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Health and Safety Executive

The burden of occupational cancer in Great Britain

Bone cancer and thyroid cancer

Prepared by the **Health and Safety Laboratory**, the **Institute of Occupational Medicine** and **Imperial College London** for the Health and Safety Executive 2012

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Research Report

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Bone cancer and thyroid cancer

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The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for cancers of the bone and thyroid derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for bone cancer related to overall occupational exposure to ionising radiation is 0.02% (no 95%Confidence Interval available), which equates to 0 attributable deaths and 0 attributable registrations. The estimated total (male and female) attributable fraction for thyroid cancer associated with occupational exposure overall and to ionising radiation is 0.05% (no 95%Confidence Interval available), which equates to 0 attributable deaths and 1 attributable registration.

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EXECUTIVE SUMMARY

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer used in this project was the attributable fraction i.e. the proportion of cases that would not have occurred in the absence of exposure; this was then used to estimate the attributable numbers. This involved obtaining data on the risk of the disease due to the exposure of interest, taking into account confounding factors and overlapping exposures, and the proportion of the target population exposed over the period in which relevant exposure occurred. Estimation was carried out for carcinogenic agents or exposure circumstances classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens. Here, we present estimates for cancers of the bone and thyroid that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

Ionising radiation has been classified by the IARC as a definite human carcinogen for bone and thyroid cancers. Ionising radiation consists of highly energetic (>12.4 electron volts) particles or waves that can ionise (detach) at least one electron from an atom or molecule. Examples of ionising radiation include X-rays, γ-rays, cosmic radiation, alpha particles and beta particles. Individuals can be exposed to radiation either externally, such as the use of X-ray equipment, or internally, such as by inhalation or ingestion of radioactive particles. Occupational exposure to external ionising radiation mainly affects nuclear industry workers, disaster clean-up workers, radiologists, technologists and military personnel (typically through weapons production and testing). Occupational exposure to internal ionising radiation occurs during underground mining, working with plutonium, reactor fuel manufacture and radium-dial painting (luminising industry). Workers who are exposed to natural sources of radiation include miners and aircrew.

Due to assumptions made about cancer latency and working age range, only cancers in ages 25+ in 2005/2004 could be attributable to occupation.

For Great Britain (GB) in 2005, there were 133 deaths in men and 100 in women aged 25+ from bone cancer; in 2004 there were 188 total registrations for bone cancer in men aged 25+ and 135 in women aged 25+. The estimated total (male and female) attributable fraction for bone cancer associated with occupational exposure overall and to ionising radiation is 0.02% (no 95%Confidence Interval available), which equates to 0 attributable deaths and 0 attributable registrations.

In 2005 in GB, there were 106 deaths in men and 231 in women aged 25+ from thyroid cancer; in 2004 there were 419 total registrations for thyroid cancer in men aged 25+ and 1100 in women aged 25+. The estimated total (male and female) attributable fraction for thyroid cancer associated with occupational exposure overall and to ionising radiation is 0.05% (no 95%Confidence Interval available) which equates to 0 attributable deaths and 1 attributable registration.

CONTENTS

1 INCIDENCE AND TRENDS

1.1 BONE CANCER

Cancers that arise in the bone, or articular cartilage, (ICD-10 C40-C41; ICD-9 170) account for approximately 0.5% of all malignant neoplasms in humans (Miller *et al,* 2006). There are three main cell types of bone cancer: osteosarcoma, chondrosarcoma and Ewing's sarcoma. Osteosarcoma is the most common and usually develops in the growing ends of long bones, such as the lower thigh, upper shin, upper arm and lower shin. Chondrosarcoma produces cartilage in areas where no cartilage would normally grow; common sites for this tumour are the pelvis, shoulder blade and ribs. Ewing's sarcoma mainly occurs in the axial skeleton, typically starting in the pelvis, thigh or shin. Osteosarcoma has a bimodal age-distribution which peaks in adolescence (around 17 years) and then again later in life (around 80 years). Chondrosarcoma is rare in childhood and rates rise with advancing age, peaking between 70 and 80 years of age. Ewing's sarcoma has a similar age distribution to that of osteosarcoma for early years but tails off, as the condition is rare over 35 years of age.

Table 1 Number of male bone cancer registrations in England, Wales and Scotland for 1995-2004.

Year	England		Wales	Scotland	
	C40	C41	C40-C41	C40	C41
1995	120 (0.5)	125 (0.5)	8 (0.57)	5 (0.2)	9 (0.4)
1996	100 (0.4)	105 (0.4)	11 (0.79)	14 (0.6)	13 (0.5)
1997	114 (0.5)	104 (0.4)	8 (0.57)	12 (0.5)	16 (0.7)
1998	103 (0.4)	93 (0.4)	23 (1.64)	20 (0.8)	11 (0.4)
1999	102 (0.4)	130 (0.5)	20 (1.43)	14 (0.6)	13 (0.5)
2000	131 (0.5)	116 (0.5)	19 (1.35)	16 (0.6)	7 (0.3)
2001	112 (0.5)	111 (0.5)	19 (1.35)	12 (0.5)	7 (0.3)
2002	116 (0.5)	114 (0.5)	15 (1.1)	14 (0.5)	12 (0.5)
2003	106 (0.4)	110 (0.5)	16 (1.1)	14 (0.6)	9 (0.4)
2004	88 (0.4)	133 (0.5)	19 (1.3)	9 (0.4)	11 (0.4)
Average	**109 (0.5)**	**114 (0.5)**	**16 (1.1)**	**13 (0.5)**	**11 (0.4)**

Source: ONS MB1 Series (ONS 2007a), Welsh Cancer Intelligence & Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008)

Table 2 Number of female bone cancer registrations in England, Wales and Scotland for 1995-2004.

Year	England		Wales	Scotland	
	C40	C41	C40-C41	C40	C41
1995	75 (0.3)	88 (0.4)	8 (0.54)	10 (0.4)	10 (0.3)
1996	85 (0.3)	106 (0.4)	12 (1.81)	6 (0.2)	13 (0.4)
1997	73 (0.3)	83 (0.3)	14 (0.94)	12 (0.4)	11 (0.4)
1998	83 (0.3)	93 (0.4)	16 (1.07)	8 (0.3)	10 (0.3)
1999	100 (0.4)	89 (0.4)	15 (1.01)	11 (0.3)	9 (0.3)
2000	91 (0.4)	97 (0.4)	16 (1.07)	11 (0.4)	6 (0.2)
2001	90 (0.4)	117 (0.5)	15 (1.00)	5 (0.2)	9 (0.3)
2002	97 (0.4)	90 (0.4)	8 (0.5)	4 (0.2)	14 (0.5)
2003	96 (0.4)	96 (0.4)	15 (1.0)	13 (0.5)	8 (0.3)
2004	75 (0.3)	78 (0.3)	15 (1.0)	8 (0.3)	7 (0.2)
Average	**87 (0.4)**	**94 (0.4)**	**13 (1.0)**	**9 (0.3)**	**10 (0.3)**

Source: ONS MB1 Series (ONS 2007a), Welsh Cancer Intelligence & Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008)

Currently in the UK, bone cancer (including connective tissue) is ranked 19th in men and 21st in women. In Great Britain, the numbers of cancers registered (i.e., diagnosed) has been fluctuating between 450 cases and 500 cases each year (Table 1 and Table 2). The numbers who die from the condition has been steadily increasing from around 240 in 1999 to nearly 300 in 2005 (Table 3). Long-term trends in the incidence and mortality were studied based on notifications of cancer cases and deaths in England, Wales and Scotland over the past ten-years. On average 263 males and 213 females were diagnosed with bone cancer in Great Britain, with the highest average annual incidence occurring in Wales at 1.1 per 100,000 males and 1.0 per 100,000 females. The crude rate appears to be relatively stable in England for both males and females, and for females in Wales. In Wales a large increase in the crude rate for deaths amongst males during the period 1998-2001 appears to have stabilised over recent years. Crude rates for Scotland appear to be fluctuating for both males and females around 0.4 per 100,000 persons. On average 156 males and 121 females die from bone cancer in Great Britain. The crude rate in England/Wales appears to be stable at around 5 per 1,000,000 males and 4 per 1,000,000 females. In Scotland, the rates are relatively stable for malignant neoplasm of bone and articular cartilage of limbs (C40) and fluctuate for malignant neoplasm of bone and articular cartilage of other and unspecified sites (C41) for both males and females.

Table 3 Number of deaths from bone cancer in England, Wales and Scotland 1999-2005.

Year	Men			Women		
	England and Wales	Scotland		England and Wales	Scotland	
	C40-C41	C40	C41	C40-C41	C40	C41
1999	128 (5)	2 (0.1)	15 (0.6)	86 (3)	3 (0.1)	8 (0.2)
2000	112 (4)	2 (0.1)	18 (0.7)	103 (4)	3 (0.1)	15 (0.4)
2001	138 (5)	2 (0.1)	11 (0.4)	119 (4)	1 (0.0)	8 (0.3)
2002	153 (6)	5 (0.2)	11 (0.4)	89 (3)	1 (0.0)	10 (0.3)
2003	131 (5)	1 (0.0)	14 (0.5)	123 (4)	-	9 (0.3)
2004	175 (6)	3 (0.1)	10 (0.4)	125 (4)	3 (0.1)	13 (0.4)
2005	147 (5)	-	11 (0.4)	118 (4)	-	8 (0.2)
Average	**141 (5)**	**2 (0.1)**	**13 (0.5)**	**109 (4)**	**2 (0.1)**	**10 (0.3)**

Source: ONS DH2 Series (ONS 2007b), Welsh Cancer Intelligence & Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008)

Bone cancer survival rates have been improving over the past 35 years, with rates being consistently higher in females (Cancer Research UK 2007a). For patients diagnosed with this cancer in the period 1996-1999 in England and Wales, the population-based five-year relative survival rate was 44.1% for males and 54.2% for females compared to 27% in males and 36% in females diagnosed in 1971-1975. The one-year survival rates are much higher for both males (67.7% and 53%) and females (77.7% and 57%) for those diagnosed in 1996-1999 and 1971-1975 respectively. Generally bone cancer treatment is very successful if the disease has not spread to other parts of the body; overall approximately 2 out of 3 people will be cured. Generally, the five-year survival rate varies between 10% and 90% depending on the type, grade and stage of disease as well as age at diagnosis. Low-grade osteosarcomas are uncommon but they have the highest survival rate of 90%, localised tumours (irrespective of grade) have a survival rate of about 55% but if the tumour has spread to other parts of the body the survival rate can be lower than 10%. For Ewing's sarcoma that has not spread the five-year survival rate is approximately 60%. However, if it has spread this rate reduces to around 20%. The grade of the tumour is the most important factor for chondrosarcoma; if the tumour is low grade the ten-year survival rate is high at 80% whereas if the cancer is high grade the outlook is poorer with a five-year rate of about 30%. In 2004, cancer mortality to incidence ratios for bone cancer (C40 and C41) were 0.16 and 1.13 for men and 0.32 and 1.17 for women (ONS 2006).

1.2 THYROID CANCER

Cancer of the thyroid (ICD-10 C73; ICD-9 193) accounted for 141,000 new cases, and 35,000 deaths, worldwide in 2002 (Parkin *et al,* 2005). Thyroid cancer is one of the few malignancies that are more common in females than males. The disease accounts for 2.1% of all cancers in women and has a male to female sex ratio of 0.36. Diagnostic procedure can influence rates of incidence and this may account for particularly high rates observed in the US. High incidence rates are also found in Australia, New Zealand and Japan. The worldwide mortality to incidence ratio is low at 0.25, thus the disease accounts for few cancer deaths (0.5% of all cancer deaths worldwide).

Thyroid cancer is relatively uncommon, although it is the most common malignancy of the endocrine system (Ron and Schneider, 2006). The majority of cancer cases (about 95%) originate from the cells derived from the follicular epithelium. There are four main types of thyroid cancer: papillary, follicular, anaplastic and medullary. For clinical and aetiological purposes the types tend to be termed well differentiated (papillary and follicular) i.e. the cancerous cells have some features of normal thyroid cells, or are poorly differentiated (i.e., anaplastic). Other non-epithelial tumours are rare and are classified separately. Papillary thyroid cancer is the most common, accounting for about 60% of diagnosed cases (Cancer Research UK 2007b). Around 5-10% of diagnosed cases are medullary thyroid cancers. The remaining 30% of cases are equally split between follicular and anaplastic types. Papillary thyroid cancer is usually diagnosed in younger people, follicular thyroid cancer is generally a disease of the young or middle aged and anaplastic thyroid cancer is typically a disease of the elderly, with 75% of people diagnosed with this type being 60 years of age or more.

Currently the condition is within the top twenty most common cancers for UK women and top twenty-five for UK men (ranking 18th and 22nd respectively), accounting for 0.6% of all UK cancer cases diagnosed each year. In Great Britain, the numbers diagnosed has been steadily increasing from approximately 1,000 cases each year to in excess of 1,600 (Table 4). Long-term trends in the incidence and mortality were studied based on notifications of cancer cases and deaths in England, Wales and Scotland over the past ten-years. On average 360 males and 950 females were diagnosed with thyroid cancer in Great Britain. The average annual incidence rate is similar across Great Britain at around 1.4 per 100,000 males and over 3 per 100,000 for females. The crude incidence rate for females is consistently double the rate for males for all countries. On average 106 males and 210 females die from thyroid cancer in Great Britain. The crude rate for both males and females in Scotland fluctuates around 0.3 per 1,000,000 for males and 0.5 per 1,000,000 for females. The crude mortality rate is not published for England/Wales.

