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Occupational cancer in Britain

Female cancers: breast, cervix and ovary

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Overview of female cancers

The following paper reviews the three cancers in women: breast, cervical and ovarian. There is no overlap between the cancers and exposure circumstances, and thus all are considered and described separately. Data for male breast cancer are much more limited and will not be considered here.

Breast cancer Although cervical cancer is more frequent in some developing countries, female breast cancer is the most common cancer in women worldwide (Quinn *et al*, 2001; Ferlay *et al*, 2010). Incidence and mortality increase with age; although mortality continues to increase after menopause, the rate of increase of breast cancer incidence slows from a peak before menopause (Colditz *et al*, 2006). In Britain, female breast cancer increased by 53% between 1980 and 2004 (ONS, 2006a; ISD, 2008; WCISU, 2008). However, there has been a 33% decline in age-standardised breast cancer mortality since 1989 (ONS, 2006b; ISD, 2008). The five-year relative survival rate has improved from 52% in the early 1970s to 80% in the late 1990s (Quinn *et al*, 2008a). Virtually all invasive female breast cancers are adenocarcinomas (Quinn *et al*, 2001). Established risk factors for breast cancer include reproductive status, lifestyle, family history and genetics, as well as environmental and occupational exposures, which include shift work, ionising and non-ionising radiation, and exposure to chemicals such as organochlorines, PAHs and pesticides (Colditz *et al*, 2006).

Cervical cancer In terms of incidence, cancer of the cervix is the seventh most common cancer worldwide (second most common amongst women) and is much more common in developing countries where over 80% of the cases occur (Parkin *et al*, 2005). In Western countries where well-developed screening programs have been introduced, there has been a substantial decline in both incidence and mortality. In Britain, both the numbers diagnosed and deaths from the condition steadily decreased over the period from 1995 to 2005. Cervical cancer is rare below the age of 20 years, possibly because of the 10- to 20-year period required for the cancer to develop. Generally, the 5-year relative survival rate varies between 15% and 95% depending on the stage of disease and age at diagnosis, but averages at around 65% (Quinn *et al*, 2008b).

There are two main histological types of cervical cancer, the most common being squamous cell cancer and adenocarcinoma being less common. Evidence supports an association between all cervical cancers and human papillomavirus (HPV). Other risk factors that increase the risk of cervical cancers, especially if HPV is present, include socioeconomic status, oral contraceptive use, parity, body mass index and smoking (Schiffman and Hildesheim, 2006).

Ovarian cancer In terms of incidence, this is the sixth most common female cancer worldwide (in terms of mortality it is the seventh most common female cancer), with incidence rates being highest in developed countries and slowly increasing in many Western countries and Japan. In Britain, both incidence and mortality have increased and subsequently decreased, peaking in 2000 and 2002, respectively. Ovarian cancer is predominantly a disease of older, post-menopausal women, with almost 85% of cases being diagnosed in women over 50 years. This cancer has the lowest survival rate of all the gynaecological cancers, with a 5-year survival rate of 38% observed in recent years (Cooper *et al*, 2008). Between 80 and 90% of ovarian cancers are 'epithelial', with the remaining cases mainly being 'germ cell' tumours. Other types of cancer can affect the ovary (such as sarcomas), but these are very rare. Factors that increase the risks of ovarian cancer include a family history of ovarian or breast cancer, ovulation history and reproductive status, elevated body mass index, diagnosis of endometriosis and post-menopausal hormone use (Quinn *et al*, 2001; Hankinson and Danforth, 2006).

METHODS

Occupational risk factors

Group 1 and 2A human carcinogens The International Agency for Research on Cancer (IARC) has assessed the carcinogenicity of a number of substances and occupational circumstances as either definitely causing female cancer (Group 1) or probably causing

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

Table 1 Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1–77 (IARC, 1972–2001), into Groups 1 and 2A, which target the female organs 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				
No agents or occupational circumstances				
Group 2A: Probably carcinogenic to humans				
Agents, groups of agents				
Tetrachloroethylene	Production; dry cleaning; metal degreasing	Cervical *limited*	CAREX	Industry sectors categorised as highly exposed were, for example, manufacture of machinery, personal and household services, manufacture of fabricated metal products. Industry sectors categorised to low exposure, for example, in land transport, manufacture of wearing apparel and textiles. The construction industry did not contribute high numbers of exposed females.
Exposure circumstances				
Shift work	Healthcare; industrial manufacturing; mining; transport; communication; leisure and hospitality	Breast *limited*	IEH (2005)	
Hairdressers and barbers	Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols	Ovarian *limited*	LFS	
Agents/occupations not classified by IARC but included in the AF estimation				
Flight Personnel	Air travel assistants, airport-based personnel; pilots, cabin crew, ground staff	Breast *limited*	LFS and CAA	

Abbreviations: CAA = Civil Aviation Authority; CAREX = CARcinogen EXposure Database; IARC = International Agency for Research on Cancer; IEH = Institute for Environment and Health; LFS = Labour Force Survey; REP = risk exposure period.

female cancer (Group 2A); the estimated attributable fractions (AFs), deaths and registrations associated with these cancers are summarised in Table 1.

