

## Full Paper

## Occupational cancer in Britain

## Gastrointestinal cancers: liver, oesophagus, pancreas and stomach

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British Journal of Cancer (2012) 107, S33–S40; doi:10.1038/bjc.2012.116 www.bjcancer.com  
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**Keywords:** occupation; liver; oesophagus; pancreas; stomach

## OVERVIEW OF GASTROINTESTINAL CANCERS

## Liver cancer

Only primary liver tumours are considered here. Primary liver cancers are classified according to their specific histology and include hepatocellular carcinoma (HCC; liver cell carcinoma), cholangiocarcinoma (intrahepatic bile duct carcinoma (ICC)), hepatoblastoma and angiosarcoma (ASL). The majority of primary liver cancers (75–90%) are HCC, which are particularly prevalent in the developing countries of Asia and Africa, with the majority of cases being linked to infection with hepatitis B and hepatitis C. The latency period for the development of HCC has been estimated at between 10 and 25 years (Poovorawan *et al*, 2002; Hassoun and Gores, 2003), that of ICC up to 53 years (Zhu *et al*, 2004) and that of ASL between 15 and 30 years (Lelbach, 1996; Kielhorn *et al*, 2000). In England, during the period 1995–2005, the number of registrations for liver cancer has steadily increased, giving an average crude incidence rate of 4.8 per 100,000 men and 3.1 per 100,000 women (ONS, 2008). Survival rates for all types of primary liver cancer remain poor across both high- and low-rate areas (Ferlay *et al*, 2001).

## Oesophageal cancer

Cancer of the oesophagus is relatively uncommon worldwide, with the exception of the Asian 'oesophageal cancer belt' (northern Iran to northern China), which has the highest reported incidence rates. Oesophageal cancer is rare in individuals <50 years of age, and incidence is twice as high in men than in women (Wood *et al*, 2005; Cancer Research UK, 2007). In Britain, over recent years, there has been a steady increase in the total number of new cases of, and number of deaths from, oesophageal cancer among men but not among women. Five-year survival rates remain very poor at ~7.5% (Mitry *et al*, 2008). There are two main histological types of oesophageal cancer: squamous cell carcinoma and adenocarcinoma. In men, around 40% of oesophageal cancers are adenocarcinomas,

with squamous cell carcinomas accounting for ~20% of cases; this pattern is reversed in women (20% adenocarcinomas and 40% squamous cell carcinomas). In both men and women the remaining 40% of cases are because of unspecified carcinoma types (Wood *et al*, 2005). The two main histological types of oesophageal cancer have distinct aetiologies. Although tobacco smoking has been shown to be a potential risk factor for both, a link between tobacco smoking and alcohol intake has been observed to be primarily associated with squamous cell carcinoma (IARC, 2004). Other non-occupational risk factors for squamous cell carcinoma and adenocarcinoma include low consumption of fresh fruit and vegetables and consumption of exceptionally hot drinks. For adenocarcinoma only, a significant relationship has been observed with obesity (Blot *et al*, 2006).

## Pancreatic cancer

Globally, the incidence and mortality rates for pancreatic cancer show a considerable geographical variation, with the highest rates observed in the United States and lowest in Africa and Asia. Pancreatic cancer affects mainly the elderly, with low rates in individuals under the age of 45 years. Survival rates for pancreatic cancer are reported to be lower than that for any other major cancer; relative survival up to 1 year is 13% and 5-year relative survival is 2–3% in the United Kingdom (Walsh and Wood, 2005). Early symptoms are usually nonspecific, and current treatment options are very limited. The majority of the tumours (about 95%) arise from the exocrine portion of the pancreas. Causal factors include diet, obesity, physical activity, other medical conditions (including hereditary pancreatitis, stomach ulcer, diabetes, bowel inflammation, tooth/gum disease and chronic pancreatitis, which may be associated with long-term alcohol consumption), family history/genetics and a previous cancer at other sites (Walsh and Wood, 2005). However, the most well-established risk factor associated with pancreatic cancer is tobacco smoke.