Table 4 Number of thyroid cancer registrations in England, Wales & Scotland for 1995-2004.

Year	Men			Women		
	England	**Wales**	**Scotland**	**England**	**Wales**	**Scotland**
1995	229 (1.0)	12 (0.86)	30 (1.2)	624 (2.5)	41 (2.76)	97 (3.3)
1996	276 (1.1)	22 (1.57)	27 (1.1)	668 (2.7)	44 (2.95)	104 (3.7)
1997	278 (1.1)	17 (1.21)	35 (1.4)	676 (2.7)	34 (2.28)	102 (3.1)
1998	326 (1.3)	14 (1.00)	38 (1.5)	752 (3.0)	34 (2.28)	75 (2.4)
1999	300 (1.2)	21 (1.50)	39 (1.5)	753 (3.0)	58 (3.89)	97 (3.1)
2000	302 (1.3)	18 (1.28)	32 (1.2)	829 (3.3)	39 (2.61)	109 (3.7)
2001	316 (1.3)	15 (1.07)	34 (1.3)	862 (3.4)	56 (3.74)	115 (4.1)
2002	313 (1.3)	28 (2.0)	33 (1.2)	922 (3.6)	58 (3.8)	92 (3.1)
2003	343 (1.4)	26 (1.8)	46 (1.7)	936 (3.7)	42 (2.8)	109 (3.6)
2004	373 (1.5)	25 (1.7)	41 (1.5)	1002 (3.9)	55 (3.6)	112 (3.8)
Average	**306 (1.3)**	**20 (1.4)**	**36 (1.4)**	**802 (3.2)**	**46 (3.1)**	**101 (3.4)**

Source: ONS MB1 Series (ONS 2007a), Welsh Cancer Intelligence & Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008)

Table 5 Number of deaths from thyroid cancer in England, Wales & Scotland 1999-2005.

Year	Men		Women	
	England and Wales	**Scotland**	**England and Wales**	**Scotland**
1999	104	6 (0.2)	193	28 (0.6)
2000	88	13 (0.5)	171	28 (0.7)
2001	80	10 (0.4)	179	22 (0.5)
2002	100	9 (0.3)	179	12 (0.3)
2003	109	9 (0.3)	201	23 (0.5)
2004	99	11 (0.4)	185	16 (0.4)
2005	101	5 (0.2)	209	22 (0.5)
Average	**97**	**9 (0.3)**	**188**	**22 (0.5)**

Source: ONS DH2 Series (ONS 2007b), Welsh Cancer Intelligence & Surveillance Unit (WCISU 2008), Information Services Division (ISD 2008)

Thyroid cancer survival rates have been improving over the past 35 years, with rates being consistently higher in females (Cancer Research UK 2007b). For patients diagnosed with this cancer in the period 1996-1999 in England and Wales, the population-based five-year relative survival rate was around 75% for males and 79% for females compared to about 50% in males and 56% in females diagnosed in 1971-1975. The one-year survival rates are much higher for both males (81% and 61%) and females (82% and 63%) for those diagnosed in 1996-1999 and 1971-1975 respectively. If the cancer is diagnosed when young (under 40 years) the survival rate is very good at nearly 100% for both men and women. Generally, survival rates depend on the histological type of tumour, stage and age at diagnosis. In 2004, cancer mortality to incidence ratios for thyroid cancer (C73) were 0.25 for men and 0.17 for women (ONS 2006).

2 OVERVIEW OF AETIOLOGY

The main exposure that induces osteosarcoma bone cancer is ionising radiation. However Ewing's sarcoma is not induced by ionising radiation (Miller *et al,* 2006). Occupational exposure to radium has also been found to be associated with osteosarcoma. Osteosarcomas and chondrosarcomas have been linked with exposure to plutonium. Other non-occupational risk factors for bone cancer include high-dose radiation particularly used in the therapy of various cancers, presence of faulty genes and suffering from Paget's disease. Suggestions have been made of an association between an increased risk of bone cancer and medical implants.

Radiation is one of the few risk factors that is clearly associated with thyroid cancer (Ron and Schneider, 2006). The increased risk of thyroid cancer due to radiation is particularly evident in those exposed during childhood. Well-differentiated papillary cancer is the principal cell type induced by radiation, but an increase in follicular and anaplastic carcinomas may occur as the population ages. Other non-occupational risk factors for thyroid cancer include a history of benign thyroid diseases, such as nodules and goitre (an enlarged thyroid), a family history of thyroid cancer and diet, including iodine deficiency. Suggestions have been made that high vegetable consumption and consumption of fruit and grains may be protective for thyroid cancer.

Iodine is an essential element that enables the thyroid gland to produce thyroid hormones. A severe iodine deficiency can cause hypothyroidism, goitre and hyperthyroidism. Hypothyroidism and goitre can also be caused by an excessive iodine intake. There are many areas around the world where soils are deficient in iodine, and iodine must be added to individual's diets, typically via iodised salt. Dietary iodine is concentrated by the thyroid gland, and a high (or low) intake could alter its functionality and hormone production. This may lead to an enlarged thyroid and subsequently an increased risk of thyroid cancer. Studies investigating the link between thyroid cancer and iodine intake are rare, and the majority of studies use seafood consumption (as these foods tend to be high in iodine) as a surrogate measure of iodine exposure.

From epidemiological studies there appears to be inconclusive results when it comes to describing the relationship between iodine exposure and thyroid cancer. This could be due to the various methods used for exposure assessment, such as iodine excretion levels (Shakhtarin *et al,* 2003), estimates of intake based on food consumption (Horn-Ross *et al,* 2001; Kolonel *et al,* 1990) or definition of iodine deficient/sufficient areas (Pettersson *et al,* 2003). Most studies do not report overall estimates, but dose-response estimates. The majority of these dose-response relationships are non-significant, but do give increased estimates. Two studies report an increase in incidence for thyroid cancer with increasing intake (Kolonel *et al,* 1990; Pettersson *et al,* 2003); in contrast another study reports a decreasing risk with increasing intake (Shakhtarin *et al,* 2003). A further study found an excess of thyroid cancer was only evident in 'high risk' women i.e. women who had undergone medical radiation, suffered from a benign thyroid disease or had a family history of thyroid disease (Horn-Ross *et al,* 2001). As mentioned above, Pettersson *et al.* found an increased risk for overall thyroid cancer in iodine sufficient areas (high iodine intake). However, this relationship was relevant to only two of the three sub-types studied, papillary and anaplastic thyroid cancer. The other main sub-type, follicular, was found to have an increased incidence in iodine depleted areas (low iodine intake), although Kolonel *et al.* (1990) found that the increased risk with increased iodine intake was apparent for both follicular and papillary carcinomas. Kolonel *et al.* (1990) also found that the effects of dietary iodine intake were increased in women with reproductive difficulties (first pregnancy miscarriage/still birth or fertility drug use).

Shakhtarin *et al.* (2003) highlighted a joint effect of radiation exposure and iodine deficiency. They found the excess relative risk was nearly five times greater than that for just iodine intake, and again, the greatest risk was seen in iodine deficient areas. It should be noted that the study by

Shakhtarin *et al,* (2003) was conducted in regions highly contaminated by the Chernobyl power station accident; thus, results are likely to differ from the other papers.

Evidence of the carcinogenic effects of ionising radiation in humans mainly arises from epidemiological studies on the survivors of the atomic bombings in Japan, and patients exposed to radiation for medical reasons (IARC 2000, IARC 2001). Epidemiological studies have consistently reported elevated risks for bone and thyroid cancers associated with ionising radiation. Bone cancer is typically induced by internal exposure to radium and plutonium. Sufficient evidence has been provided through studies on radium dial painters, plutonium exposed workers and patients treated with radium. Infrequent or relatively high external exposure to X- and γ- rays has been found to induce bone cancer. Thyroid cancer is typically induced by early internal exposure to radioisotopes of iodine. Sufficient evidence has been provided through studies on atomic bomb survivors and inhabitants of the Marshall Islands after fall-out from nuclear weapons testing. External exposure to X- and γ- rays readily induces cancer of the thyroid, especially following irradiation during childhood. In these studies clear dose-response relationships for thyroid cancer have been demonstrated. Other sites that are frequently associated with ionising radiation are leukaemia, lung, skin, breast, lymphoma and CNS. These cancers will not be discussed in the following report as they are discussed elsewhere individually. In addition to the level of radiation received, the age at which exposure occurs, the length of time of exposure and the gender of the individual can modify the risk of cancer. These additional risk factors must be taken into account, if possible, when assessing the associations between cancer and occupational exposure.

The Occupational Health Decennial Supplement reported mortality (1979-1980, 1982-1990) and cancer incidence (1981-1987) in men and women aged 20-74 years in England (Drever, 1995). For bone cancer it was observed that the risk was greatest in male woodworking machinists and female press and automatic machine operators. For thyroid cancer high risks were observed for male brewery workers and female hospital porters and ward orderlies. These results can be seen by the elevated PRRs and PMRs (Table 6 and Table 7).

No raised PRRs for bone cancer were found. Occupation as a male electrician was associated with a significantly elevated mortality rate for both bone cancer and thyroid cancer; this may indicate an occupational exposure common to both aetiologies. Exposure to ionising radiation has also been shown to induce these conditions; however, related occupations did not appear to have elevated risks. Other exposures that have been shown to be associated with bone cancer include radium, plutonium and thorotrast (i.e., a suspension of particles of radioactive thorium dioxide used as a contrast medium in X-ray diagnostics in the 1930s and 40s) (Miller *et al,* 2006). Other exposures that have been shown to be associated with thyroid cancer include iodine, hydrocarbons and silica (Ron and Schneider, 2006).

Table 6 Job codes with significantly high PMRs for bone cancer. Men and women aged 20-74 years, England, 1981-87.

Job Group		Deaths	PMR	95% CI
SIC code	**Description**	**(1979-1980 and 1982-1990)**		
Men				
005	Computer programmers	11	247	123-442
013	Welfare Workers	10	225	108-413
108	Woodworking machinists	9	344	157-653
137	Electricians	25	167	108-247
192	Refuse collectors	6	287	106-626
Women				
125	Press and automatic machine operators	4	594	162-1522

Source: (Drever 1995) Occupational Health Decennial Supplement

Table 7 Job codes with significantly high PRRs and PMRs for thyroid cancer. Men and women aged 20-74 years, England.

Job Group		Registrations	PRR	95% CI	Deaths	PMR	95% CI
SIC code	Description	(1981 – 1987)			(1979 – 1980 and 1982 – 1990)		
Men							
011	Teachers nec				21	199	123-305
060	Other service personnel				24	158	101-236
074	Other textile workers	7	397	160-819			
077	Brewery workers	3	562	116-1643			
137	Electricians				18	183	109-290
143	Electrical engineers (so described)				11	273	136-489
Women							
061	Hospital porters and ward orderlies	13	195	104-335			

Source: (Drever 1995) Occupational Health Decennial Supplement

More recent results for mortality for the period 1991-2000 in men and women aged 20-74 years in England are shown in Table 8 and 9. For bone cancer it was observed that the risk was greatest in male moulders, core makers and die casters. No significantly increased risk was observed for bone cancer in women. In comparison to the previous supplement, no occupations re-appear with significantly elevated risks. For thyroid cancer the greatest risks were observed in fire service personnel for men and physiotherapists for females. In comparison to the previous supplement, one occupation re-appears with an elevated PMR. Previously male welfare workers had an increased risk whereas in the current supplement female welfare workers are at increased risk.

Table 8 Job codes with significantly high PMRs for bone cancer. Men and women aged 20-74 years, England.

Job Group		Deaths	Expected deaths	PMR	Lower 95% CI	Upper 95% CI
SIC code	Description	1991 - 2000				
Men						
025	Professional athletes, sports officials	5	1.4	355.9	115.6	830.5
050	Fire Service Personnel	7	2.0	341.5	137.3	703.7
116	Moulders, Core Makers, Die Casters	4	0.9	431.2	117.5	1104.0
129	Tool Makers, Tool Fitters & Markers-Out	10	3.0	329.7	158.1	606.3
176	Mine (excluding coal) & Quarry Workers	4	0.9	421.7	114.9	1079.7
Women						
None identified						

Source: Coggon *et al.* (2009) Occupational mortality in England and Wales, 1991-2000.

Table 9 Job codes with significantly high PMRs for thyroid cancer. Men and women aged 20-74 years, England 1991-2000.

Job Group		Deaths	Expected deaths	PMR	Lower 95% CI	Upper 95% CI
SIC code	Description	1991 - 2000				
Men						
049	Police	11	4.8	231.6	115.6	414.3
050	Fire Service Personnel	7	1.7	414.7	166.7	854.5
Women						
013	Welfare Workers	17	7.4	230.4	134.0	368.9
020	Physiotherapists	3	0.6	499.8	103.0	1460.6

Source: Coggon *et al.* (2009) Occupational mortality in England and Wales, 1991-2000.

IARC have assessed the carcinogenicity of a number of substances and occupational circumstances with those classified as Group 1 having sufficient evidence in humans and those classified as Group 2A having limited evidence in humans. Ionising radiation has been classified as a Group 1 carcinogen for human bone and thyroid cancer (Table 10). From the information included in the IARC assessments Siemiatycki *et al.* (2004) further classified the evidence for occupational causation as strong or suggestive, which can also be found in Table 10. There is strong evidence that exposure to ionising radiation is associated with an increased risk of work-related bone cancer and thyroid cancer.

Table 10 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, for bone and thyroid cancers.

