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Occupational cancer in Britain

Skin cancer

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OVERVIEW OF SKIN CANCER

Non-melanoma skin cancer

This is the most common neoplasm in Caucasian populations around the world. There are two main forms of the cancer, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), of which the former is by far the most common malignancy in white people (Miller, 1995). The incidence of non-melanoma skin cancer (NMSC) shows a marked geographical variation (Diepgen and Mahler, 2002), with incidence rapidly increasing in white populations in proportion to proximity to the equator; in particular, incidence of SCC doubles for each 8- to 10-degree decline in latitude (Giles *et al*, 1988). The UK Office of National Statistics reports that incidence of NMSC is greatly under-reported; however, it is rarely fatal (accounting for $\sim$500 deaths per year), with a cure rate close to 99% if detected in the early stages.

Melanoma of the skin (malignant cutaneous melanoma)

Melanoma of the skin is common among white populations living in sunny climates. Rapid increases in incidence and mortality are being observed in both men and women in many countries. In Britain, the number of people diagnosed has been steadily increasing from $\sim$5500 cases each year to in excess of 8500, and nearly 2000 people die from the condition each year. Survival from melanoma is relatively high in developed countries (81% in Europe) and lower in developing countries (typically around 40%). A recent analysis of survival in the UK from melanoma found that after adjustment for deprivation the 5-year survival rate for men reached 78%, and for women the rate reached was higher at 90% (Rachet *et al*, 2008). The authors comment that survival is higher for melanomas <1.5 mm in thickness at diagnosis.

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

METHODS

Occupational risk factors

Groups 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 NMSC or melanoma are summarised in Table 1. Carcinogens such as soots (Group 1), coke production (Group 1) and creosotes (Group 2A) are included within the estimation of other exposures (Table 1).

It is well established that ultraviolet radiation (UVR) from the sun and artificial sources is the dominant risk factor for both NMSC and melanoma (IARC, 1992; Kricker *et al*, 1994). The relationship with UVR as an occupational risk is often confounded by concurrent exposure to UV light (from the sun) from leisure pursuits. Increased risk for melanoma is most strongly linked to intermittent exposure to high-intensity sunlight (i.e., usually recreational exposure resulting in sunburn), rather than chronic exposure typical of outdoor occupations (Diepgen and Mahler, 2002; Gruber and Armstrong, 2006). Artificial UV radiation sources, such as sunbeds and sunlamps, are also linked to an increased risk (Gallagher and Lee, 2006).

Occupational exposure to tar and tar pitches, mineral oils, infrared radiation, burns and trauma, cutting oils, ionising radiation and bipyridyl/paraquat have been identified as causative agents for NMSC. Predisposing factors thought to affect susceptibility to melanoma include skin type, hair and eye colour, and the presence of freckles and nevi.

Choice of studies providing risk estimates for non-melanoma and melanoma skin cancer

Detailed reviews of occupational risk factor studies identified for melanoma and NMSC are provided in the relevant Health and Safety Executive technical reports (HSE, 2012a, b).

Occupational exposures common to NMSC and melanoma

Solar radiation The risk for NMSC and melanoma caused by exposure to solar radiation is difficult to estimate because everyone at some time is exposed. Exposure to solar radiation is

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 skin 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 REP	Comments
Group 1: Carcinogenic to humans				
Agents, groups of agents				
Mineral oils, untreated and mildly treated	Production; used as lubricant by metal workers, machinists, engineers; printing industry (ink formulation); used in cosmetics, medicinal and pharmaceutical preparations	NMSC *sufficient*	LFS	In addition includes shale oils or shale-derived lubricants
Solar radiation	Outdoor workers	NMSC *sufficient* Melanoma *sufficient*	CAREX	
Coal tar and pitches (Polycyclic aromatic hydrocarbons)	Production of refined chemicals and coal tar products (patent fuel); coke production; coal gasification; aluminium production; foundries; road paving and construction (roofers and slaters)	NMSC *sufficient*	LFS	In addition includes soots, and creosotes
Group 2A: Probably carcinogenic to humans				
Agents, groups of agents				
Ultraviolet radiation (A, B and C) from artificial sources	Arc welding; industrial photoprocesses; sterilisation and disinfection; phototherapy; operating theatres; laboratories; ultraviolet fluorescence in food industry; insect traps	Melanoma of skin *inadequate*		Predominantly harms the eyes thus calculated for melanoma of the eye only