## Stomach cancer

Rates of incidence of stomach cancer have declined globally (10–20% per decade), from being the most common cancer in

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

1980 to around the fourth most frequent today (Shibata and Parsonnet, 2006). However, survival rates are low, and stomach cancer mortality still represents a significant proportion of all cancer deaths. In the United Kingdom, survival rates are around 33% for 1-year survival and 13% for survival up to 5 years, which is below the European survival average (Stewart and Wood, 2005). Stomach cancer occurs mainly in older people, with <10% of patients presenting before 45 years of age. Over 90% of all stomach cancers are adenocarcinomas (Coleman *et al*, 1993), and the development is associated with a number of risk factors, including chronic infection with *Helicobacter pylori*, smoking, high dietary intake of preserved or salty foods and other medical conditions (stomach ulcers, acid reflux, stomach polyps, lowered immunity and use of non-steroidal anti-inflammatory drugs). There is currently a lack of evidence to support an association between stomach cancer and alcohol intake (IARC, 2010).

## 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 definitely causing gastrointestinal cancers (Group 1), or probably causing gastrointestinal cancers (Group 2A), are summarised in Table 1. The IARC has identified other carcinogens for liver cancer, these being arsenic and arsenic compounds (Group 1), aflatoxin (Group 1) and polychlorinated biphenyls (PCBs) (Group 2A). However, there is insufficient epidemiological evidence to calculate attributable numbers for these substances.

### Choice of studies providing risk estimates for liver cancer, oesophageal cancer, pancreatic cancer and stomach cancer

A detailed technical review of studies identified is given in the relevant Health and Safety Executive (HSE) technical reports (HSE, 2012a, b, c, d). There are no agents or exposure scenarios common to all cancer sites.

### Occupational exposures considered for liver cancer

**Ionising radiation** The relative risks (RR) for occupational exposure to ionising radiation were obtained using models of excess relative risk per unit of radiation dose for workers exposed

**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 have the GI tract as the target organ 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 the REP
<b>Group 1: Carcinogenic to humans</b>			
<b>Agents, groups of agents</b>			
Ionising radiation and sources, notably X rays, $\gamma$ rays, neutrons and radon gas	Radiologists; technologists; nuclear workers; radium-dial painters; underground miners; plutonium workers; clean-up workers following nuclear accidents; aircraft crew	Liver <i>sufficient</i>	CIDI LFS British Airways Stewards and Stewardesses Association
Asbestos	Mining and milling; by-product manufacture; insulating shipyard workers; sheet-metal workers; asbestos cement industry	Stomach <i>sufficient</i>	CAREX
Soots	Chimney sweeps; heating unit service personnel; brick masons and helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials	Oesophageal <i>sufficient</i>	UK Chimney Sweep Union LFS
Monomers: vinyl chloride	Production: production of polyvinyl chloride and co-polymers; refrigerant before 1974; extraction solvent in aerosol propellants	Liver <i>sufficient</i>	CAREX
<b>Exposure circumstances</b>			
Painters	Ammonia; acrylate resins; dyes	Stomach <i>sufficient</i>	LFS
Rubber industry	Aromatic amines; solvents	Stomach <i>sufficient</i>	LFS
<b>Group 2A: Probably carcinogenic to humans</b>			
<b>Agents, groups of agents</b>			
Tetrachloroethylene	Production; dry cleaning; metal degreasing	Oesophageal <i>limited</i>	CAREX
Trichloroethylene	Production—dry cleaning, metal degreasing	Liver <i>limited</i>	CAREX
Acrylamide	Chemical industry; water and wastewater treatment; textile, steel and lumber industries, petroleum refining, mineral processing, sugar production, hospitals	Pancreas <i>inadequate</i>	CAREX
Lead and inorganic lead compounds	Lead smelters; plumbers; solderers; occupations in battery recycling smelters; refining industries; painting and printing; firing ranges; vehicle repair services	Stomach <i>limited</i>	CAREX

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

to ionising radiation from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2008). By using this method, an RR estimate of 1.01 was obtained for men and women exposed to ionising radiation (with an estimated average lifetime dose of 15.3 mSv).

**Risk estimates for occupational exposure to ionising radiation and liver cancer** Several studies of workers exposed to ionising radiation have shown elevated risks for liver cancer, including a cohort of 27,011 radiologists and radiological technologists in China working during the period 1950–1995 (standardised incidence ratio (SIR) = 1.2,  $P < 0.05$ ) (Wang *et al*, 2002). Employees working before 1970 had an increased risk (SIR = 1.39,  $P < 0.05$ ) in comparison with those employed after 1970 (SIR = 0.85); this probably reflects improvements in protection procedures from that time. The standardised mortality ratio (SMR) for liver cancer was found to be raised in a cohort of US radiologists employed before 1940 (SMR = 1.45) (Matanoski *et al*, 1984), and risk of mortality from liver cancer in a cohort of British Risk for radiologists after 40 years of employment was also significantly increased (SMR = 1.41, 95% CI = 1.03–1.90) (Berrington *et al*, 2001).