Agents, Mixture, Circumstance	Main industry, Use	Evidence of carcinogenicity in humans*	Strength of evidence[$]	Other target organs
Group 1: Carcinogenic to Humans				
Agents, groups of agents				
Ionising Radiation	Radiologists, technologists, nuclear workers, radium-dial painters, underground miners, plutonium workers, cleanup workers following nuclear accidents, aircraft crew	Sufficient	Strong	Leukaemia Lung Liver Others
Exposure circumstances				
None identified				
Group 2A: Probably Carcinogenic to Humans				
Agents & groups of agents				
None identified				
Exposure circumstances				
None identified				

* Evidence according to the IARC monograph evaluation; [$] taken from Siemiatycki *et al,* (2004)

2.1 EXPOSURE TO IONISING RADIATION

2.1.1 Introduction

Ionising radiation consists of highly energetic (>12.4 electron volts) particles or waves that can ionise (detach) at least one electron from an atom or molecule. Examples of ionising radiation include X-rays, γ-rays, cosmic radiation, alpha particles and beta particles. Ionising radiation is found in solid or gaseous radioactive elements, such as uranium, cobalt, plutonium and radon. Occupational exposure to ionising radiation occurs in many settings: mainly medical, research and construction industries. Natural background radiation is released via cosmic radiation, solar radiation and radon. Individuals can be exposed to radiation either externally, such as the use of X-ray equipment, or internally, such as by inhalation or ingestion of radioactive particles. Ionising radiation can penetrate matter, thus the main use in industry is for measuring; X- and γ- rays are used in industrial production to reveal internal defects of materials. Level indicators and thickness gauges measure the presence/absence and thickness of material using γ-rays. In biology, radiation is typically used for sterilisation and enhancing mutations. Radiation is also used for the sterilisation of medical equipment and food preservation. Another major use of X-rays, γ-rays and other radiation sources is radiotherapy for treating many medical conditions, such as ankylosing spondylitis and cancer. Occupational exposure to external ionising radiation mainly affects nuclear industry workers, disaster clean-up workers, radiologists, technologists and military personnel (typically through weapons production and testing). Occupational exposure to internal ionising radiation occurs in many situations, including underground mining, working with plutonium, reactor fuel manufacture and radium-dial painting (luminising industry). Workers who are exposed to natural sources of radiation, such as minors and aircrew, are not usually individually monitored for exposure via dosimeters. During the period 1985-1989 there were just over 5,000,000 workers worldwide exposed to natural radiation. In total in this period there were over 9,000,000 workers worldwide exposed to radiation (IARC 2000).

2.1.2 Population Studies

Fincham *et al*. (2000) conducted a Canadian case-control study on 1,272 thyroid cancer patients and 2,666 controls to explore the risk of thyroid cancer and occupational exposures. Cases were identified through cancer registries in British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia and Newfoundland and via hospital records in Quebec. Individuals diagnosed with thyroid cancer between 1986 and 1988 were included in the analysis. Controls were randomly selected from electoral registers, taxation lists, telephone directories and population based health care system files. All participants completed self-reporting questionnaires, which collected information on demographics, radiation exposure (diagnostic, therapeutic and occupational), smoking, medical history and occupational history. Individuals that reported being exposed to radiation at work were further classified from their job titles as possibly being exposed to ionising radiation, possible exposure to electromagnetic radiation or unlikely to be exposed to either. For self reported exposure to radiation at work, odds ratios were calculated adjusted for age, sex and cigarette smoking. Possible exposure to ionising radiation was associated with a slightly increased risk of thyroid cancer with an OR of 1.03 (95% CI=0.60-1.77, cases=65, controls=95). The authors conclude that from this information it is difficult to confirm or disconfirm an association between thyroid cancer risk and workplace exposure to ionising radiation.

In the US the number of women employed in ‘traditionally’ female occupations is growing and there is limited occupational health research on these occupations, thus Robinson *et al.* (1999) conducted a cancer mortality study paying particular attention to these occupations. In total there were 458,690 US women studied, who died of cancer aged 65 or under, between 1984 and 1995 and were not listed as homemaker on the death certificate. Women in all occupations were used as the reference group. Proportionate cancer mortality ratios were adjusted for race and age. PCMRs

were reported for the whole 12 year period, 1984-1995 and for two six year periods, 1984-1989 and 1990-1995. Excess risk was observed for thyroid cancer in health service occupations, this excess was significant for the whole period and for the last six years (1984-1995: PCMR=194, 95% CI=123-290, n=23, 1984-1989: PCMR=172, 95% CI=82-316, n=10 and 1990-1995: PCMR=214, 95% CI=114-367, n=13). Very high and significant excesses of thyroid cancer were also observed in women whose usual occupation was as a therapist for the whole period (PCMR=820, 95% CI=301-1786, n=6) and for both six-year periods (PCMR=945, 95% CI=195-2760, n=3 and PCMR=725, 95% CI=150-2119, n=3 for 1984-1989 and 1990-1995 respectively). No results for bone cancer were reported. The authors note that health aids may be exposed to chemotherapeutic agents and ionising radiation through diagnostic and therapeutic procedures, which may account for the excess of thyroid cancer observed.

2.1.3 Registry Studies

Ashmore *et al.* (1998) carried out a cohort mortality study of occupational radiation exposure in Canada. The cohort consisted of 206,620 individuals (105,456 males and 101,164 females) who were registered in the National Dose Registry between January 1951 and December 1983. The National Dose Registry of Canada is a centralised registry of records of occupational exposure to ionising radiation from 1950 onwards; it includes individual dosimetry information on industrial, medical and dental workers as well as nuclear power workers. Mortality follow-up was through December 1987 and cause of death for the cohort was determined via linkage of records to the Canadian Mortality Data Base. A total of 5,426 deaths (4,210 males and 1,216 females) were identified. The mortality experience of the Canadian population was used for reference. Standardised mortality ratios were adjusted for age and calendar period. There was an elevated risk of thyroid cancer for males, although it was non-significant (SMR=1.49, 90% CI=0.59-3.14, n=5). No cases of thyroid cancer were observed among the female sub cohort. Bone cancer was non-significantly elevated for females (SMR=1.14, 90% CI=0.39-2.61, n=4); however, it was significantly reduced for males (SMR=0.36, 90% CI=0.10-0.93, n=3). It should be noted that although the cohort under study is relatively large, there are very few cases of bone and thyroid cancer, and therefore interpretation of results should be made with caution.

A cohort study investigating cancer incidence and occupational exposure to ionising radiation was conducted in Canada from 1969 to 1988 (Sont *et al,* 2001). The study used a smaller cohort to that of the mortality study described above by Ashmore. Individuals who had no exposure data after 1969 (the first year incidence data is available) were excluded. The cohort consisted of 191,333 individuals (95,643 males and 95,690 females) who had one or more dose records in the National Dose Registry between January 1969 and December 1983. Again individuals were linked with the Canadian Cancer Data Base, for incidence follow-up through 1988. In total 3,737 cases of cancer (2,098 males and 1,639 females) were recorded. Standardised incidence ratios were calculated using Canadian cancer incidence rates stratified by age, sex and calendar year. For bone cancer there were non-significant deficits found for males (SIR=0.70, 90% CI=0.38-1.19, n=10), females (SIR=0.69, 90% CI=0.30-1.35, n=6) and both combined (SIR=0.70, 90% CI=0.44-1.06, n=16). There was an elevated risk of thyroid cancer in the cohort which was of borderline significance for males (SIR=1.32, 90% CI=0.97-1.75, n=35), and highly significant for females (SIR=1.42, 90% CI=1.19-1.69, n=94), and male and females combined (SIR=1.39, 90% CI=1.20-1.61, n=129). The author notes that the excess risks observed for thyroid cancer is mainly due to the medical workers. They give a possible explanation for this as the effects of whole body doses, internal doses from radioisotopes and other risk factors not related to radiation. The conclusion given is that further investigation is needed to assess the association between thyroid cancer incidence and occupational radiation exposure.

Kendall *et al.* (1992) undertook a cohort study on 95,217 radiation workers in the UK. The National Registry for Radiation Workers was used to identify individuals who were employed in radiation

work. Generally the follow-up was until December 1988. However, if individuals had left employment before the study began and had been included in a previous study, the previously published follow-up date was used. Personal data and radiation dose histories were collected from employer records. Follow-up information was primarily obtained from the National Health Service Central Registers, as well as the records branch of the Department of Social Security. The authors conducted two types of analysis on the cohort. The first was an external analysis, producing standardised mortality ratios, using the general population of England and Wales for reference. The second was an internal analysis, to investigate dose-response relationships. Standardised mortality ratios were adjusted for age, calendar year and sex. No confidence intervals were published; instead, significance was indicated based on the p-value. In addition, two results were reported, for an unlagged analysis and a lagged (i.e. excluding the most recent 10 years exposure) analysis resulting from including a ten-year latency period. For bone cancer the risk was not elevated or significant in either external analysis (unlagged: SMR=70, n=6 and lagged: SMR=68, n=3). In contrast, there were significantly elevated risk estimates found for thyroid cancer in both the unlagged analysis (SMR=214, n=9, $p<0.05$) and the lagged analysis (SMR=303, n=9, $p<0.01$). Results from the internal analysis also included a ten-year latency period and were adjusted for age, calendar period, sex, industrial classification and first employer. There was a negative dose trend reported for bone cancer; however, this was non-significant (p=0.19) and was based on 3 cases (2 cases with <10mSv exposure and 1 case each with 20-50mSv exposure). A positive trend was associated with thyroid cancer; again, this was non-significant (p=0.59) and based on 9 cases (4 cases with <10mSV exposure, 1 case with 10-20mSv, 20-50mSv and >400mSv exposure and 2 cases with 50-100mSv exposure). The authors note that there is strong evidence of a healthy worker effect in this study, and the observed significant excess risk of thyroid cancer may be due to chance since there is no detectable trend with recorded radiation dose.

A second analysis of the National Registry for Radiation Workers was published in 1999 (Muirhead *et al,* 1999). This analysis used an enlarged cohort of 124,743 workers, updated dosimetry and personal data and longer follow-up through 1992. The methods for obtaining estimates were similar to those used in the first analysis. In this further follow-up mortality from bone cancer remained below that expected in the unlagged analysis (SMR=75, 95% CI=36-138, n=10) and the lagged analysis (SMR=52, 95% CI=14-134, n=4). Risk of thyroid cancer continued to be elevated; however, results were now non-significant (unlagged: SMR=152, 95% CI=79-266, n=12 and lagged: SMR=180, 95% CI=90-321, n=11). In the internal analysis, there was a non-significant negative dose trend for bone cancer (p=0.28) from 4 deaths (3 with <10mSv exposure and 1 with 20-50mSv exposure). There was also a non-significant positive trend associated with thyroid cancer (p=0.31) as found in the first analysis, from 11 deaths (4 with <10mSv exposure, 2 with 10-20mSv and 50-100mSv exposure and 1 with 20-50mSv, 100-200mSv and >400mSv exposure).

2.1.4 Industry Workers

In 2000, a mortality study of 2,514 white male workers at a US uranium processing plant was published (Dupree-Ellis *et al,* 2000). Individuals who were employed between 1942 and 1966 at Mallinckrodt Chemical Works were identified through plant records. Individual exposure was monitored via film badges. Vital status through 1993 was obtained using Social Security Administration, Pension Benefit Information and the National Death Index Database. The underlying cause of death was used to calculate standardised mortality ratios. US white males were used for comparison. Estimates were adjusted for age and calendar period. No deaths from thyroid cancer were observed. There was 1 observed death from bone cancer resulting in an elevated SMR of 1.20 (95% CI=0.07-5.26). The authors note that this was a small cohort and there was an indication of the presence of a healthy worker effect, so results should be interpreted with caution.

Cardis *et al.* (1995) presented the results of an internationally combined analysis of mortality data from 95,673 workers monitored for external exposure to ionising radiation. Cohort studies of

nuclear industry workers that were published before 1989 and met specified criteria were included in the analysis. The chosen studies were conducted in the US, UK and Canada. The study population included individuals who were monitored for radiation exposure by the use of personal dosimeters and were employed for at least 6 months. Internal comparisons of mortality by level of external radiation dose were made. A latency of 10 years was used for analysis for both bone and thyroid cancer. Results were adjusted for sex, socio-economic status, study population, age and calendar period (in 5 year intervals). Overall, there were 11 deaths from bone cancer and 15 deaths from thyroid cancer. For bone cancer 10 individuals had a cumulative does of 0-10mSv and 1 individual had a cumulative dose of 20-50mSv. For thyroid cancer 10 individuals had cumulative dose of 0-10mSv, 2 individuals had cumulative dose of 10-20mSv and the remaining 3 individuals had a cumulative dose of 20-50mSv, 50-100mSv and 400+mSv. No evidence was found for an association between cumulative radiation dose and bone or thyroid cancer (1-sided p-value: 0.358 and 0.281 respectively). No risk estimates are given in the study, as confidence intervals were large and non-significant for most cancers. The authors note that the nature of the combined analysis could have resulted in a lack of power to detect risk. From the data provided in the published article it was possible to calculate risk estimates for both bone and thyroid cancer. Both cancers had an overall SMR of 1 (Bone: SMR=1, n=11, 95% CI=0.5-1.8 and Thyroid: SMR=1, n=15, 95% CI=0.6-1.7).