Abbreviations: CAREX = CARcinogen EXposure database; IARC = International Agency for Research on Cancer; LFS = Labour Force Survey; REP = risk exposure period.

usually estimated using exposure categorisation (recreational or occupational) or job categorisation (indoor or outdoor). However, not all studies attempt to adjust occupational risks for non-occupational exposure to solar radiation. Furthermore, epidemiological evidence suggests that for occupational exposure to UV radiation excess risk can only be demonstrated for SCC (Diepgen and Mahler, 2002), with the majority of these tumours occurring on the head and neck areas of the body most exposed to sunlight. There is uncertainty about how patterns of solar exposure (frequent or intermittent) and potential cofactors (such as age, gender and social class) affect the risk of melanoma.

Risk estimates for occupational exposure to solar radiation and NMSC To estimate the number of NMSC registrations and deaths attributable to occupational solar radiation, a US-based case–control study (Freedman *et al*, 2002) was used. This compared predominantly indoor work with 'mixed', outdoor and farming work, and obtained a risk estimate for 'mixed' indoor and outdoor work of 1.01 (95% confidence interval (CI) = 0.93–1.09). For mainly outdoor work a risk estimate of 1.30 (95% CI = 1.14–1.47), and for farmers a risk estimate of 1.15 (95% CI = 1.00–1.32), was obtained. The study by Freedman *et al* (2002) considered 6565 cases of NMSC between 1984 and 1995 across 24 states and for each case 25 controls were chosen, matched by the 5-year age group. The usual occupation from the death certificate was used to classify occupation as indoor, mixed indoor/outdoor, outdoor non-farmer and outdoor farmer, and the estimates were adjusted for critical demographics. The effects of occupational exposure on risk increased when combined with medium residential exposure (mixed: odds ratio (OR) = 1.03, outside: OR = 1.41 and farmers: OR = 1.20).

A key observation is that studies of BCC and SCC have shown an increased risk of NMSC in individuals whose occupation entails working many hours outdoors (Gallagher *et al*, 1995a, 1995b), with suggestions that exposure to sunlight in the 10 years before diagnosis may be an important individual risk for development of SCC.

Risk estimates for occupational exposure to solar radiation and melanoma Because of the varying risk estimates reported for melanoma, and the difficulty in separating the contribution of occupational versus non-occupational exposures, no risk estimate was carried out for melanoma.

Generally, outdoor work has been associated with an elevated risk of malignant melanoma (Garland *et al*, 1990; Goodman *et al*, 1995; Puntoni *et al*, 2005). However, because of difficulties in classifying solar exposure as occupational or recreational, and thus being treated as a single exposure, negative associations have been reported (Vagero *et al*, 1986; Elwood and Jopson, 1997; Gandini *et al*, 2005). Inconsistencies in the estimates for occupational melanoma were demonstrated in the systematic review of Elwood and Jopson (1997), which considered 29 published case–control studies of melanoma and sun exposure. The exposures were classified as intermittent, occupational or total sun exposure, and the highest reported exposure category was compared with the lowest exposure category. These estimates were adjusted for critical demographic factors, and studies were excluded if either no OR or 95% CI was reported. A significant positive risk (OR = 1.71, 95% CI = 1.54–1.90, 6934 cases, 23 studies) was estimated for intermittent exposure but a significantly reduced risk (OR = 0.86, 95% CI = 0.77–0.96, 6517 cases, 20 studies) for heavy occupational exposure. Twelve studies evaluated occupational exposure and yielded reduced risk estimates; eight yielded increased risk estimates, four of these contributing most to the heterogeneity.