Gilbert *et al* (2000) reported a significant excess risk of liver cancer (in particular ASL) in plutonium workers employed between 1948 and 1958 at the Mayak facility in Russia, but no such effect has been identified in a series of cohorts of United States and United Kingdom nuclear industry workers. The difference in response is probably a consequence of the marked differences in exposure between the Western and Russian plants. No excess risk of liver cancer has been found for workers in other nuclear industries, underground (coal or uranium) miners or aircraft crew.

**Vinyl chloride (VC)** Vinyl chloride monomer is used in the manufacture of polyVC resin, with the highest exposure occurring during the cleaning of reactors in which polymerisation reactions take place, a process that traditionally was done manually by workers.

**Risk estimates for occupational exposure to VC and liver cancer** Risk estimates were taken from a European retrospective cohort study covering the period 1955–1986 (Simonato *et al*, 1991). In the study, a significantly increased excess of liver cancer (particularly ASL) was observed (SMR = 2.86, 95% CI = 1.83–4.25), with a significant exposure–response relationship ( $P < 0.001$ ) being demonstrated. Owing to the absence of sufficient dose–response data specific to VC, an RR of 1.89 was estimated for the ‘low-exposure’ category. This was based on a harmonic mean of the high/low ratios across all other cancer–exposure pairs in the overall project for which data were available.

**Risk estimates for occupational exposure to trichloroethylene (TCE) and liver cancer** Trichloroethylene is widely used as a degreaser. A meta-analysis of 14 occupational cohort studies and 1 case–control study (Alexander *et al*, 2007) was used for the RR estimate for high exposure. Across the studies providing the most accurate estimate of TCE exposure through biomonitoring (sub-cohort of studies specifically identifying TCE as a workplace exposure), a combined RR of 1.30 (95% CI = 1.09–1.55) was reported for liver and biliary tract cancer, and has been used for the high exposure in burden estimation; this association was slightly stronger but less precise for primary liver cancer only (SRRE = 1.41, 95% CI = 1.06–1.87). ‘Low exposures’ were set to 1 to reflect scarcity of exposure–response data.

Wartenberg *et al* (2000) also reviewed evidence for an association between cancer and TCE exposure, on the basis of all identified cohort and case–control studies up to the year 2000. Within those studies giving an accurate exposure estimate through biomonitoring, there was evidence of an increased incidence of,

and mortality from, primary liver cancer, with an average RR of 1.9 (95% CI = 1.0–3.4) and 1.7 (95% CI = 0.2–16.2), respectively. In addition, an IARC working group (IARC, 1995) reported excess risk for cancer of the liver and biliary tract (SIR = 2.3, 95% CI = 0.74–5.3; SMR = 1.1, 95% CI = 0.14–4.0) in workers specifically exposed to TCE.

### Other occupational exposures considered for liver cancer

**Aflatoxin** Aflatoxins are naturally occurring fungal products that can be present in some human foodstuffs such as grains, milk and dairy products. Overall, the evidence from occupational studies supports a role for aflatoxin in the development of liver cancer, for example, in studies of livestock feed processing workers (Olsen *et al*, 1988), warehouse workers and oil mill workers (Dossing *et al*, 1997). However, exposure to aflatoxin is only suggestive, and in most studies adjustment for confounding factors has not been carried out. Given these limitations, the robustness of risk estimates could not be confirmed, and the data set was considered inappropriate to proceed with an attributable fraction (AF) calculation.

**Arsenic and arsenical compounds** There is limited evidence to suggest an association between ingestion of arsenic and arsenical compounds and the development of liver tumours, especially ASL. Although most arsenic and arsenical compounds have been eliminated from the workplace over the past 30 years, because of a latency period of up to 30 years it is still feasible that cases of ASL reported between 1999 and 2005 may have been caused by historic occupational exposure to this agent. However, the available studies were considered inadequate to support the derivation of an AF, and therefore a formal AF calculation has been omitted (HSE, 2012a).

