1)/\{1+Pr(E)*(RR-1)\}$

Where RR = relative risk, Pr(E) = proportion of the population exposed

2. Miettinen's equation

$AF = Pr(E|D)*(RR-1)/RR$

Where Pr(E | D) = proportion of cases exposed (E = exposed, D = case)

3. Turnover equation to estimate numbers ever employed during the REP

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

Where $N_{e(REP)}$ = numbers ever employed in the REP

n_0 = numbers employed in the exposed job/industry at a mid-point in the REP

TO = staff turnover per year

R = retirement age (65 for men, 60 for women)

$l_{(adj15)i}$ = the proportion of survivors to age i of those alive at age 15 (from GB life tables)

a to b = age range achieved by the original cohort members by the target year (2004) (eg 65 to 100 for the solid tumour REP)

c to d = age range achieved by the turnover recruited cohort members by the target year (25 to 64 for the solid tumour REP)

age(u) and age(l) = upper and lower recruitment age limits (24 and 15)

The derivation and assumptions underlying this formula are described in the methodology technical report (http://www.hse.gov.uk/research/rrhtm/rr595.htm). The equation can be represented as a single factor acting as a multiplier for n_0, calculated by setting n_0 to 1 in the above equation, so that the factor varies only with TO (see table A1).

4. Equation to estimate the proportion of the population exposed

$Pr(E) = N_{e(REP)}/N_{p(REP)}$

where $N_{p(REP)}$ = numbers ever of working age during the REP from population estimates for the relevant age cohorts in the target year (2004)

5. Equation for combining AFs where exposed populations overlap but are independent and risk estimates are assumed to be multiplicative

$AF_{overall} = 1 - \prod_k (1 - AF_k)$ for the k exposures in the set

Table A1 Employment level adjustment and turnover factors used in the calculation of attributable fraction

	Main industry sector	Adjustment factor for change in employment levels*	Turnover per year (%)	Equivalent turnover factor to apply to point estimate of numbers exposed†
Men	Agriculture, hunting and forestry; fishing	1	9	3
	Mining and quarrying, electricity, gas and water; manufacturing industry	1.4	9	4
	Construction	1	13	5
	Service industries	0.9	11	4
	Total	1	10	4
Women	Agriculture, hunting and forestry; fishing	0.75	10	4
	Mining and quarrying, electricity, gas and water; manufacturing industry	1.5	14	6
	Construction	0.67	16	6
	Service industries	0.8	15	6
	Total	0.9	15	6

*Applied to CAREX data only. Exposed numbers are obtained for a mid-point year in the REP where national employment data sources have been used (the LFS or CoE).
†Based on a 40-year (solid tumour) REP and life expectancy tables.
CoE, Census of Employment; LFS, Labour Force Survey; REP, relevant exposure period.