The mortality of all 14,327 people (11,604 men and 2,633 women) who were known to have been employed at the Sellafield plant of British Nuclear Fuels at any time between the opening of the site in 1947 and 1975 was studied through 1983 (Smith, Douglas 1986). Staff of British Nuclear Fuels searched personnel records in order to identify individuals who had ever worked at the Sellafield plant. Follow-up was primarily done through the National Health Service Central Register. Other sources of vital status were the records branch of the Department of Health and Social Security and the medical and pensions records of British Nuclear Fuels. Overall there were 2,277 deaths recorded, of which 572 were cancer deaths (2 bone and 2 thyroid). At the Sellafield plant, personal radiation dose records, from personal dosimeters, were kept for all workers who entered controlled areas (where exposure to radiation was likely) frequently. Other workers who entered these controlled areas less frequently were also issued with dosimeters, but records were not kept for these individuals. These two subgroups are termed “radiation workers” and “other workers” respectively. In the following estimates the general population of England and Wales was used for reference. All estimates were adjusted for age, sex and calendar period. No confidence intervals were published with the results; instead, significance was based on the p-value. No significant results were recorded for bone cancer or thyroid cancer. Bone cancer was elevated in “other workers” (SMR=122, n=1) but not for “radiation workers” (SMR=56, n=1) or “all workers” (SMR=76, n=2). Thyroid cancer was elevated for “all workers” (SMR=153, n=2). Both cases of thyroid cancer occurred in “radiation workers” which also resulted in an elevated estimate (SMR=241, n=2). A further analysis of this cohort was conducted by Omar *et al.* (1999), which extended the follow-up period through 1992. For this update cancer incidence and mortality from 1971 to 1986 were investigated. Individuals who had ever been monitored for plutonium exposure, via urine samples, were also analysed as a separate group to those monitored for radiation exposure. There were 2 observed deaths from bone cancer, 1 in radiation workers and 1 in non-radiation workers, yielding non-significant SMRs of 81 and 98 respectively. The resulting rate ratio of radiation exposure vs. non-radiation exposure was 1.12 and was non-significant. There was 1 case of bone cancer identified, which occurred among the radiation workers, resulting in a non-significantly elevated SRR of 166. There were 6 deaths from thyroid cancer, 1 plutonium worker, 3 radiation workers and 2 non-radiation workers. The overall SMR was significantly elevated (SMR=278, n=6, $p<0.05$), and also significantly elevated in the radiation workers (SMR=429, n=3, $p<0.05$), but not in the plutonium workers (SMR=150, n=1) or non-radiation workers (SMR=253, n=2). The corresponding rate ratios for plutonium vs. radiation workers and radiation workers vs. non-radiation workers were 0.28 and 2.45 respectively, and neither were significant. There were 3

observed cases of thyroid cancer, all occurring among the radiation workers, resulting in a significantly elevated SRR of 371 (p-value<0.05).

Mortality during 1946-1988 was analysed in 75,006 employees of three United Kingdom Nuclear Industry Workforces (Carpenter *et al,* 1994). Individuals were employed by the Atomic Energy Authority prior to 1980, the Atomic Weapons Establishment prior to 1983 and employed at the Sellafield plant of British Nuclear Fuels Limited prior to 1976. Employment histories for all three workforces were updated to the end of 1986. Follow-up was conducted through 1988 via the National Health Service central registers, the Department of Social Security and company records. For individuals that had died death certificates were obtained. Data on external radiation dose were obtained from records held by the three industries. In the analysis, "monitored workers" refers to employees for whom personal dose records were maintained (N=40,761). The general population of England and Wales was used for reference. Estimates were adjusted for age, sex and calendar year. Internal analysis were also conducted to compare monitored workers to non-monitored workers and to investigate dose-response relationships. These estimates were further adjusted for establishment and social class. Although standardised mortality ratios for bone cancer were below 100 for monitored workers (SMR=79, n=6), other workers (SMR=41, n=3) and all workers (SMR=60, n=9), the rate ratio for monitored workers compared to non-monitored workers was elevated (RR=2.74, 95% CI=0.68-11.81). Mortality from thyroid cancer was elevated in all three groups with SMRs of 188 (95% CI=81-369, n=8), 176 (95% CI=81-334, n=9) and 181 (95% CI=106-290, n=17, p<0.05) for monitored, other and all workers respectively. The corresponding rate ratio was also elevated but did not reach statistical significance (RR=1.18, 95% CI=0.37-3.77). There were no significant dose trends discovered for bone or thyroid cancer, in either an unlagged analysis or a lagged analysis using a ten-year latency period. However, further analyses suggested a dose-response relationship with thyroid cancer after a twenty-year latency period (p=0.02, full results not shown).

A further paper was published in 1998 based on the monitored workers (Carpenter *et al,* 1998). Follow-up and analysis was conducted as described in the previous report. This analysis concentrated on particular exposures that were monitored (tritium, plutonium and other radionuclides). Individuals that were not monitored for exposure to any radionuclide were used for reference in the internal analysis. There were 4 observed deaths from bone cancer in the internal reference group (SMR=83). Of those monitored for radionuclides elevated SMRs of 181 (n=1), 100 (n=2) and 142 (n=2) were observed for tritium, plutonium and other respectively. Rate ratios were found to be elevated but not significantly (tritium: RR=1.31, 95% CI=0.05-14.71, plutonium: RR=1.01, 95% CI=0.12-7.35 and other: RR=2.07, 95% CI=0.21-18.61). There were no thyroid deaths in the tritium and other radionuclides subgroups, and only 1 observed death in the plutonium subgroup (SMR=85). A significantly elevated SMR of 269 (n=7, p<0.05) for thyroid cancer was observed in the internal reference group, resulting in a significantly lower rate ratio (RR=0.15, 95% CI=0.01-0.89) for the group monitored for plutonium.

Atkinson *et al.* (2004) conducted a mortality analysis of employees of the United Kingdom Atomic Energy Authority (UKAEA). The cohort consisted of 51,367 employees who were followed up from January 1946 until December 1997. The study includes all employees who had ever worked at Culham, Dounreay, Harwell, London or Winfrith between 1946 and 1996, and employees at Risley and Culcheth recruited between 1965 and 1996. Vital status and cause of death (where applicable) were obtained from the National Health Service central registers, Pensions Administration Office and the Department of Social Security mortality Study Service. Individuals who have been issued routinely with a dosimeter and have maintained records are termed "radiation workers" in the results. All occupational radiation doses incurred before 1996 are considered in the analysis. Standardised mortality ratios are adjusted for age sex and calendar year, using mortality rates for England and Wales for reference. Mortality rate ratios were used to compare mortality in radiation workers to that of non-radiation workers. Rate ratios were further adjusted for social class and last

UKAEA establishment. No results for bone cancer are presented. Overall, there were 11 deaths due to thyroid cancer resulting in an elevated SMR of 152 (95% CI=75.8-272.1), which was elevated among female workers (SMR=160, 95% CI=43.0-409.0, n=4); no results for male workers were given. Increased risk of death from thyroid cancer was observed among the non-radiation workers (SMR=188, 95% CI=75.3-387.3, n=7) and the radiation workers (SMR=114, 95% CI=30.7-291.7, n=4), this resulted in a low rate ratio of 0.83 (95% CI=0.18-3.28). In terms of dose, there was no observed trend (p=0.65), but this was based on small numbers (2 deaths with 20-50mSv exposure and 1 with 50-100mSv and >100mSv exposure). The authors note that there may be a healthy worker effect in this cohort.

A retrospective follow-up of 5,657 employees of the former Spanish Nuclear Energy Board (JEN) found an excess mortality risk for bone cancer (Rodriguez Artalejo *et al,* 1997). All individuals in the study had been in the boards' direct employment for over six months between January 1954 and January 1993. Follow-up of each worker began six months after employment began through 1992. Information on cancer incidence and individual dosimetry was collected from JEN's records. Individual exposure to ionising radiation exposure was available from 1954 to 1992. Standardised mortality ratios were produced using the Spanish population for reference, adjusting for sex, age and calendar period. Analysis was conducted on the whole JEN cohort and three sub-cohorts (employees of the Madrid facilities, JEN miners and JEN non-miners). These sub-cohorts are not exclusive (a JEN miner/non-miner can be employed at a Madrid facility). No results for thyroid cancer are presented. For the cohort as a whole, death from bone tumours gave a significantly increased risk (SMR=2.95, 95% CI=1.08-6.43, n=6). In the sub-cohorts, this excess continued to be present but did not reach significance (Madrid: SMR=3.36, 95% CI=0.67-9.81, n=3, miner: SMR=4.39, 95% CI=0.88-12.84, n=3 and non-miner: SMR=2.22, 95% CI=0.45-6.50, n=3). The authors note that the elevated risk observed for bone cancer is based on few numbers and further follow-up should be done to confirm the excess.

Telle-Lamberton *et al.* (2007) conducted a cohort study to analyse the effect external radiation exposure had on the mortality of French nuclear workers. The cohort included 29,204 workers who were employed for at least one year between 1950 and 1994 at the French Atomic Energy Commission (in CEA or Cogema). All individuals were monitored for external radiation after 1956 and records were held in the centralised dosimetry archives. Information on subjects was obtained from personnel files, vital status was ascertained from the municipality of birth and cause of death was obtained from the national cause of death registry. Follow-up of the cohort was the period 1968-1994 because data from the national registry of causes of death is not available prior to 1968. The mortality observed in the cohort was compared to that expected from national mortality rates. Estimates were adjusted for sex, age and calendar year. In the follow-up period there were 5 observed deaths from bone cancer (SMR=0.65, 90% CI=0.26-1.36) and 1 death from thyroid cancer (SMR=0.36, 90% CI=0.00-2.00). For bone cancer 3 deaths had recorded exposure <5mSv and 2 had recorded exposure between 5 and 49mSv, this resulted in no dose trend being observed (p=0.62), after introducing a ten year latency period and further adjusting for socioeconomic status, duration of employment and company. The authors note that there was a healthy worker effect present in this cohort.

2.1.5 Other Workers

Cancer incidence among radiologic technologists in the US was conducted for the follow-up period 1983-1998 (Sigurdson *et al,* 2003). The cohort consisted of 90,305 radiologic technologists (69,524 males and 20,781 females) who were listed on the American Registry of Radiologic Technologists. Individuals were included if they were registered for 2 years or more over the period 1962-1982 and resided in the US or one of its territories. Questionnaires were sent to participants collecting information on work history, radiation protection methods, lifestyle characteristics, demographic factors and health outcomes (including cancer occurrence). If individuals died during follow-up,

cause of death was ascertained from death certificates or the National Death Index. To confirm reported cancer cases, medical records from the diagnosing physician or hospital were obtained. Cancer incidence rates from the Surveillance, Epidemiology and End Results Program of the National Cancer Institute were used for reference. Estimates were adjusted for five-year age group, gender, race and five-year calendar period. The observed excess from cancer of the bones and joints was non-significant (SIR=1.11, 95% CI=0.39-2.48, n=6) and only present in males (SIR=1.71, 95% CI=0.28-5.47, n=3, females: SIR=0.86, 95% CI=0.18-2.48, n=3). A significantly elevated risk of thyroid cancer were found with SIR=1.61 (95% CI=1.34-1.88, n=124), which persisted among both males (SIR=2.23, 95% CI=1.29-3.59, n=17) and females (SIR=1.54, 95% CI=1.24-1.83, n=107). The authors note that 40% of the cohort started working as a radiologic technologist before the age of 20, which may be a vulnerable age for radiation exposure and thyroid cancer. However, further analysis controlling for age at first employment, did not alter results (estimates not given). They concluded that the observed excess of thyroid cancer may reflect, at least in part, earlier detection of tumours among medical workers who have easy access to health care.

Cancer incidence among medical diagnostic x-ray workers in China was reported in 1988 (Wang *et al,* 1988). Overall 27,011 diagnostic x-ray workers were compared to 25,782 other medical specialists employed between 1950 and 1980 in major hospitals. The radiation workers included both radiologists and technicians. The comparison population consisted of surgeons, physicians and otolaryngologists who worked in the same hospitals during the same period but did not use x-ray equipment. The follow-up period was from January 1950 through December 1980. Rate ratio (RR) estimates were adjusted for age, calendar year and sex. No numerical confidence intervals were published. Incidence of bone cancer was significantly elevated with RR=9.56 (n=5, $p<0.05$), this excess was observed in the three categories of employment duration for which cases were observed (<5years: RR=10.0, n=1, 5-9years: RR=13.6, n=3, $p<0.05$ and 10-14years: RR=6.7, n=1). By calendar year of first employment elevated risks of bone cancer were observed for <1950-1959 (RR=3.57, n=1) and 1960-1969 (RR=4.17, n=1). Incidence of thyroid cancer was elevated with RR=2.14 (n=7), this excess was observed in the three categories of employment duration for which cases were observed (5-9years: RR=3.7, n=2, 10-14years: RR=4.7, n=2, $p<0.05$ and 15-19years: RR=2.5, n=2). By calendar year of first employment significant risk of thyroid cancer was observed for <1950-1959 (RR=2.84, n=4, $p<0.05$) and elevated risks for 1960-1969 (RR=1.64, n=2) and 1970-1980 (RR=1.56, n=1). The authors concluded that repeated exposure to radiation over many years increased the occurrence of cancer of the thyroid. They also stated due to the low number of cases of bone cancer, the observed excess may be a chance finding but an association cannot be discounted, and due to the relative low age of the cohort the follow-up may not be long enough to adequately evaluate exposure impact. Unfortunately, individual dosimetry readings were not collected and this limits the study in terms of risk quantification, as duration of employment was used as a surrogate for radiation dose.