**PCBs** The evidence to support a positive association between occupational exposure to PCBs and development of liver cancer is limited. The total number of workers in the United Kingdom exposed to PCBs during the period 1990–1993 is low (1860), with only 54 of those estimated to have a ‘high’ exposure level (CAREX, 1999). In addition, the use of PCBs in new ‘closed-use’ equipment was banned in 1981, by which time the majority of production had also ceased. It was therefore not considered appropriate to proceed with an AF calculation.

### Occupational exposures considered for oesophageal cancer

**Soots** Soots contain various potentially carcinogenic substances including arsenic, nickel and several polycyclic aromatic hydrocarbons (PAHs). The highest occupational exposure to soot is likely to occur among chimney sweeps.

**Risk estimates for occupational exposure to soots and oesophageal cancer** A Swedish cohort study (Evanoff *et al*, 1993) was used for the risk estimate for exposure to soots. After adjusting estimates for smoking and alcohol intake, a significant increase in both oesophageal cancer incidence and mortality was found, that is, SIR = 3.87 (95% CI = 1.93–6.93,  $n = 11$ ) and SMR = 3.86 (95% CI = 2.00–6.75,  $n = 12$ ), respectively. In addition, there was a positive association between duration of employment and oesophageal cancer, with a significant estimate for >30 years in active employment (SMR = 6.74,  $n = 6$ ,  $P < 0.05$ ). The authors concluded that the alcohol and tobacco consumption habits of the chimney sweeps could not explain the excesses observed.

**Tetrachloroethylene (perchloroethylene (PCE))** The highest occupational exposure to the solvent tetrachloroethylene is likely to occur among dry cleaning and metal degreasing workers. Other

occupational exposures may occur among workers involved in fluorocarbon production.

**Risk estimates for occupational exposure to PCE and oesophageal cancer** A study by Ruder *et al* (2001) of 1708 dry cleaners who were primarily exposed to PCE for at least 1 year in the period 1940–1960 was used to obtain the RR. A significant excess of oesophageal cancers was found overall, SMR = 2.47 (95% CI = 1.35–4.14), and this has been used for high exposure in the burden estimate. Statistically significant excess risks were also found for over a 5-year duration of employment and 20-year latency (SMR = 5.03, 95% CI = 2.41–9.47,  $n = 10$ ). There were no data available on potential confounders, but the authors suggested that the magnitude of the results were greater than could be explained by smoking alone. Adequate dose–response data were not available. An RR of 1.63 (95% CI = 0.24–3.85) has therefore been estimated for the low-exposure-level category. This was based on a harmonic mean of the high/low ratios across all other cancer–exposures pairs in the overall project for which data were available.

Consistent associations between PCE and excess oesophageal cancers have been shown in several other studies including that by Blair *et al* (2003) in a study of US dry cleaners over the period 1948–1993 (SMR = 2.2, 95% CI = 1.5–3.3). Elevated risks were found in three of the gender–race sub-cohorts (white men, non-white men and white women), but the excess was found to be only significant in the non-white male sub-cohort. Neither level of exposure or date of employment (pre-1960) were found to be associated with increased risk. Tobacco usage was not taken into account in this study, but the authors conclude that confounding by smoking is unlikely to fully explain the observed two-fold excess.

### Occupational exposures considered for pancreatic cancer

**Acrylamide** Acrylamide is used in the manufacture of dyes and to synthesise polyacrylamides, which are used as water-soluble thickeners in wastewater treatment, papermaking, ore processing and in the manufacture of permanent press fabrics. It is found in many cooked starchy foods as a by-product of the heating process, as well as in tobacco smoke.

**Risk estimates for occupational exposure to acrylamide and pancreatic cancer** A limited number of epidemiological studies have evaluated the association between cancer and occupational exposure to acrylamide. The study used for the burden estimation was a mortality study by Marsh *et al* (2007) from 1925 to 2002 of a cohort of 8508 workers (of which 2004 were categorised as potentially exposed to acrylamide) at three US plants, and 344 workers (including 273 exposed to acrylamide) in a plant in the Netherlands. Estimates based on the US plants have been used. Exposure to acrylamide was assessed by combining measured airborne exposures with work history information on jobs and duration in each job; adjustment of estimates for potential smoking or time since first exposure to acrylamide did not significantly affect outcome. SMRs from this study for mean intensity of acrylamide exposure have been used; SMR = 1.85 (95% CI = 0.68–4.03) for mean intensity of exposure of  $\geq 0.30 \text{ mg m}^{-3}$  has been used for the high-exposure category. An inverse-variance-weighted pooled estimate of the SMRs for the mean intensities 0.001–0.029 and 0.03–0.29  $\text{mg m}^{-3}$  has been calculated by the research team (1.22 (95% CI = 0.66–2.27)) and has been used for the low-exposure category. The risk for cumulative exposures  $< 0.001 \text{ mg m}^{-3}$  years was 0.8; an SMR of 1 has thus been used for the background exposure category.