Choice of studies providing risk estimates for breast, cervical and ovarian cancers

A detailed review of occupational risk factor studies identified for breast, cervical and ovarian cancers is provided in the relevant HSE technical reports (HSE, 2012a, b, c).

Occupational exposure circumstances considered for breast cancer

Shift work Approximately 15–20% of the working population in Europe and North America are involved in shift work that involves working at night (Straif *et al*, 2007). The percentage of women working in shifts has increased over the past two decades, with about one-third working in some form of night shift. Exposure to light at night disturbs the circadian system, causing alterations to sleep-activity patterns, increased oxidative stress, suppression of melatonin production and deregulation of circadian genes involved in cancer-related pathways (Stevens *et al*, 2007; Straif *et al*, 2007). Stevens (1987) first put forward the hypothesis that exposure to light at night leads to increased female breast cancer risk via perturbation of melatonin homoeostasis (Cohen *et al*, 1978). The IARC Working Group has concluded that 'shift work that involves circadian disruption is probably carcinogenic to humans', and hence a Group 2A carcinogen (Straif *et al*, 2007).

Nurses (Dimich-Ward *et al*, 2007; Lie *et al*, 2007) and flight personnel are two of the main occupational groups considered in epidemiological studies of shift workers. A number of cohort and case–control studies have evaluated the association between female breast cancer and shift work in nurses, flight personnel and other occupational groups exposed to night-time shift work (HSE, 2012a).

Risk estimates for female night workers (excluding air flight personnel) For the present work, a systematic review and meta-analysis by Megdal *et al* (2005) was used to obtain risk estimates for night shift work (defined as 'high exposure'). An aggregate risk estimate of 1.48 (95% confidence interval (CI) = 1.36–1.61) was calculated, including flight personnel and other female night

Table 2 Female cancer burden estimation results

Agent	Number of women ever exposed	Proportion of women ever exposed	AF women (95% CI)	Attributable deaths (women) (95% CI)	Attributable registrations (women) (95% CI)
Breast cancer					
Shift work	1,953,645	0.0930	0.0453 (0.0323–0.0594)	552 (393–724)	1957 (1395–2568)
Flight personnel	13,902	0.0007	0.0003 (0.0002–0.0004)	4 (2–5)	13 (7–19)
Totals[a]			**0.0456 (0.0326–0.0597)**	**555 (397–727)**	**1969 (1407–2579)**
Cervical cancer					
Tetrachloroethylene	189,605	0.0090	0.0068 (0.0000–0.0213)	7 (0–22)	18 (1–56)
Ovarian cancer					
Hairdressers and barbers	631,937	0.0301	0.0054 (0.0000–0.0122)	23 (0–52)	33 (0–76)

Abbreviations: AF = attributable fraction; CI = confidence interval. [a]Totals are the product sums and are not therefore equal to the sums of the separate estimates of attributable fraction, deaths and registrations for each agent. The difference is especially notable where the constituent attributable fractions (AFs) are large.

workers. This study noted that the highest risk estimates from each of the cohorts and case–control studies corresponded to long periods of night-work employment, with lag times and increased incidence in breast cancer in those over 50 years, or exposed before the age of 30 years. To avoid double counting, flight personnel were excluded, giving a meta-relative risk (RR) for female night workers of 1.51 (95% CI = 1.36–1.68) based on six studies with adjustment for confounding factors.

Published risk estimates for <15 years of night shift work have varied from 0.3 (95% CI = 0.1–1.2) to 3.2 (95% CI = 0.6–17.3) (Tynes *et al*, 1996), with most falling close to 1 (Davis *et al*, 2001; Schernhammer *et al*, 2001; Lie *et al*, 2006; Schernhammer *et al*, 2006). Therefore, excluding the extremes of the range provided by Tynes *et al* (1996), a risk estimate of 1 is appropriate for all shift-work patterns with no night work or shift work for less than a year. Although there have been a number of other meta-analyses producing slightly different risk estimates often from the same studies, the estimates of risk used in this study are within similar orders of magnitude to other published estimates (e.g., Erren *et al*, 2008).