Other studies have reported an increased risk for melanoma skin cancer for farmers (Freedman *et al*, 1997; Cerhan *et al*, 1998; Settimi *et al*, 1999) and veterinarians (Miller and Beaumont, 1995; Travier *et al*, 2003). However, a meta-analysis (Acquavella *et al*, 1998)

of 37 studies assessed whether farmers had an elevated cancer incidence. Studies included in the meta-analysis were those previously analysed by Blair *et al* (1992) and other publications through to 1994. Twenty-one studies of malignant melanoma and 19 studies of NMSC in white male farmers were analysed, yielding a pooled random-effects estimate of 0.95 (95% CI = 0.82 – 1.09) and 1.15 (95% CI = 1.00 – 1.33), respectively, but with evidence of heterogeneity.

Other occupational exposures considered for NMSC

Mineral oils Exposure to mineral oils and in particular shale oil is of historical interest, but metalworking fluids (MWFs) appear to be the relevant route for exposure to minerals oils for the exposure period considered in the present study.

Risk estimates for occupational exposure to mineral oils and NMSC A paper by Mitropoulos and Norman (2005) investigated the associations between occupational and non-occupational exposures and the risk of SCC in a population-based case – control study ($n = 795$) in Arizona. There was a slightly elevated risk associated with automobile and machine work (OR = 1.21, 95% CI = 0.48 – 3.06), adjusted for skin reaction to sun exposure, history of actinic keratoses and current number of freckles. As this study had substantial data on occupational and non-occupational exposures and is adjusted for confounders, it has been used for the high level of exposure groups in the present study. As many studies provide negative risk estimates, the relative risk (RR) for low levels of exposure was taken as 1.

An early review by Tolbert (1997) was limited to substantial occupational exposure to mineral oils and risk of cancers of the skin or respiratory tract (e.g., metal workers and printers). The review considered studies from Sweden and the United States. One Swedish study reported a significant standard incidence ratio (SIR) of 16.6 (P-value < 0.001), based on only five exposed cases for SCC compared with the general male population. The US study also reported a significantly increased risk (RR = 10.5, 95% CI = 4.0 – 36.9) of scrotal SCC cancer among workers exposed to MWFs.

Calvert *et al* (1998) conducted a systematic review of cancer risk among workers exposed to MWFs and concluded that MWF exposure (primarily straight oil MWF) is associated with an increased risk of skin cancer and scrotal cancer. They noted that as a result of formulation changes in the composition of MWFs, and the reduction of impurities, recent exposures to straight oil may be associated with a substantially reduced risk of these two cancers. Other studies reviewed included one cohort study of skin cancer mortality in three automobile plants with no significant excesses in risk; three proportionate mortality studies that did not observe significant increase in risk; and a fourth study that did (proportional mortality ratio = 1.88, 95% CI = 0.51 – 4.80), based on four cases. The authors concluded that there is substantial evidence for an increased risk of skin cancer associated with the use of some types of MWFs before the mid 1970s.

A more recent study by Eisen *et al* (2001) considered mortality among a cohort of 46,399 workers in the US car industry during the period 1941 – 1994. This study reported a significant deficit for skin cancer overall, but for exposure to soluble MWFs a RR estimate of 1.48 (95% CI = 1.17 – 1.53) for each one standard deviation change in cumulative exposure (30 mg m^{-3} years) was found. However, the paper does not state the type of skin cancers, and it now appears that all the skin cancer deaths were in fact melanomas (Kriebel, personal communication).

Polycyclic aromatic hydrocarbons (coal tars and pitches) Exposure to polycyclic aromatic hydrocarbons (PAHs) is mainly via inhalation, which, similar to ingestion, does not increase the risk of NMSC (ATSDR, 1995). There is little evidence of a direct association between dermal exposure to individual PAHs and NMSC. However, a risk for this cancer may exist among individuals exposed to mixtures of PAHs in certain industrial processes/exposures (coal tar and pitches, soots, coal gasification, coke production, asphalt workers and roofers and creosotes).