### Occupational exposures considered for stomach cancer

**Risk estimates for occupational exposure to asbestos and stomach cancer** A large number of studies have reported an association

between asbestos exposure and stomach cancer, and there have been many reviews (Morgan *et al*, 1985; Goodman *et al*, 1999). Two large UK asbestos data sources, the national (GB) mesothelioma register and the HSE's British Asbestos Workers Survey, have been analysed in relation to asbestos-related diseases including cancer of the stomach (Hutchings *et al*, 1995). Stomach cancer was significantly elevated in workers first exposed after 1970 and with  $> 10$  years recorded latency (SMR = 1.43, 95% CI = 1.05–1.89); smokers and, to a lesser extent, ex-smokers were shown to be at increased risk. An update of this study to 2005 reported an overall SMR of 1.66 (95% CI = 1.49–1.86), which, when adjusted for age, sex and smoking, was 1.50 (95% CI = 1.03–2.17) for former smokers and 1.58 (95% CI = 1.12–2.24) for current smokers (Harding *et al*, 2009).

A systematic review and meta-analysis of 38 cohorts from 35 studies investigating occupational exposure to asbestos was also carried out by the cancer burden project research team; a meta-SMR of 1.16 (95% CI = 1.02–1.32, 31 studies) for men and a meta-SMR of 0.92 (95% CI = 0.66–1.28, 14 studies) for women were determined (HSE, 2012d). As this is lower than that reported by Harding *et al* (2009), the estimate of excess risk of 1.66 (95% CI = 1.49–1.86) from Harding *et al* (2009) has been used for the high-exposure group for men (as most asbestos-exposed workers are men). The research team removed the data of Harding *et al* (2009) from the meta-analysis and estimated a meta-SMR of 1.21 (95% CI = 1.06–1.38) for men; this value has been used for the low-exposure group for men. As the pooled estimate from the meta-analysis for women was  $< 1$ , a risk estimate of 1 has been used for all industry sectors for women.

**Inorganic lead** Lead and inorganic lead have widespread uses in industry, with applications in building construction and paints, lead-acid batteries, bullets and shot, weights, and as part of solders, pewter, fusible alloys and, until 2000, petrol (Fu and Boffetta, 1995).

**Risk estimates for occupational exposure to inorganic lead and stomach cancer** Two meta-analyses provided evidence for the reclassification of inorganic lead as a Group 2A carcinogen (IARC, 2006). Fu and Boffetta (1995) used data from 16 cohort and 13 case–control studies, and reported a significant excess risk for stomach cancer, as did a smaller study by Steenland and Boffetta (2000) for a range of industries/occupations including battery workers, smelters, glassworkers and workers exposed to pigments. Both studies report similar overall RRs of 1.33 (95% CI = 1.18–1.49) (Fu and Boffetta, 1995) and 1.34 (95% CI = 1.14–1.57) (Steenland and Boffetta, 2000), although the former meta-analysis also provided a separate estimate of 1.50 for the highest-exposed subgroups of worker. The study reported by Fu and Boffetta (1995) is considered to be most relevant to the UK population, and has therefore been used in this study. It is noted that this study provided some evidence of a possible dose–response relationship, as well as providing the two risk estimates. As no dose–response data are available, a relative risk based on a harmonic mean of the high/low ratios across all other cancer–exposures pairs in the overall project for which data were available has been estimated for the low-exposure-level category. As this was  $< 1$ , the RR for low exposure has been set to 1.

**Risk estimates for employment as a painter and stomach cancer** Paints contain various resins, dyes and organic solvents. A number of epidemiological studies have considered the risk of cancer in painters (HSE, 2012d). Chen and Seaton (1998) carried out a meta-analysis of 58 studies of workers exposed to paints published between 1966 and 1995. The SMR for stomach cancer among painters was 1.27 (95% CI = 1.01–1.60) and has been used for the AF calculation.