Risk estimates for shift work and flight personnel Although not explicitly listed as a Group 1 or 2A carcinogen, occupation as airline flight personnel has been linked to increased female breast cancer risk in a number of studies. There is uncertainty regarding causal factors (ionising radiation *vs* shift work) for breast cancer in female flight personnel; a number of studies have reported risk estimates for cancer incidence and mortality, but there was concern that these estimates varied according to flight routes and duration of employment. As such, European studies are more appropriate to the UK work force, and a meta-RR of ~1.4 has been reported in four meta-analyses (Ballard *et al*, 2000; Megdal *et al*, 2005; Buja *et al*, 2006; Tokumaru *et al*, 2006). The meta-standardised incidence ratio (SIR) of 1.44 (95% CI = 1.26–1.65) derived by Megdal *et al* (2005) has been used for the present study as it accurately reports the RRs provided in seven source studies. This study refers to employment as 'flight personnel', and thus differences between long- and short-haul flight are not relevant.

Occupational exposures considered for cervical cancer

Tetrachloroethylene (perchloroethylene) The highest occupational exposure to tetrachloroethylene is likely to occur among dry cleaning and metal degreasing workers; other occupational exposures may occur in fluorocarbon production. Exposure is most likely by inhalation or ingestion, but exposure via skin contact may also occur. Increased cervical cancer rates have been observed in studies of dry cleaners and laundry workers (Ruder *et al*, 2001; Blair *et al*, 2003).

Risk estimates for occupational exposure to PCE and cervical cancer The risk estimate for occupational exposure to PCE was taken from the study by Ruder *et al* (2001) who derived (using national rates) a significant standardised mortality ratio (SMR) of 1.95 (95% CI = 1.00–3.40, $P<0.05$, $n=12$). This was based on an extended follow-up of 1708 dry cleaners (in California, Michigan, Illinois and New York) primarily exposed to PCE for at least 1 year between 1940 and 1960. Individuals were classified as using only PCE or as using other substances, as well as PCE. Three mortality rates, with different reference populations, were produced for the entire study period (1940–1996). Despite the absence of data on potential confounders, the authors noted that the magnitude of the results were greater than could be explained by smoking alone. This risk estimate falls within the middle of a range of published results, which includes an SIR of 2.35 (95% CI = 1.08–4.46) (Anttila *et al*, 1995) and an SMR of 1.6 (95% CI = 1.0–2.3) (Blair *et al*, 2003), and is applicable to high-exposure occupational categories. Because of the absence of sufficient dose–response data specific to PCE, an RR of 1.29 has 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.

Occupational exposure circumstances considered for ovarian cancer

Risk estimates for employment as hairdressers and barbers (cosmetologists/beauticians) and ovarian cancer A risk estimate based on an overall SIR of 1.18 (95% CI = 0.98–1.40, $n=127$) was chosen from a study of 29 279 female hairdressers by Boffetta *et al* (1994). The hairdressers were identified from the 1970 censuses of Sweden, Norway, Finland (aged 25–64 years) and Denmark (aged 20–64 years). National Cancer Registries from these countries were used to identify the 127 attributable ovarian cancer cases (Denmark: 36, Sweden: 44, Norway: 14 and Finland: 33). The overall female population from the censuses was used as the reference, and all estimates were age adjusted (covering the period 1971–1985 in Sweden, Norway and Finland and 1971–1987 in Denmark). The risk estimates were elevated in Denmark and Finland over the full 16 years examined, but only for the first 9 years of follow-up in Sweden and Norway.

Shields *et al* (2002) reported a similarly elevated risk for female hairdressers with long-term exposure (RR = 1.21, 95% CI = 0.9–1) in Sweden between the 1960 and 1970 censuses and followed up from 1971 to 1990. Czene *et al* (2003) also reported a slightly elevated risk (SIR = 1.11; 95% CI = 0.96–1.28) for ovarian cancer in female hairdressers, with data taken from the Swedish censuses of 1960, 1970, 1980 and 1990 with follow-up until 1998. Other studies suggest that risks associated with ovarian cancer have declined over time, but there is uncertainty as to whether this is a true trend.

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.

In 1992, shift work was first included as a category in the UK Labour Force Survey (LFS), and hence data are only available for the very end of the 1956–1995 REP. A total of 1 282 042 women in GB were recorded in 1992 as shift workers by the LFS, and it was assumed that ~31% (IEH, 2005) were employed at night time, suggesting an exposed population of 400 611. To prevent double counting of flight personnel who may be exposed to shift-work patterns and ionising radiation, the 1979 UK LFS flight personnel numbers were subtracted from the shift-work numbers generating a conservative estimate of 387 045 female (non-flight personnel) night-time workers.

RESULTS

Because of the assumptions made about cancer latency and working age range, only cancers in patients aged 25 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 all female cancers. Table 2 provides a summary of the attributable deaths and registrations in Britain for 2005 and 2004 and shows the separate estimates for men and women, respectively.