The most recent follow-up through 1995 was published in 2002 (Wang, *et al,* 2002). Since individual dose monitoring was not available prior to 1985, a mathematical model and computerised system was used to reconstruct average annual doses for each year up to 1985. Overall, there were 15 cases of bone cancer reported; unfortunately, no numerical risk estimates are published. There were 14 cases of thyroid cancer resulting in an elevated RR of 1.58 (95% CI=0.9-2.6). The thyroid cases were split evenly between males (RR=1.96, n=7) and females (RR=1.33, n=7). To investigate the changes in equipment, procedures and protection over time, the cohort was divided into two. Cohort I contained individuals who were employed before 1970 and cohort II contained individuals who were employed between 1970 and 1980. The risk of thyroid cancer was only significantly raised in the first cohort (RR=2.06, n=13, $p<0.05$) and appeared reduced in the second cohort (RR=0.39, n=1). In the earlier cohort the highest risk was seen among those who started work under 20 years (RR=3.23, n=2) or 25 years (RR=3.29, n=8, $p<0.05$) of age, which persisted among the whole cohort (under 20: RR=3.08, n=2 and 20-25 years: RR=2.92, n=8, $p<0.05$). The authors conclude that occupational exposure to X-rays may increase the risk of

thyroid cancer, however this excess only appeared in cohort I, which may relate to larger doses in earlier years and short latency of the disease, resulting in a large risk no longer being evident.

2.1.6 Exposed Veterans

Darby *et al.* (1988) conducted a mortality case-control analysis of men who participated in the United Kingdom's atmospheric nuclear weapons tests and experimental programmes in Australia and the Pacific Ocean. Individuals who participated between 1952 and 1967 were identified from the archives of the Ministry of Defence, and were followed through 1983. From the archives 22,326 controls were chosen matched by age, type of armed service, rank and date of entry to the study. Controls were servicemen who did not participate in the weapon test programme but had served in tropical or subtropical areas during the test period. Three sources of information were used to ascertain vital status; these were the National Health Service central registers, the Department of Health and Social Security records and the Medical Research Council's Epidemiological Monitoring Unit. Standardised mortality ratios were calculated for both cases and controls, using national mortality statistics as a reference. Estimates were adjusted for age and calendar year. In addition, relative risks were also calculated to compare mortality of cases and controls. Estimates were adjusted for age, calendar year, armed service and rank. For bone cancer there were non-significant deficits in the SMRs of 63 (n=2) and 33 (n=1) for cases and controls respectively. The corresponding risk ratio was elevated but not significantly (RR=1.34, 90% CI=0.09-31.38). For thyroid cancer, the results were similar. There were non-significant deficits for cases and controls (SMR=92, n=1 and SMR=90, n=1 respectively) and the relative risk was close to that expected (RR=1.01, 90% CI=0.04-27.70). The authors note that individuals who served in the tropics and subtropics had been selected to do so due to their physical fitness, which could have a substantial effect on mortality.

The first extended follow-up of this cohort was published in 1993 (Darby *et al,* 1993). The follow-up was extended by 7 years until 1990. The updated analysis was conducted on 21,358 cases (1,503 cases from the previous analysis were excluded as it was unlikely they had been exposed to excess radiation, and others were included that had been discovered in archival material), and 22,333 controls. Standardised mortality ratios and risk ratios were calculated as before, however, estimates were lagged by 10 years to account for possible latency. No more deaths from bone cancer were observed, resulting in risk estimates being reduced (cases: SMR=0.42, n=1, controls: SMR=0.41, n=1 and RR=1.07, 90% CI=0.04-29.19). After introducing the ten-year latency period, only 1 thyroid cancer was observed; this was in the control group, thus no risk estimate for exposure could be calculated.

Muirhead *et al.* (2003) conducted the second extended follow-up of this cohort. The follow-up period was extended a further 8 years through 1998. The same study population was used as the first update and estimates were calculated similarly, including the ten-year latency period. In this follow-up the deficits in the SMRs persist (bone: 2 cases SMR=61, 1 control SMR=30 and thyroid: 1 case SMR=37, 1 control SMR=35), with an elevated RR for bone cancer (RR=2.11, 90% CI=0.19-44.14) and an RR of 1 (90% CI=0.04-27.44) for thyroid cancer. Muirhead *et al.* also investigated cancer incidence in this further follow-up and found excesses in risk for both bone cancer (RR=1.16, 90% CI=0.35-3.86, 5 cases, 5 controls) and thyroid cancer (RR=1.92, 90% CI=0.51-7.97, 6 cases, 3 controls).

2.1.7 Commercial Airline Crew

A record linkage cancer incidence study was conducted amongst 1,577 female and 187 male cabin attendants who had worked for a Finnish airline company (Pukkala *et al,* 1995). Recruitment for the study started in the late 1940s with the cancer follow-up being from 1967 until 1992. Length of employment was recorded from the files of the Finnair Flight Company. A unique personal

identification number given to all residents in Finland since 1967 was used to ascertain cancer incidence from the Finnish cancer registry. Standardised incidence ratios were calculated, adjusted for age, sex and period, using national cancer incidences as reference. A non-significant deficit for thyroid cancer was observed (SIR=0.62, 95% CI=0.02-3.42, n=1). A significantly elevated risk was observed for bone cancer incidence (SIR=15.1, 95% CI=1.82-54.4, n=2). The authors state that due to the small numbers of bone cancer, although the estimate is significant the result may be due to chance.

A retrospective cohort study was conducted in order to describe the cancer pattern of commercial pilots using follow-up through the Icelandic Cancer Registry (Rafnsson *et al,* 2000). The cohort comprised of 458 men who were all licensed commercial pilots in Iceland according to the computerised files from the Icelandic Aviation Authority. Of these, 265 pilots had been employed by Icelandair; the study is primarily restricted to these individuals. For all employees, after 1985 there was information on the type of aeroplane and number of block hours flown each year. The personal identification number of each individual was used for linkage to the National Registry and the Icelandic Cancer Registry. Follow-up started in 1955 and ended in 1997 with a time lag of 5 years. The reference group used was the male population of Iceland. Risk estimates were adjusted for age. Among the whole cohort (458 pilots) there was 1 observed case of thyroid cancer resulting in an increased SIR estimate of 1.49 (95% CI=0.02-8.30). This case occurred in the smaller sub-cohort (SIR=2.27, 95% CI=0.03-12.64). No results for bone cancer were given. The authors note that the study is small resulting in wide confidence intervals, possibly handicapping the study.

Pukkala *et al.* (2002) studied the incidence of cancer among Nordic airline pilots, specifically focusing on the relation to cosmic radiation. National cohorts of airline pilots were identified from registers in Denmark, Finland, Iceland, Norway and Sweden. In Denmark all members of commercial cockpit crews on file since 1946 in the National Clinic of Aviation Medicine were enrolled (3,790 men), along with 793 male pilots from Finland flying for Finnair up to 1996, and 239 men who were commercial pilots in Iceland. In Norway there were 3,752 male commercial pilots who held a valid licence between January 1946 and February 1994 and in Sweden there were 1,478 male aircraft pilots of the Scandinavian Airline System employed between 1957 and 1994. This cohort overlaps with the cohorts of Pukkala *et al.* (1995), Rafnsson *et al.* (2000) and Blettner *et al.* (2003). The cohorts were linked to the national population registers and cancer registries. The cancer follow-up period varied for each country (Denmark: 1943-1996, Finland: 1953-1997, Iceland: 1984-1997, Norway: 1962-1996 and Sweden: 1961-1996). The flight histories of the pilots, before the cancer follow-up period, were also taken into account when evaluating exposure to radiation. National cancer rates were used for reference and estimates were adjusted for age and period. In total there were 10,032 men undergoing follow-up, of which 3 cases of thyroid cancer were observed. No cases of bone cancer were observed. There was a reduced risk estimate for thyroid cancer of 0.88 (95% CI=0.18-2.58). However, the risk increased slightly with increasing estimated exposure to radiation during flight (p=0.54) with SIRs of 1.42 for 1-2999μSv (95% CI=0.17-5.14, n=2) and 1.63 for 10000-19999μSv (95% CI=0.04-9.10, n=1).

Blettner *et al.* (2003) analysed cancer mortality among male airline cockpit crew from Denmark, Finland, Germany, Great Britain, Greece, Iceland, Italy, Norway and Sweden; this study overlaps with the study by Pukkala *et al.* (2002). Follow-up was carried out through centralised or local population registries. Deaths for the period 1960-1997 were compared based on national mortality rates. Risk estimates were adjusted for age, period and country. In total there were 27,797 male cockpit crew members resulting in 2,251 deaths, of which 5 were from thyroid or other endocrine cancer. No results for bone cancer were provided. Mortality from thyroid and other endocrine cancer was increased (SMR=1.48, 95% CI=0.47-3.48). The authors note that there is a strong healthy worker effect present and information on potential confounders, such as smoking and recreational UV exposure was not available.

Table 11 Summary of reviewed papers

Reference	Data/Exposure Source	Country	Type of Study	Follow-up	Study Size	Exposure Assessment	Bone Cancer	Thyroid Cancer	Adjusted For	Over-lap
Population Studies										
Fincham *et al.* (2000)	Occupation	Canada	Case Control	1986-1988	1,272 Cases 2,666 Controls	Self-reported Job title	None	65 Cases 95 Controls OR=1.03	Age Sex Smoking	Ashmore *et al.* (1998) Sont *et al.* (2001)
Robinson *et al.* (1999)	Occupation	US	Cohort Mortality	1984-1995	458,690 F	None	None	23 Health Service PCMR=194 6 Therapist PCMR=820	Race Age	None
Registry Studies										
Ashmore *et al.* (1998)	National Dose Registry	Canada	Cohort Mortality	1951-1987	206,620 105,456 M 101,164 F	Dosimeter	3 M SMR=0.362 4 F SMR=1.141	5 M SMR=1.492 0 F	Age Period	Fincham *et al.* (2000) Sont *et al.* (2001)
Sont *et al.* (2001)	National Dose Registry	Canada	Cohort Incidence	1969-1988	191,333 95,643 M 95,690 F	Dosimeter	16 Total SIR=0.70 10 M SIR=0.70 6 F SIR=0.69	129 Total SIR=1.39 35 M SIR=1.32 94 F SIR=1.42	Age Sex Year	Fincham *et al.* (2000) Ashmore *et al.* (1998)
Kendall *et al.* (1992)	National Registry for Radiation Workers	UK	Cohort Mortality	1976-1988	95,217	Company records (Dosimeter)	6 Total SMR=70 3 10yr lag SMR=68	9 Total SMR=214 9 10yr lag SMR=303	Age Sex Year	Muirhead *et al.* (1999) Cardis *et al.* (1995) Smith *et al.* (1986) Omar *et al.* (1999) Carpenter *et al.* (1994) and (1998) Atkinson *et al.* (2004)
Muirhead *et al.* (1999)	National Registry for Radiation Workers	UK	Cohort Mortality	1976-1992	124,743	Company records (Dosimeter)	10 Total SMR=75 4 10yr lag SMR=52	12 Total SMR=152 11 10yr lag SMR=180	Age Sex Year	Kendall *et al.* (1992) Cardis *et al.* (1995) Smith *et al.* (1986) Omar *et al.* (1999) Carpenter *et al.* (1994) and (1998) Atkinson *et al.* (2004)
Industry Workers										
Dupree-Ellis *et al.* (2000)	Uranium processing plant	US	Cohort Mortality	1942-1993	2,514 M	Film badges	1 M SMR=1.20	None	Age Period	None

Reference	Data/Exposure Source	Country	Type of Study	Follow-up	Study Size	Exposure Assessment	Bone Cancer	Thyroid Cancer	Adjusted For	Over-lap
Cardis *et al.* (1995)	Nuclear Industry Workers	US UK Canada	Cohort Mortality	1943-1988	95,673 81,745 M 13,928 F	Dosimeter	11 Total Calculated SMR=1	15 Total Calculated SMR=1	Age Sex Period Socio-economic status Study population 10yr lag	Kendall *et al.* (1992) Muirhead *et al.* (1999) Smith *et al.* (1986) Omar *et al.* (1999) Carpenter at al. (1994) and (1998) Atkinson *et al.* (2004)
Smith *et al.* (1986)	Sellafield plant	UK	Cohort Mortality	1947-1983	14327 11,604 M 2,633 F	Dosimeter	2 Total SMR=76 1 Radiation SMR=56 1 Other SMR=122	2 Total SMR=153 2 Radiation SMR=241	Age Sex Period	Kendall *et al.* (1992) Muirhead *et al.* (1999) Cardis *et al.* (1995) Omar *et al.* (1999) Carpenter *et al.* (1994) and (1998)
Omar *et al.* (1999)	Sellafield plant	UK	Cohort Mortality Incidence	1947-1992 1971-1986	14327 11,604 M 2,633 F	Dosimeter	1 Radiation SMR=81 1 Non-Radiation SMR=98 RR=1.12 (Rad Vs Non) 1 Radiation SRR=166	6 Total SMR=278 1 Plutonium SMR=150 3 Radiation SMR=429 2 Non-Radiation SMR=253 RR=0.28 (Plut Vs Rad) RR=2.45 (Rad Vs Non) 3 Radiation SRR=371	Age Sex Period	Kendall *et al.* (1992) Muirhead *et al.* (1999) Cardis *et al.* (1995) Smith *et al.* (1986) Carpenter at al. (1994) and (1998)
Carpenter *et al.* (1994)	Nuclear Industry Workforces	UK	Cohort Mortality	1946-1988	75,006	Company records (Dosimeter)	9 Total SMR=60 6 Monitored SMR=79 3 Other SMR=41 RR=2.74 (Mon Vs Other)	17 Total SMR=181 8 Monitored SMR=188 9 Other SMR=176 RR=1.18 (Mon Vs Other)	Age Sex Year Establishment Class	Kendall *et al.* (1992) Muirhead *et al.* (1999) Cardis *et al.* (1995) Smith *et al.* (1986) Omar *et al.* (1999) Carpenter at al. (1998) Atkinson *et al.* (2004)
Carpenter *et al.* (1998)	Nuclear Industry Workforces	UK	Cohort Mortality	1946-1989	75,006	Company records (Dosimeter)	4 Reference SMR=83 1 Tritium SMR=181 2 Plutonium SMR=100 2 Other SMR=142 RR=1.31 (Tri Vs Ref) RR=1.01 (Plut Vs Ref) RR=2.07 (Other Vs Ref)	7 Reference SMR=269 1 Plutonium SMR=85 RR=0.15 (Plut Vs Ref)	Age Sex Year Establishment Class	Kendall *et al.* (1992) Muirhead *et al.* (1999) Cardis *et al.* (1995) Smith *et al.* (1986) Omar *et al.* (1999) Carpenter *et al.* (1994) Atkinson *et al.* (2004)
Atkinson *et al.* (2004)	Atomic Energy Authority	UK	Cohort Mortality	1946-1997	51,367	Dosimeter	None	11 Total SMR=152 4 F SMR=160 4 Radiation SMR=114	Age Sex Year	Kendall *et al.* (1992) Muirhead *et al.* (1999) Cardis *et al.* (1995)