**Risk estimates for employment in the rubber industry and stomach cancer** Work in the rubber industry involves potential exposure

to several different carcinogenic agents. Results therefore differ between studies, with risks of cancer not being consistently raised (IARC, 1982). Sorahan *et al* (1989) conducted a mortality study of 13 British rubber industry factories, mostly tyre manufacturers from 1946 to 1985, which included 36 691 male rubber workers employed for at least 12 months during 1946–1960. Detailed job histories were recorded for each subject, and the mean duration of exposed employment was reported to be 10.5 years. The SMR was 1.13 (observed cases: 359, expected cases: 316.5). A confidence interval was not provided, and thus was determined by the research team (95% CI = 1.02–1.25) using the Byar's approximation proposed in Breslow and Day (1987). These figures were used in the present study to calculate the AF for the high-exposure level. Because of the absence of sufficient dose–response data specific to the rubber industry, an RR of 1 has been used for the low-exposure-level category. This was based on a harmonic mean of the high/low ratios across all other cancer–exposures pairs in the overall project for which data were available.

### 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, are given in Table 1.

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

Exposures in the textile/clothing industries and in the manufacture of finished metal products where TCE was used as a degreaser were allocated to the high category for TCE. Textile industry workers may also have been exposed to TCE as a spot-cleaning agent, along with dry cleaners who were considered to come under the personal and household services category; these were also allocated to the high-exposure category.

Worker exposures in the manufacture of industrial chemicals and chemical products and manufacture of plastic products were allocated to the high-exposure category for VC.

There were an estimated 2500 chimney sweeps (99.5%, 2488 male) in the United Kingdom in 2006, with 250 affiliated to a representative trade association (McAlinden, 2006). According to the 2006 LFS data, chimney sweeps were included within the 12,421 men classified as road sweepers. The proportion estimated to be chimney sweeps in 2006 was thus 2488/12,421 (0.20). This proportion was applied to the most relevant job category, cleaners, in the LFS data for 1979.

High exposure to tetrachloroethylene was assumed for the manufacture of machinery, personal and household services, and manufacture of fabricated metal products and low exposure in industries such as construction, land transport and manufacture of wearing apparel.

High exposure to asbestos was assumed for all manufacturing industry sectors, electricity and gas utilities and land transport.

Mining of metal ores, manufacture of industrial chemicals, chemical products, plastic products and electrical machinery, iron and steel and non-ferrous metal basic industries and construction have all been assigned high exposures for inorganic lead.

High exposure to acrylamide was assumed for manufacture of industrial chemicals and other chemical products, and low exposure was allocated to the manufacture of rubber products and research and scientific institutes.

## RESULTS

Because of assumptions made about cancer latency and working age range, only cancers in patients aged 25 years and above in 2005/2004 could be attributable to occupation. A latency period of at least 10 years and up to 50 years has been assumed for all gastrointestinal cancers. Attributable fractions have been calculated for liver cancer and ionising radiation, VC and TCE; oesophageal cancer and exposure to soots and tetrachloroethylene; pancreatic cancer and exposure to acrylamide; stomach cancer and asbestos, inorganic lead, occupation as a painter and employment in the rubber industry. Table 2 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.

The estimated overall AFs and cancer deaths and registrations attributable to occupational exposures were as follows: for liver cancer the AF is 0.18% (95% CI = 0.11–0.29), with 5 (95% CI = 3–8) attributable deaths and 5 (95% CI = 3–8) attributable registrations; for oesophageal cancer the AF is 2.54% (95% CI = 1.07–5.88), with 184 (95% CI = 78–429) attributable deaths and 188 (95% CI = 80–439) attributable registrations; for pancreatic cancer the AF is 0.01% (95% CI = 0.00–0.05), with 1 (95% CI = 0–4) attributable death and 1 (95% CI = 0–4) attributable registration; and for stomach cancer the AF is 1.95% (95% CI = 1.00–3.39), with 108 (95% CI = 55–187) attributable deaths and 157 (95% CI = 81–274) attributable registrations.

### Exposures affecting liver cancer

For those occupational exposures relevant to the risk of liver cancer, the following total AFs and attributable deaths and registrations were estimated.