For all exposure scenarios, the combined AFs, numbers of deaths and registrations for each type of cancer were as follows: for breast cancer the total AF was 4.56% (95% CI = 3.26–5.97%), giving in total 555 (95% CI = 397–727) attributable deaths and 1969 (95% CI = 1407–2579) registrations. For cervical cancer, the AF was 0.68% (95% CI = 0.03–2.13%), giving in total 7 (95% CI = 0–22) attributable deaths and 18 (95% CI = 1–56) registrations. For ovarian cancer, the AF was 0.54% (95% CI = 0.00–1.22%), giving in total 23 (95% CI = 0–52) attributable deaths and 33 (95% CI = 0–76) registrations.

Exposures affecting breast cancer

An estimated 1,953,645 women were ever exposed to shift (night) work over the 40-year exposure period, 1956–1996. The estimated AF was 4.53% (95% CI = 3.23–5.94), with 552 (95% CI = 393–727) deaths in 2005 and 1957 (95% CI = 1395–2568) registrations in 2004 attributable to exposure to shift work at night. Further breakdown by employment industry/service was not possible given current data on employment patterns for shift workers. For flight personnel, a separate AF of 0.03% was estimated with 4 (95% CI = 2–5) breast cancer deaths in 2005 and 13 (95% CI = 7–19) breast cancer registrations in 2004, all potentially linked either to disruption of the light at night/circadian rhythm and/or due to elevated exposure to ionising radiation.

Exposures affecting cervical cancer

An estimated 189,605 women were ever exposed to tetrachloroethylene over the 40-year relevant exposure period. The estimated AF was 0.68% (95% CI = 0.03–2.13%), with an estimated 7 (95% CI = 0–22) deaths in 2005 and 18 (95% CI = 1–56) registrations in 2004 for cervical cancer attributable to tetrachloroethylene exposure. Women engaged in personal and household services had the highest numbers attributable to occupation, with 11 registrations and 4 deaths. Manufacture of machinery, except electrical, accounted for two attributable registrations and one attributable death.

Exposures affecting ovarian cancer

An estimated 631 937 women were ever employed as a hairdresser or a barber over the 40-year relevant exposure period. The estimated AF was 0.54% (95% CI = 0.00–1.22%), with 23 (95% CI = 0–52) cancer deaths in 2005 and 33 (95% CI = 0–76) registrations in 2004 for ovarian cancer attributable to occupation as a hairdresser or a barber.

DISCUSSION

Exposure to night shift working patterns has been identified as the most significant occupational agent/exposure associated with female cancers, potentially accounting for over 4.5% of all breast cancer cases. As shift work has only recently been listed as a carcinogen by IARC, this finding has potential far-reaching implications globally. As a first step, more data are required to clarify the proportion of women who are exposed to night shift work. For example, the term ‘nursing jobs’ potentially obscures other occupational causal factors, including exposure to ionising radiation (medical radiography) and chemicals (pharmaceutical products and cleaning chemicals such as ethylene oxide). However, Franzese and Nigri (2007) reported a correlation between breast tumour onset and altered blood melatonin levels in nurses working in night shifts. Similarly, flight personnel are exposed to a number of potential breast cancer occupational risk factors including various volatile organic compounds, engine exhaust gases, pesticides and ionising radiation (Blettner *et al*, 1998). It is difficult to separate the individual effect of each potential risk factor, particularly the impact of ionising radiation and shift work in this group (Mawson, 1998). A recent review by Kolstad (2008) reported that definitions of ‘night work’ vary from study to study, and a consistent classification has not yet been developed. Direct comparison of different studies, particularly the difference, if any, between fixed (or permanent) night shifts and non-fixed (or rotating/mixed) and temporary night workers is problematic. Recall bias may also influence the inferred association between breast cancer and shift work (Kolstad, 2008).

Other potential carcinogen exposures for female cancers for which estimation was not carried out include asbestos, which has recently been re-categorised as an IARC Group 1 carcinogen for ovarian cancer, and ethylene oxide, which has been re-categorised as a Group 2A carcinogen for breast cancer (Baan *et al*, 2009). Inclusion of these would further increase the attributable estimates for female cancers. In addition, estimation has not been carried out for ionising radiation and breast cancer. Overall, ionising radiation is not considered to be a Group 1 or 2A carcinogen for breast cancer in occupational settings. However, in non-occupational exposures such as chest fluoroscopy and for atomic bomb survivors, a statistically significant association has been reported between pre-menopausal breast cancer and ionising radiation. Although radiographers may be at higher risk of exposure to ionising radiation, more rigorous health and safety regulations introduced since the 1940s have considerably reduced exposures and hence breast cancer risk (Doody *et al*, 2006).

Conflict of interest

The authors declare no conflict of interest.

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Appendix

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