Reference	Data/Exposure Source	Country	Type of Study	Follow-up	Study Size	Exposure Assessment	Bone Cancer	Thyroid Cancer	Adjusted For	Over-lap
								7 Non-Radiation SMR=188 RR=0.83 (Rad Vs Non)	Establishment Class	Carpenter at al. (1994) and (1998)
Rodriguez Artalejo *et al.* (1997)	Nuclear Energy Board	Spain	Cohort Mortality	1954-1992	5,657	Dosimeter	6 Total SMR=2.95 3 Madrid SMR=3.36 3 Miner SMR=4.39 3 Non-Miner SMR=2.22	None	Sex Age Period	None
Telle-Lamberton *et al.* (2007)	Nuclear Workers	France	Cohort Mortality	1968-1994	29,204	Dosimeter	5 Total SMR=0.65	1 Total SMR=0.36	Age Sex Year	None
Other workers										
Sigurdson *et al.* (2003)	Radiologic technologists	US`	Cohort Incidence	1983-1998	90,305 69,524 M 20,781 F	Self-reported	6 Total SIR=1.11 3 M SIR=1.71 3 F SIR=0.86	124 Total SIR=1.61 17 M SIR=2.23 107 F SIR=1.54	Age Sex Race Period	None
Wang *et al.* (1988)	Medical diagnostic X-ray workers	China	Cohort Incidence	1950-1980	27,011 X-ray workers 25,782 Other workers	None	5 Total RR=9.56	7 Total RR=2.14	Age Sex Year	Wang *et al.* (2002)
Wang *et al.* (2002)	Medical diagnostic X-ray workers	China	Cohort Incidence	1950-1995	27,011 X-ray workers 25,782 Other workers	Pre 1985: dose reconstruction models Post 1985: Dosimeter	15 Total (No numerical estimate published)	14 Total RR=1.58 7 M RR=1.96 7 F RR=1.33 Pre 1970: 13 Total RR=2.06 Post 1970: 1 Total RR=0.39	Age Sex Year	Wang *et al.* (1988)
Exposed Veterans										
Darby *et al.* (1988)	Nuclear weapons test	UK	Case Control Mortality	1952-1983	22,347 M Cases 22,326 Controls	None	2 Cases SMR=63 1 Control SMR=33 RR=1.34	1 Case SMR=92 1 Control SMR=90 RR=1.01	Age Year Service Rank	Darby *et al.* (1993) Muirhead *et al.* (2003)
Darby *et al.* (1993)	Nuclear weapons test	UK	Case Control Mortality	1952-1990	21,358 Cases 22,333 Controls	None	1 Case SMR=0.42 1 Control SMR=0.41 RR=1.07	1 Control SMR=0.60	Age Year Service Rank 10yr lag	Darby *et al.* (1988) Muirhead *et al.* (2003)
Muirhead *et al.*	Nuclear weapons	UK	Case Control	1952-1998	21,358	None	2 Cases SMR=61	1 Case SMR=37	Age	Darby *et al.* (1988) and

Reference	Data/Exposure Source	Country	Type of Study	Follow-up	Study Size	Exposure Assessment	Bone Cancer	Thyroid Cancer	Adjusted For	Over-lap
(2003)	test		Mortality Incidence		Cases 22,333 Controls		1 Control SMR=30 RR=2.11 (Mortality) 5 Cases 5 Controls RR=1.16 (Incidence)	1 Control SMR=35 RR=1 (Mortality) 6 Cases 3 Controls RR=1.92 (Incidence)	Year Service Rank 10yr lag	(1993)
Aircraft Personnel										
Pukkala *et al.* (1995)	Finnair flight company	Finland	Cohort Incidence	1967-1992	187 M 1,577 F	None	2 Total SIR=15.1	1 Total SIR=0.62	Age Sex Period	Pukkala *et al.* (2002) Blettner b*et al.* (2003)
Rafnsson *et al.* (2000)	Commercial pilots (male)	Iceland	Cohort Incidence	1955-1997	458 M Total 265 M Icelandair	None	None	1 Total SIR=1.49 1 Icelandair SIR=2.27	Age	Pukkala *et al.* (2002) Blettner *et al.* (2003)
Pukkala *et al.* (2002)	Airline pilots (male)	Denmark Finland Iceland Norway Sweden	Cohort Incidence	1943-1996 1953-1997 1984-1997 1962-1996 1961-1996	3,790 M 793 M 239 M 3,752 M 1,478 M	None	None	3 Total SIR=0.88	Age Period	Pukkala *et al.* (1995) Rafnsson *et al.* (2000) Blettner *et al.* (2003)
Blettner *et al.* (2003)	Cockpit crew	Denmark Finland Germany GB Greece Iceland Italy Norway Sweden	Cohort Mortality	1960-1997	27,797 M	None	None	5 Total SMR=1.48 NB. Includes other endocrine cancer as well as thyroid cancer	Age Period Country	Pukkala *et al.* (1995) and (2002) Rafnsson *et al.* (2000)

3 ATTRIBUTABLE FRACTION ESTIMATION

3.1 GENERAL CONSIDERATIONS

Substances and Occupations

IARC have assessed the carcinogenicity of a number of substances and occupational circumstances with those classified as Group 1 being definite human carcinogens and those classified as Group 2A having being probable human carcinogens. Table 12 shows agents and exposure circumstances classified as Group 1 or 2A for bone cancer and thyroid cancer.

Table 12 Substances considered in the estimation of the attributable fraction for bone cancer and thyroid cancer

Agents, Mixture, Circumstance	AF calculation	Strength of evidence	Comments
Group 1: Carcinogenic to Humans			
Agents, groups of agents			
Ionising radiation	Yes	Strong	
Exposure circumstances			
None identified			
Group 2A: Probably Carcinogenic to Humans			
Agents & groups of agents			
None identified			
Exposure circumstances			
None identified			

Data Relevant to the Calculation of AF

The two data elements required are an estimate of relative risk (RR), and either (1) an estimate of the proportion of the population exposed (Pr(E)) from independent data for Great Britain, or (2) an estimate of the proportion of cases exposed (Pr(E|D)) from population based study data.

The RR chosen from a 'best study' source is described for each exposure, with justification of its suitability. Information on the 'best study' and independent data sources for the proportion of the population exposed are also summarised for each exposure in the appropriate section below. In the absence of more precise knowledge of cancer latency, for solid tumours a latency of up to 50 years and at least 10 years has been assumed for all types of the cancer. Therefore it is assumed that exposure at any time between 1956 and 1995 (the Risk Exposure Period, REP) can result in a cancer being recorded in 2004 as a registration or in 2005 as an underlying cause of death. Although strictly speaking the REP for cancer registrations recorded in 2004, the year for which estimation has been carried out, would be 1955-1994, for simplification the years 1956 to 1995 have also been used, as for deaths, as the proportion exposed will not be affected.

For an independent estimate of the proportion of the population exposed, numbers of workers ever exposed during this period are estimated by extrapolating from a point estimate of exposed workers taken from the period. If this is from CAREX relating to 1990-93, an adjustment is made to take account of gross changes in employment levels which have occurred particularly in manufacturing industry and the service sector across the REP. Otherwise a point estimate that represents numbers employed as close as possible to about 35 years before the target year of 2005 is used, as this is thought to represent a 'peak' latency for the solid tumours, and is also close to the mid-point of the REP for estimating numbers ever exposed across the period (for which a linear change in employment levels is implicitly assumed). Where the Census of Employment is used, the data are for 1971. Where the LFS is used, the first year available and therefore used is 1979. A turnover factor is applied to

estimate numbers ever exposed during the REP, determined mainly by the estimate of staff turnover per year during the period. For each exposure therefore, if an AF has been based on independent estimates of numbers exposed, the table of results includes the point estimate of numbers employed, the adjustment factor for CAREX if applicable, the staff turnover estimate, and the resulting estimate of numbers ever exposed during the REP. Other estimates used in the calculations that remain constant across exposures (unless otherwise stated) are given below:

- Number of years in REP = 40

- Proportion in the workplace ever exposed is set to one, i.e. all are assumed to be exposed, in the absence of more detailed information. Where sources other than CAREX are used for the point estimate of numbers exposed, such as the LFS or Census of Employment, a precise as possible definition of workers exposed is sought.

- Numbers ever of working age during the target REP = 19.4 million men, 21.0 million women. This is the denominator for the proportion of the population exposed, and is based on population estimates by age cohort in the target year.

- Total deaths from bone cancer in GB in 2005 = 133 for men aged 25+ (125 England and Wales and 8 Scotland), 100 for women aged 25+ (97 England and Wales and 3 Scotland).

- Total registrations for bone cancer in GB in 2004 = 188 for men aged 25+ (157 England, 17 Wales and 14 Scotland), 135 for women aged 25+ (116 England, 12 Wales and 7 Scotland).

- Total deaths from thyroid cancer in GB in 2005 = 106 for men aged 25+ (101 England and Wales and 5 Scotland), 231 for women aged 25+ (209 England and Wales and 22 Scotland).

- Total registrations for thyroid cancer in GB in 2004 = 419 for men aged 25+ (355 England, 25 Wales and 39 Scotland), 1100 for women aged 25+ (948 England, 46 Wales and 106 Scotland).

Attributable numbers are estimated by multiplying the AF by the total number of cancers in GB. Only cancers which could have been initiated during the risk exposure period are counted, taking normal retirement age into account. Therefore for solid tumour cancers, total deaths or registrations recorded at all adult ages (25+) are used to estimate attributable numbers, and for short latency cancers, deaths and registrations for ages 15-84 for men and 15-79 for women are used.

For each agent where data on worker numbers are only available for men and women combined (CAREX data), the assumed percentage of men is given in addition to the numbers exposed. The allocation to high and low, and occasionally negligible, exposure level categories, or division into separate exposure scenarios, is also included in these tables. Where no separate estimate of relative risk is available for the low exposure level category, an estimate is based on an average of the high/low ratios for cancer-exposure pairs for which data were available.

Full details of the derivation of the above factors and the methods of calculating AF are published separately. Unless otherwise stated, Levin's method is used for estimates using independent estimates of numbers exposed, and Miettinen's method is used for study based estimates. A summary of the methodology is given in the Statistical Appendix 6.1.

3.2 IONISING RADIATION

Occupational exposure to ionising radiation occurs in a number of occupations. Healthcare workers, especially radiographers and radiologists, nuclear workers and airline cabin crew are exposed. The risk for bone cancer and thyroid cancer caused by occupational exposure to ionising radiation may be difficult to estimate because individuals can be exposed to background radiation from solar radiation

and radon. Individuals may also be exposed to non-occupational radiation through diagnostic procedures and medical treatment. However, the majority of workers who are exposed to occupational ionising radiation are issued with personal dosimeters, and records of doses received and cumulative dose are held by employers. Through this information, epidemiological studies interested in the effects of occupational exposure tend to overcome the difficulty.

There is considerable overlap between the study cohorts described in Section 2.1. This overlap needs to be considered when choosing the most appropriate study and subsequent exposed numbers to be used for the AF calculation. For details on which of these studies overlap see Table 11.

Four of the more recent studies are follow-ups of previous studies (Omar *et al,* 1999 from Smith and Douglas, 1986; Muirhead *et al,* 2003 from Darbyl *et al,* 1988, 1993; Muirhead *et al,* 1999 from Kendall *et al,* 1992; Wang *et al,* 2002 from Wang *et al,*1988).

The UK National Registry for Radiation Workers includes information on British Nuclear Fuels plc (including the Sellafield plant), Ministry of Defence Atomic Weapons Establishment and UK Atomic Energy Authority. The studies by Carpenter *et al.* in 1994 and 1998 include sub-cohorts from all three of the radiation worker cohorts mentioned above. Workers from the British Nuclear Fuels plc Sellafield plant were specifically studied by Smith *et al.* (1986) and Omar *et al.* (1999) as were workers from the UK Atomic Energy Authority (Atkinson *et al,* 2004).

The two most recent studies on aircraft personnel (Pukkala *et al,* 2002; Blettner *et al,* 2003) overlap with the male cohorts from the other two studies (Pukkala *et al,* 1995; Rafnsson *et al,* 2000). Both studies include further recruitment periods and follow-up. The study conducted by Blettner includes the same five cohorts as Pukkala *et al.* (2002) from Denmark, Finland, Iceland, Norway and Sweden. Additional cohorts are included from Germany, Greece, Italy and the UK, making the Blettner study larger and possibly more informative than the Pukkala study.