Risk estimates for occupational exposure to PAHs and NMSC For the present study, a combined overall RR of 1.74 (95% CI = 1.07 – 2.65) was obtained from Partanen and Boffetta (1994) who carried out a meta-analysis of 20 studies of asphalt workers and roofers, of which four reported results for skin cancer. For pavers and road maintenance workers an RR of 2.18 (95% CI = 1.19 – 3.66), for roofers an RR of 4.00 (95% CI = 0.83 – 11.7) and for other workers an RR of 0.82 (95% CI = 0.22 – 2.09) was obtained. This observed excess could not be explained by smoking as a confounder or from the excess risk among the roofers, and was therefore attributed to PAHs from coal-tar products. It should be noted, however, that it appears that at least one of the four papers may include some melanoma cases, although these are reported as NMSC.

More recently, Boffetta *et al* (1997) conducted a general review of epidemiological evidence for a relationship between PAHs and cancer, and reported two studies relevant to skin cancer. A Polish study (Kubasiewicz and Starzynski, 1989; Kubasiewicz *et al*, 1991) identified significantly increased risks for skin cancer associated with exposure to any PAH for 30 or more years (OR = 1.5, 95% CI = 1.1 – 2.1), tar (OR = 1.1, $P < 0.05$), soot (OR = 1.2, $P < 0.05$) and coke (OR = 1.3, $P < 0.05$). A Canadian study (Gallagher *et al*, 1996) reported a nonsignificant increase in risk for BCC (OR = 1.2, 95% CI = 0.7 – 2.1) and a nonsignificant decrease in risk for SCC (OR = 0.9, 95% CI = 0.5 – 1.7) when exposed to pitch tar and tar products. These estimates were adjusted for key demographics.

Other occupational exposures considered for melanoma

Ultraviolet radiation from artificial sources Exposure to UVR from artificial sources is a potential cause of melanoma. However, from the literature there appears to be no association with cutaneous melanoma and it predominantly affects ocular melanoma, particularly in welders; an estimate for this is not presented in this paper but is given in the technical report (HSE, 2012b).

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.

Occupational exposure to solar radiation was categorised as 'outdoor' (e.g., the construction industry, public administration, defence and service industry), 'mixed' exposure or 'lower' exposed (e.g., wholesale and retail trade, restaurants and hotels, financing, insurance, real estate, business services, health and veterinary services) or exposed in 'farming or agriculture'.

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 at least 10 years and up to 50 years has been assumed for NMSC. Attributable fractions (AFs) for NMSC have been calculated for mineral oils, solar radiation and PAHs (coal tars and pitches). 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.

For all exposure scenarios, the estimated total AF for NMSC is 4.50% (95% CI = 0.77 – 9.94%), with 23 (95% CI = 4 – 50) attributable deaths and 2862 (95% CI = 478 – 6347) attributable registrations.

Table 2 Skin cancer 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)
Non-melanoma skin cancer										
Mineral oils	5,462,177	473,380	0.2816	0.0225	0.0215 (0.0000–0.1069)	0.0039 (0.0000–0.0210)	6 (0–31)	1 (0–4)	781 (0–3889)	121 (0–648)
PAHs – coal tars and pitches	346,466	0	0.0179	0	0.0130 (0.0022–0.0297)	0 (0)	4 (1–9)	0	475 (72–1094)	0
Solar radiation	3,735,036	1,781,937	0.1925	0.0849	0.0361 (0.0186–0.0550)	0.0074 (0.0018–0.0135)	11 (5–16)	2 (0–3)	1312 (678–2003)	229 (57–416)
Totals[a]					**0.0691 (0.0131–0.1498)**	**0.0113 (0.0000–0.0291)**	**20 (4–44)**	**2 (0–6)**	**2513 (478–5448)**	**349 (0–899)**
Melanoma: AF not determined										

Abbreviations: AF = attributable fraction; PAH = polycyclic aromatic hydrocarbon. [a]Totals are the product sums and are not therefore equal to the sums of the separate estimates of AF, deaths and registrations for each agent. The difference is especially notable where the constituent AFs are large.