In total, there were 252 035 men and 39 420 women ever exposed to ionising radiation over the REP. The total AF for liver cancer associated with ionising radiation is 0.01% (95% CI = 0.01–0.01%), which resulted in no attributable deaths and no attributable registrations.

There were 43 861 men and 42 288 women ever exposed to TCE during the REP. The total AF for liver cancer associated with TCE is 0.06% (95% CI = 0.02–0.11%), with 2 (95% CI = 1–3) attributable deaths and 2 (95% CI = 1–3) attributable registrations.

There were 14 756 men and 9151 women ever exposed over the REP to VC. The total AF for liver cancer associated with TCE is 0.11% (95% CI = 0.05–0.20%), with 3 (95% CI = 2–6) attributable deaths and 3 (95% CI = 2–6) attributable registrations.

### Exposures affecting oesophageal cancer

For those occupational exposures relevant to the risk of oesophageal cancer, the following total AFs and attributable deaths and registrations were estimated.

There were 84 585 men ever exposed to soots over the REP. The total AF for oesophageal cancer and exposure to soots was 0.81% (95% CI = 0.29–1.75), with 59 (95% CI = 21–128) attributable deaths and 60 (95% CI = 22–130) attributable registrations.

There were 373 376 men and 189 605 women ever exposed to tetrachloroethylene over the REP. The overall total AF for oesophageal cancer and exposure to PCE was 1.74% (95% CI = 0.41–5.05), with 126 (95% CI = 30–368) attributable deaths and 130 (95% CI = 31–377) attributable registrations. Both men and women engaged in personal and household services had the highest numbers attributable to occupation, with 65 registrations and 64 deaths. Manufacture of machinery, except electrical, was the next highest, with 14 attributable registrations and deaths (11 men and 3 women for each), and construction accounted for 10 male registrations and deaths.

### Exposures affecting pancreatic cancer

There were 7045 men and 8395 women ever exposed to acrylamide over the REP. The estimated total AF for pancreatic cancer and

**Table 2** GI cancer burden estimation results (male and female)

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)
<b>Liver cancer</b>										
Ionising radiation	252,035	39,420	0.0130	0.0019	0.0000	0	0	0	0	0
Trichloroethylene	43,861	42,288	0.0023	0.0020	0.0007 (0.0002–0.0012)	0.0006 (0.0002–0.0011)	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–1)
Vinyl chloride	14,756	9151	0.0008	0.0004	0.0014 (0.0007–0.0024)	0.0007 (0.0004–0.0014)	2 (1–4)	1 (0–2)	2 (1–4)	1 (0–2)
<b>Totals<sup>a</sup></b>					<b>0.0021 (0.0013–0.0033)</b>	<b>0.0013 (0.0008–0.0021)</b>	<b>4 (2–6)</b>	<b>2 (1–2)</b>	<b>4 (2–6)</b>	<b>1 (1–2)</b>
<b>Oesophageal cancer</b>										
Soots	84,585	0	0.0044	0	0.0124 (0.0045–0.0269)	0 (0)	59 (21–128)	0	60 (22–130)	0
Tetrachloro-ethylene	373,376	189,605	0.0192	0.0090	0.0208 (0.0046–0.0626)	0.0109 (0.0032–0.0278)	99 (22–297)	28 (8–70)	101 (22–303)	29 (9–74)
<b>Totals<sup>a</sup></b>					<b>0.0329 (0.0148–0.0754)</b>	<b>0.0109 (0.0032–0.0278)</b>	<b>156 (70–358)</b>	<b>28 (8–70)</b>	<b>159 (71–365)</b>	<b>29 (9–74)</b>
<b>Pancreatic cancer</b>										
Acrylamide	7045	8395	0.0004	0.0004	0.0002 (0.0000–0.0007)	0.0001 (0.0000–0.0004)	1 (0–2)	0 (0–1)	1 (0–2)	0 (0–1)
<b>Stomach cancer</b>										
Asbestos	350,302	82,336	0.0181	0.0039	0.0094 (0.0071–0.0120)	0 (0)	32 (24–41)	0	47 (36–60)	0
Inorganic lead	805,981	411,339	0.0414	0.0196	0.0039 (0.0023–0.0061)	0.0010 (0.0006–0.0015)	14 (8–21)	2 (1–3)	20 (11–31)	3 (2–4)
Painters	1,118,813	130,630	0.0577	0.0062	0.0155 (0.0008–0.0334)	0.0017 (0.0001–0.0037)	53 (3–114)	4 (0–8)	78 (4–168)	5 (0–11)
Rubber industry	146,089	62,237	0.0075	0.0030	0.0010 (0.0002–0.0019)	0.0004 (0.0001–0.0007)	3 (1–6)	1 (0–2)	5 (1–10)	1 (0–2)
<b>Totals<sup>a</sup></b>					<b>0.0295 (0.0152–0.0514)</b>	<b>0.0030 (0.0014–0.0053)</b>	<b>101 (52–176)</b>	<b>6 (3–11)</b>	<b>149 (77–258)</b>	<b>9 (4–15)</b>