(a) Risk Estimate for Bone Cancer:

Key Studies in GB

Due to the rarity of the disease, all the studies mentioned involve relatively low numbers (typically fewer than 6 cases). Occupational exposure from employment as a technologist appears to have an increased risk in the US (Sigurdson *et al,* 2003) and China (Wang *et al,* 1988). However, a study conducted on UK radiologists (Berrington *et al,* 2001) found no increased risk from bone cancer (results not published). In addition, there is limited evidence for an association of bone cancer in aircraft personnel. Only one study reported increased incidence with an SIR of 15.1 (Pukkala *et al,* 1995). More recent studies and follow-up do not report results for bone cancer (Rafnsson *et al,* 2000; Pukkala *et al,* 2002; Blettner *et al,* 2003).

From UK studies of radiation exposure in various jobs, it appears that not all radiation workers are at increased risk from bone cancer. The registry studies consistently show a reduced risk (Kendall *et al,* 1992; Muirhead *et al,* 1999), whereas the studies conducted on nuclear industry workforces show an elevated risk for incidence (Omar *et al,* 1999) and mortality (Carpenter *et al,* 1998). The paper published in 1998 by Carpenter was favoured as the best study as it was conducted on a larger cohort than the study by Omar (it includes all nuclear workforces in the UK as oppose to just Sellafield workers). Unfortunately, results are presented in terms of the different sources of exposure that have been monitored (tritium, plutonium and other radiation), and not for total radiation; information to derive the proportion of the GB population exposed is only available for total radiation.. A combined SMR, for all monitored workers, can be calculated based on the information provided in the paper giving an elevated SMR of 1.26 (95% CI=0.41-2.95, n=5) for all monitored nuclear industry workers.

Another study conducted a mortality analysis on 40,761 employees from three United Kingdom Nuclear Industry Workforces (Carpenter *et al,* 1998). All employees were monitored for exposure to

tritium, plutonium or other radiation sources. Data on external radiation dose were obtained from personal dose records held by the three industries. Individuals were employed by the Atomic Energy Authority prior to 1980, the Atomic Weapons Establishment prior to 1983 and employed at the Sellafield plant of British Nuclear Fuels Limited prior to 1976. Follow-up was conducted through 1988 via the National Health Service central registers, the Department of Social Security and company records. The general population of England and Wales was used for reference. The estimates produced were adjusted for age, sex and calendar year.

The UNSCEAR model

Airline cockpit crews are occupationally exposed to ionising radiation (IR) of cosmic origin. Radiation workers in the nuclear industry and medical and laboratory staff are the other principal group exposed. Strong non-occupational evidence of the carcinogenic potential of ionising radiation includes the 'Life Span Study', an ongoing study (45+ years) of the long-term health of survivors of the atomic bomb detonations at Hiroshima and Nagasaki (Japan) in 1945 (Pierce *et al.*, 1996; UNSCEAR, 2000). The most recent report from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2006) provides, for several cancer sites, models of excess relative risk (ERR) per unit of radiation dose, estimated as RR=1+ERR. The relative risks for occupational exposure to ionising radiation for bone cancer have been derived using these models; details of the model are described below.

From UNSCEAR 2006, Table 52, generalized ERR incidence model, quadratic dose response:

$ERR(a) = \beta . D^2 . \exp[\kappa_1 \ln([a]]$,

Where $\beta = 6.90379 \times 10^7$ Sv^{-2}

$\kappa_1 = -4.472$

From Table D10: Model Deviance = 236.222, df = 42,703

ERR is obtained as average ERR(a), averaged over a = 25-100 (long latency REP 1956-1995).

Dose was assumed to be an individual's cumulative dose received over the risk exposure period (REP) for each cancer (1956-1995 for the solid tumours). For workers exposed to ionising radiation, doses were estimated using data from the Central Index of Dose Information (CIDI, see below). To estimate lifetime dose from the CIDI data, the following procedure was used. Data on collective doses for the years 1990 to 2004 were used to estimate total collective dose for the REP, by assuming a constant 1990 rate prior to 1990 for the 1956-1995 REP. The estimated REP collective dose was then divided by an estimate of the numbers ever exposed to ionising radiation during the REP. These estimates were obtained by multiplying the CIDI point estimates of IR exposed workers (see below) by the employment turnover factors in Table A1 and by the number of years in the REP (40 for the solid tumours).

For aircrew who are not covered by the CIDI data, an estimate of lifetime dose from Langner, Blettner et al, 2004 was used. In a large seven country European cohort of airline pilots employed from the earliest days of air transport (1921, Finland to 1965, Italy) up to between 1994 and 1997, the mean total lifetime radiation dose per pilot for all pilots in the cohort was 15.3 mSv, (median 10.7 mSv, maximum 78.5 mSv). The annual mean dose rate of all active pilots was 2.96 μSv per block hour flying time, for an average of 7,031 block hours. Pilots in the cohort were employed for an average 14.6 years. The lifetime dose estimate of 15.3 mSv per worker is used to estimate ERR for aircrew.

ERR(a) was estimated for ages (a) that could be attained by workers in 2005 who had been exposed during the REP between the ages of 15 and 65 (an even distribution of ages from 15 to 65 in the exposed cohorts was assumed). ERR (all ages) was then obtained as the average across these ages. Standard errors were not available from the UNSCEAR data so no confidence intervals are given.

The RR estimate is 1.09 for men and women for ionising radiation exposed workers (excluding aircrew) (with an estimated average lifetime dose of 15.3 mSv) and the same for aircrew (also with an estimated average lifetime dose of 15.3 mSv).

(b) Risk Estimate for Thyroid Cancer:

Key Studies for GB

Occupational exposure from employment as a technologist appears to have an increased risk from thyroid cancer in the US (Sigurdson *et al,* 2003) and China (Wang *et al,* 1988; Wang *et al,* 2002). However, a study conducted on UK radiologists (Berrington *et al,* 2001) found no increased risk from thyroid cancer (results not published). In addition, there is conflicting evidence for an association of thyroid cancer in aircraft personnel, although these studies are based on few cases. Two studies reported increased risks (Rafnsson *et al,* 2000; Blettner *et al,* 2003) and two studies reported reduced risk estimates (Pukkala *et al,* 1995; Pukkala *et al,* 2002). For aircraft personnel the analysis by Blettner is most relevant for GB being the largest study available and included sub-cohorts from the other available studies as well as a cohort from Great Britain. The risk estimate for aircraft personnel from this study is SMR=1.48 (95% CI=0.47-3.48, n=5).

There are several studies available that have been conducted on UK cohorts investigating exposure to radiation in various jobs. From the UK studies, it appears that all radiation workers are at increased risk from thyroid cancer. The registry studies consistently showed an increased risk, with and without a ten-year latency period (Kendall *et al,* 1992; Muirhead *et al,* 1999). The studies conducted on only nuclear industry workforces continued to show an elevated risk for incidence (Smith 1986; Omar *et al,* 1999) and mortality (Carpenter *et al,* 1994, 1998). The registry study by Muirhead *et al,* (1999) had one of the most recent follow-up periods and included all radiation workers (excluding aircraft personnel). From the paper, it appears that the excess risk reported is only evident after a cumulative exposure of 50mSv. A combined SMR, for all workers exposed to greater than 50mSv in their lifetime, gives an elevated SMR of 1.30 (95% CI=0.35-3.31, n=4) for workers other than aircraft personnel exposed to ionising radiation. Based on person-years of follow-up and numbers in the study an average of twenty working years since first exposure is assumed, resulting in an average annual dose from ionising radiation of greater than 2mSv.

The UNSCEAR model

As for bone cancer, the estimate of relative risk was derived using the models in UNSCEAR 2006. Details of the model used are described below.

From UNSCEAR 2006, Table 57, generalized ERR incidence model, linear dose response

$$ERR(a) = \alpha \,.\, D \,.\, \exp[\kappa_1 \ln[e] + \kappa_2 \ln([a]]$$

where $\alpha = 3.80452 \times 10^4\ Sv^{-1}$
$\kappa_1 = -0.4405$
$\kappa_2 = -2.197$
e = 20 years

From Table D15: Model Deviance = 2,890.965, df = 42,697

ERR is obtained as average ERR(a), averaged over a = 25-100 (long latency REP 1956-1995).

The RR estimate is 1.03 for men and women for ionising radiation exposed workers (with an estimated average lifetime dose of 15.3 mSv) and the same for aircrew (also with an estimated average lifetime dose of 15.3 mSv).

(c) Numbers Exposed:

Data from the HSE's Central Index of Dose Information (CIDI, 1998) indicates that there were 43,805 people exposed above 0.1mSv in GB in 1990. The data exclude aircrew. A breakdown by occupation is in Table 13 below. Estimated numbers exposed over 0.1mSv are split between men and women in proportion to the proportion of men (93%) with recorded doses between 1997 and 2004. Estimates of numbers of aircraft flight deck officers and male travel and flight attendants estimated from the LFS for 1979, are also given in Table 13. CIDI data from 1990 and LFS data from 1979 are used as a best available point estimate for numbers exposed in the 'solid tumour' REP, 1956-1995.

For female air stewardesses, full data of numbers employed since 1958 was available from the British Airways Stewards and Stewardesses Union (for women only). Noting that in 2003 the number of women stewardesses employed by BA (11,479) was 48% of the LFS 'air travel assistants' total (23,890), and 55% of the CAA 'cabin attendants' total (20,761), doubling the BA numbers of new starters during the REP gives an appropriate estimate of stewardesses 'ever employed' in the period (13,902 in 1956-95). These 'ever exposed' numbers for air stewardesses are given in Table 13, and are used in the estimation of AF for this part of the exposed population (bypassing the usual turnover equation estimate).

Table 13: Numbers of workers exposed to >0.1mSv ionising radiation in GB in 1990, from CIDI, numbers of aircrew in 1979, from LFS data, and air stewardesses from BA union data

	Industry/occupation	***Numbers exposed >0.1 mSv***			
	REP 1956-95	***M***	***F***	***Total***	***%male***
	CIDI 1990				
C-E	Nuclear Power	13414	1010	14424	93%
C-E	Nuclear Fuel Fabrication/ Reprocessing	7376	555	7931	93%
C-E	General Industry	7489	564	8053	93%
C-E	Industrial Radiography	2614	197	2811	93%
C-E	Non-coal Mining	264	20	284	93%
C-E	Radiation Protection	2407	181	2588	93%
C-E	Waste Treatment	1202	90	1292	93%
C-E	Nuclear Industry Misc.	683	51	734	93%
C-E	Other	4275	322	4597	93%
	Sub-total	*39724*	*2990*	*42714*	
G-Q	Medical/Dental	408	31	439	93%
G-Q	Transport	179	13	192	93%
G-Q	Academic	428	32	460	93%
	Sub-total	*1015*	*76*	*1091*	
	CIDI Total >0.1 mSv	***40739***	***3066***	***43805***	
	LFS 1979				
G-Q	Aircraft Flight Deck Officers	6915	-	6915	
G-Q	Supervisors of Travel Stewards and Attendants	258			
G-Q	Travel Stewards and Attendants	6248			
	BA stewards and stewardesses union data				
	Air stewardesses, number employed 1956-1995		13,902		
	Aircrew Total	***13421***			

(d) AF Calculation for Bone Cancer:

The estimated total (male and female) attributable fraction for bone cancer associated with occupational exposure to ionising radiation is 0.02% (no 95%Confidence Interval obtained), which equates to 0 attributable deaths and 0 attributable to registrations. The estimated AF for men is 0.04%, resulting in 0 attributable deaths and 0 attributable registrations. The estimated AF for women was 0.01% resulting in 0 attributable deaths and 0 attributable registrations (Table 14).

(e) AF Calculation for Thyroid Cancer:

The estimated total (male and female) attributable fraction for thyroid cancer associated with occupational exposure to ionising radiation is 0.05% (no 95%Confidence Interval obtained) which equates to 0 attributable deaths and 1 attributable registration. The estimated AF for men is 0.12%, resulting in 0 attributable deaths and 1 attributable registrations. For women the estimated AF is 0.02% resulting in 0 attributable deaths and 0 attributable registrations (Table 15).