Exposures affecting NMSC

Mineral oils are predominantly used in MWFs, and in total there were an estimated 5,805,643 men and 581,140 women 'ever exposed' over the 40-year REP. The estimated total AF for NMSC caused by exposure to mineral oils is 1.42% (95% CI = 0.00–7.11%). There were in total 7 (95% CI = 0–36) attributable deaths (6 men and 1 woman) and 902 (95% CI = 0–4537) attributable registrations (781 males and 121 females). Metal workers were at the most risk (658 male and 120 female registrations), especially machine tool operators, both men (446 registrations and 4 deaths) and women (87 registrations and 1 death).

Overall, there were 346 466 men ever exposed to PAHs from coal tars and pitches during the REP. The estimated total AF for NMSC caused by exposure to PAHs from coal tars and pitches is 0.76% (95% CI = 0.13–1.73%), with 4 (95% CI = 1–9) attributable deaths and 475 (95% CI = 80–1080) attributable registrations. Male roofers and glaziers had the most registrations and deaths attributable to occupation (254 and 2, respectively), followed by road workers, with 1 death and 138 registrations (85 roadmen and 53 road surfacers and concreters).

Occupational solar radiation occurs in various outdoor occupations. There were 3 735 036 men and 1 781 937 women ever exposed to solar radiation during the relevant exposure period. The estimated total AF for NMSC caused by exposure to solar radiation is 2.41% (95% CI = 1.16–3.77%), with 12 (95% CI = 6–19) attributable deaths and 1541 (95% CI = 735–2419) attributable registrations. In predominantly outdoor occupations, there were 11 attributable deaths (10 men and 1 woman) and 1379 attributable registrations (1192 men and 187 women). For mixed occupations, this reduced to 39 attributable registrations (21 men and 18 women) and no deaths. In farmers, there was 1 attributable male death and 123 attributable registrations (99 men and 24 women). Individuals in the construction and in the public administration and defence industry had the majority of attributable registrations (786 and 222, respectively) and deaths (6 and 2, respectively) for men. For women, the industries with the most attributable registrations were construction (55 registrations), sanitary and similar services (37 registrations), as well as recreational and cultural services (30 registrations).

DISCUSSION

These results for NMSC update those previously published (HSE, 2007). Because of the availability of more recent data, the overall attributable fraction estimate for both men and women has reduced from 11.8 to 6.91% and 3.0 to 1.13%, respectively. Our estimates are lower than those obtained by Doll and Peto (1981), that is, 10% for men and 2% for women. A study by Nurminen and Karjalainen (2001) also gave higher estimates for skin cancer than this study (13% for men and 4% for women), although Steenland *et al* (2003) gave a lower estimate of 1.5–6.0% for men. Our estimates appear to be consistent with current literature. However, because of the under-reporting of NMSC, these are likely to underestimate the true burden. Assessment of the literature relating to occupational solar radiation is often hampered by inadequate definition of the type of skin cancer studied, the use of different methods for assessing exposure and variable adjustment for non-occupational exposure (if any) and other risk factors. Risk estimates thus vary substantially between studies, particularly for melanoma.

More recently, interest has centred on evaluating the nature of sun exposure and occurrence of melanoma on different parts of the body, and there has been discussion about whether melanomas at different anatomic sites may be due to different causal pathways. Chang *et al* (2009) in a pooled analysis of 15 case–control studies found that excess sunbathing and total recreational sun exposure increased the risk of melanoma of the trunk and limbs but not melanoma of the head and neck. Occupational sun exposure appeared neither to increase nor decrease the risk of melanoma on the trunk and limbs but tended to increase the risk of melanoma on the head and neck, especially at low latitudes (OR = 1.7 95% CI = 1.0–3.0; adjusted for effects of age, sex, hair colour, ability to tan and freckling).

Other carcinogens identified by IARC were either not included in the review, as very little epidemiological evidence relating to occupational exposure was identified (e.g., arsenic and arsenic compounds), or were included within other estimates (e.g., soots and PAHs).

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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