Abbreviations: AF = attributable fractions; GI = gastrointestinal. <sup>a</sup>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 AF is large.

exposure to acrylamide is 0.01% (95% CI = 0.00–0.05%), with 1 (95% CI = 0–4) attributable death and 1 (95% CI = 0–4) attributable registration.

### Exposures affecting stomach cancer

For those occupational exposures relevant to the risk of stomach cancer, the following total AFs and attributable deaths and registrations were estimated.

There were 350 302 men and 82 336 women ever exposed to asbestos over the REP. The estimated total AF for stomach cancer and exposure to asbestos is 0.58% (95% CI = 0.44–0.74%), with 32 (95% CI = 24–41) attributable deaths and 47 (95% CI = 36–60) attributable registrations. The highest number of attributable deaths (24 in total) and registrations (35 in total) was for men employed in the construction industries.

There were 805 981 men and 411 339 women ever exposed to inorganic lead over the REP. The estimated total AF for stomach cancer and exposure to inorganic lead is 0.28% (95% CI = 0.16–0.43%), which equates to 16 (95% CI = 9–24) attributable deaths and 23 (95% CI = 13–35) attributable registrations. Manufacturing and construction industries dominated the attributable occupations, with no deaths or registrations associated with low exposures in either male or female workers.

A total of 1,118,813 men and 130,630 women were ever exposed as painters over the REP. The estimated total AF for stomach cancer and work as a painter is 1.03% (95% CI = 0.06–2.22%), which equates to 57 (95% CI = 3–122) attributable deaths and 83 (95% CI = 5–179) attributable registrations. For men, employment as a painter in the construction industries resulted in the highest attributable deaths (43) and registrations (63), whereas for women it was employment in other industries (3 deaths and 4 registrations) that dominated.

There were 146,089 men and 62,237 women ever exposed in the rubber industry over the REP. The estimated total AF for stomach cancer and work in the rubber industry is 0.08% (95% CI = 0.01–0.15%), which equates to 4 (95% CI = 1–8) attributable deaths and 6 (95% CI = 1–12) attributable registrations.

### DISCUSSION

The majority of GI deaths and registrations that could be attributable to occupational exposure were from oesophageal cancer in relation to both exposures to tetrachloroethylene and soots, and stomach cancer in painters (deaths) or exposure to asbestos (for registrations). Our estimate for oesophageal cancer (2.54%) is higher than that of Nurminen and Karjalainen (2001),

but their estimates for the other GI tract cancers are higher than that obtained by us (liver: 0.7% vs 0.18%, pancreas: 3.0% vs 0.01%, stomach: 3.0% vs 1.96%).

In addition to the carcinogens evaluated for a GI tract cancer, there are other occupationally related agents that may have a role in the development of these cancers. For example, associations have been shown for pancreatic cancer, with exposure to chlorinated hydrocarbon solvents and related compounds, nickel and chromium compounds, PAHs, insecticides, silica dust and electromagnetic fields. Occupations showing particular evidence of elevated risk are laundry/dry cleaning workers and metal-

plating workers, with a suggestion of an association also being found for printers and pressmen, plywood and fibreboard workers and electrical/electronic workers (HSE, 2012c). There is also considerable epidemiological evidence that associates occupational exposure with dusts (including coal dust and wood dust) as carcinogens associated with stomach cancer (HSE, 2012d). In addition, the IARC has recently held a series of monograph meetings to update the classifications for all Group 1 carcinogens; rubber manufacture is now classified as a Group 2A carcinogen for oesophageal cancer (Baan *et al*, 2009) and asbestos as a Group 2A carcinogen for colorectal cancer (Straif *et al*, 2009).

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## Appendix

### British Occupational Cancer Burden Study Group

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