Table 14 Results for Bone Cancer and Exposure to Ionising Radiation

				Data		Calculations				Attributable Fraction (Levins[8]) [9]			Attributable Deaths			Attributable Registrations		
	Risk Estimate Reference	Exposure	Main Industry Sector[1]	RR[2]	Ne[3]	Carex adj[4]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	UNSCEAR 2006	H	C-E	1.03	39724	1.4	0.09	192147	0.0099	0.0003			0			0		
		H	G-Q	1.03	1015	0.9	0.11	3816	0.0002	0.0000			0			0		
		H	All		40739			195964	0.0101	0.0003			0			0		
		L	G-Q	1.03	13421	0.9	0.11	56071	0.0029	0.0001			0			0		
		L	All		13421			56071	0.0029	0.0001			0			0		
		All	**All**		**54160**			**252035**	**0.0130**	**0.0004**			**0**			**0**		
Women	UNSCEAR 2006	H	C-E	1.03	2990	1.5	0.14	25154	0.0012	0.0000			0			0		
		H	G-Q	1.03	76	0.8	0.15	364	0.0000	0.0000			0			0		
		H	All		3066			25518	0.0012	0.0000			0			0		
		L (Aircrew)	G-Q	1.03	-			13902	0.0007	0.0000			0			0		
		L (Aircrew)	All					13902	0.0007	0.0000			0			0		
		All	**All**		**3066**			**39420**	**0.0019**	**0.0001**			**0**			**0**		

1. Specific scenario or main industry code (Table A1)
2. Relative risks selected from the best study
3. Numbers exposed, allocated to men/women
4. CAREX adjustment factor to mid-REP (Table A1)
5. Staff turnover (TO, Table A1)
6. Number ever exposed during the REP (Statistical Appendix equation 3)
7. Proportion of the population exposed (Pr(E), Statistical Appendix equation 4)
8. Statistical Appendix 6.0 equation 1
9. Standard errors were not available from the UNSCEAR data so no confidence intervals are given

Table 15 Results for Thyroid Cancer and Exposure to Ionising Radiation

				Data		Calculations				Attributable Fraction (Levins[8]) [9]			Attributable Deaths			Attributable Registrations		
	Risk Estimate Reference	Exposure	Main Industry Sector[1]	RR[2]	Ne[3]	Carex adj[4]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	UNSCEAR 2006	H	C-E	1.09	39724	1.4	0.09	192147	0.0099	0.0009			0			0		
		H	G-Q	1.09	1015	0.9	0.11	3816	0.0002	0.0000			0			0		
		H	All		40739			195964	0.0101	0.0009			0			0		
		L	G-Q	1.09	13421	0.9	0.11	56071	0.0029	0.0003			0			0		
		L	All		13421			56071	0.0029	0.0003			0			0		
		All	All		54160			252035	0.0130	0.0012			0			1		
Women	UNSCEAR 2006	H	C-E	1.09	2990	1.5	0.14	25154	0.0012	0.0001			0			0		
		H	G-Q	1.09	76	0.8	0.15	364	0.0000	0.0000			0			0		
		H	All		3066			25518	0.0012	0.0001			0			0		
		L (Aircrew)	G-Q	1.09	-			13902	0.0007	0.0000			0			0		
		L (Aircrew)	All					13902	0.0007	0.0000			0			0		
		All	All		3066			39420	0.0019	0.0002			0			0		

1. Specific scenario or main industry code (Table A1)
2. Relative risks selected from the 'best study'
3. Numbers exposed, allocated to men/women
4. CAREX adjustment factor to mid-REP (Table A1)
5. Staff turnover (TO, Table A1)
6. Number ever exposed during the REP (Statistical Appendix equation 3)
7. Proportion of the population exposed (Pr(E), Statistical Appendix equation 4)
8. Statistical Appendix 6.0 equation 1
9. Standard errors were not available from the UNSCEAR data so no confidence intervals are given

4 OVERALL ATTRIBUTABLE FRACTION

4.1 EXPOSURE MAP

No exposure map is given since there is only one exposure substance.

4.2 SUMMARY OF RESULTS

The results are summarised in Table 16 to Table 19.

Table 16 Summary of RR used to calculate AF for Bone Cancer

Agent	Exposure	RR	LL	UL
Ionising radiation	L	1.03	NA	NA
Ionising radiation	H	1.03	NA	NA

Table 17 Summary of RR used to calculate AF for Thyroid Cancer

Agent	Exposure	RR	LL	UL
Ionising radiation	L	1.09	NA	NA
Ionising radiation	H	1.09	NA	NA

Table 18 Results for Bone Cancer

Agent	Numbers of Men Ever Exposed	Numbers of Women Ever Exposed	Proportion of Men Ever Exposed	Proportion of Women Ever Exposed	AF Men	MCLL Men	MCUL Men	AF Women	MCLL Women	MCUL Women	Attributable Deaths (Men)	Attributable Deaths (Women)	Attributable Registrations (Men)	Attributable Registrations (Women)
Ionising radiation	252035	39420	0.0130	0.0019	0.0004			0.0001			0	0	0	0

Table 19 Results for Thyroid Cancer

Agent	Numbers of Men Ever Exposed	Numbers of Women Ever Exposed	Proportion of Men Ever Exposed	Proportion of Women Ever Exposed	AF Men	MCLL Men	MCUL Men	AF Women	MCLL Women	MCUL Women	Attributable Deaths (Men)	Attributable Deaths (Women)	Attributable Registrations (Men)	Attributable Registrations (Women)
Ionising radiation	252035	39420	0.0130	0.0019	0.0012			0.0002			0	0	1	0

4.3 EXPOSURES BY INDUSTRY/JOB

As the numbers of deaths and registration from both bone and thyroid cancers are less than 1, the tables by industry sector are not given.

5 BIBLIOGRAPHY

Ashmore JP, Krewski D, Zielinski JM, Jiang H, Semenciw R, Band PR (1998) First analysis of mortality and occupational radiation exposure based on the National Dose Registry of Canada. *Am J Epidemiol* **148(6):** 564-74

Atkinson WD, Law DV, Bromley KJ, Inskip HM (2004) Mortality of employees of the United Kingdom Atomic Energy Authority, 1946-97. *Occup Environ Med* **61(7):** 577-85

Berrington A, Darby SC, Weiss HA, Doll R (2001) 100 years of observation on British radiologists: mortality from cancer and other causes 1897-1997. *British Journal Radiology* **74(882):** 507-519

Blettner M, Zeeb H, Auvinen A, Ballard TJ, Caldora M, Eliasch H, Gundestrup M, Haldorsen T, Hammar N, Hammer GP, Irvine D, Langner I, Paridou A, Pukkala E, Rafnsson V, Storm H, Tulinius H, Tveten U, Tzonou A (2003) Mortality from cancer and other causes among male airline cockpit crew in Europe. *International Journal Cancer* **106(6):** 946-952

Cancer Research UK, 2007a-last update, UK bone and connective tissue cancer statistics. Available: http://info.cancerresearchuk.org/cancerstats/types/bone/?a=5441 [June, 2008]

Cancer Research UK 2007b-last update, UK thyroid cancer statistics. Available: http://info.cancerresearchuk.org/cancerstats/types/thyroid/?a=5441 [June, 2008]

Cardis E, Gilbert ES, Carpenter L, Howe G, Kato I, Armstrong BK, Beral V, Cowper G, Douglas A, Fix, J (1995) Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. *Radiat Res* **142(2):** 117-32

Carpenter L, Higgins C, Douglas A, Fraser P, Beral V, Smith, P (1994) Combined analysis of mortality in three United Kingdom nuclear industry workforces, 1946-1988. *Radiat Res* **138(2):** 224-38

Carpenter LM, Higgins CD, Douglas AJ, Maconochie NE, Omar RZ, Fraser P, Beral V, Smith PG (1998) Cancer mortality in relation to monitoring for radionuclide exposure in three UK nuclear industry workforces. *Br J Cancer* **78(9):** 1224-32

Coggon D, Harris EC, Brown T, Rice T, Palmer KT (2009) Occupational mortality in England and Wales, 1991-2000. Office of Public Sector Information, London

HSE, CIDI, 1998. Occupational exposure to ionising radiation 1990-1996. Analysis of doses reported to the Health and Safety Executive's Central Index of Dose Information. Available: http://www.hse.gov.uk/pubns/cidi2.pdf [July, 2008]

Darby SC, Kendall GM, Fell TP, Doll R, Goodill AA, Conquest AJ, Jackson DA, Haylock RG (1993) Further follow up of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes. *BMJ* **307(6918):** 1530-5

Darby SC, Kendall GM, Fell TP, O'hagan JA, Muirhead CR, Ennis JR, Ball AM, Dennis JA, Doll R (1988) A summary of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes. *Br Med J* **296(6618):** 332-8

Drever, F., 1995. Occupational Health Decennial Supplement. London: HMSO

Dupree-Ellis E, Watkins J, Ingle JN, Phillips J (2000) External radiation exposure and mortality in a cohort of uranium processing workers. *Am J Epidemiol* **152(1):** 91-5

Fincham SM, Ugnat AM, Hill GB, Kreiger N, Mao Y (2000) Is occupation a risk factor for thyroid cancer? Canadian Cancer Registries Epidemiology Research Group. *J Occup Environ Med* **42(3):** 318-22

Horn-Ross PL, Morris JS, Lee M, West DW, Whittemore AS, McDougall IR, Nowels K, Stewart SL, Spate VL, Shiau AC, Krone MR (2001) Iodine and thyroid cancer risk among women in a multiethnic population: the Bay Area Thyroid Cancer Study. *Cancer Epidemiology, Biomarkers & Prevention* **10(9):** 979-985

HSE (1998). Occupational exposure to ionising radiation 1990-1996, analysis of doses reported to the Health and Safety Executive's Central Index of Dose Information

IARC (2000) *Ionizing Radiation, Part 1: X- and Gamma- Radiation, and Neutrons:* Volume 75 Lyon: International Agency for Research on Cancer

IARC (2001). *Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides* Volume 78. Lyon: International Agency for Research on Cancer

ISD, 2008. *ISD Cancer Information Programme*. Available at http://www.isdscotland.org

Kendall GM, Muirhead CR, Maggibbon CR, Macgibbon BH, O'hagen JA, Conquest AJ, Goodill AA, Buland BK, Fell TP, Jackson DA, Webb MA (1992) Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers. *BMJ* **304(6821):** 220-5

Kolonel LN, Hankin JH, Wilkens LR, Fukunaga FH, Hinda MW (1990) An epidemiologic study of thyroid cancer in Hawaii. *Cancer Causes and Control* **1(3):** 223-234

Langner I, Blettner M, Gundestrup M, Storm H, Aspholm R, Auvinen A, Pukkala E, Hammer GP, Zeeb H, Hrafnkelsson J, Rafnsson V, Tulinius H, De Angelis G, Verdecchia A, Haldorsen T, Tveten U, Eliasch H, Hammar N, Linnersjö A (2004) Cosmic radiation and cancer mortality among airline pilots: results from a European cohort study (ESCAPE). Radiat. Environ. Biophys **42(4):** 247-256

Miller RW, JD, B, Jr, Curtis RE (2006) Bone Cancer. In: D. Schottenfeld And J.F. Fraumeni, eds, *Cancer Epidemiology and Prevention.* 3rd edn. Oxford: Oxford University Press **946-958**: 48

Muirhead CR, Bingham D, Haylock RG, O'Hagan JA, Goodill AA, Berridge GL, English MA, Hunter N, Kendall GM (2003) Follow up of mortality and incidence of cancer 1952-98 in men from the UK who participated in the UK's atmospheric nuclear weapon tests and experimental programmes. *Occup Environ Med* **60(3):** 165-72

Muirhead CR, Goodill AA, Haylock RG, Vokes J, Little MP, Jackson DA, O'hagan JA, Thomas JM, Kendall GM., Silk TJ, Bingham D, Berridge GL (1999) Occupational radiation exposure and mortality: second analysis of the National Registry for Radiation Workers. *J Radiol Prot* **19 (1):** 3-26

Omar RZ, Barber JA, Smith PG (1999) Cancer mortality and morbidity among plutonium workers at the Sellafield plant of British Nuclear Fuels. *Br J Cancer* **79(7-8):** 1288-301

ONS, 2007a. *Cancer Statistics: Registrations.* No. 25-35. Available at http://www.statistics.gov.uk/statbase/Product.asp?vlnk=8843

ONS, 2007b. *Mortality statistics: Cause.* No. 26-32. Available at http://www.statistics.gov.uk/statbase/Product.asp?vlnk=618

ONS, 2006. *Cancer Statistics, Registrations. Registrations of Cancer Diagnosed in 2004, England.* No. 35. London: Office for National Statistics. Available at http://www.statistics.gov.uk/statbase/Product.asp?vlnk=8843

Parkin D, Bray MF, Ferlay J, Pisani P (2005) Global Cancer Statistics, 2002. *CA: A Cancer Journal for Clinicians* **55(2):** 74-108

Pettersson B, Coleman MP, Ron E, Adami HO (1996) Iodine supplementation in Sweden and regional trends in thyroid cancer incidence by histopathologic type. *Int. J Cancer* **65(1):** 13-19

Pierce DA, Shimizu Y, Preston DL, Vaeth M, Mabuchi K (1996) Studies of the mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950-1990. *Radiat Res* **146(1)**: 1-27

Pukkala E, Aspholm R, Auvinen A, Eliasch H, Gundestrup M, Haldorsen T, Hammar N, Hrafnkelsson J, Kyyronen P, Linnersjo A, Rafnsson V, Storm H, Tveten U (2002) Incidence of cancer among Nordic airline pilots over five decades: occupational cohort study. *BMJ* **325(7364):** 567

Pukkala E, Auvinen A, Wahlberg G (1995) Incidence of cancer among Finnish airline cabin attendants, 1967-92. *BMJ* **311(7006):** 649-652

Rafnsson V, Hrafnkelsson J, Tulinius H (2000) Incidence of cancer among commercial airline pilots. *Occupational Environmental Medicine* **57(3)**:175-179

Robinson CF, Walker JT (1999) Cancer mortality among women employed in fast-growing U.S. occupations. *Am J Ind Med* **36(1):** 186-92

Rodriguez Artalejo F, Castano Lara S, De Andres Manzano B, Garcia Ferruelo M, Iglesias Martin L, Calero JR (1997) Occupational exposure to ionising radiation and mortality among workers of the former Spanish Nuclear Energy Board. *Occup Environ Med* **54(3):** 202-8

Ron E, Schneider AB (2006) Thyroid Cancer. In: D. Schottenfeld and J.F. Fraumeni, eds, *Cancer Epidemiology and Prevention.* 3rd edn. Oxford: Oxford University Press **975-994;** 50

Shakhtarin VV, Tsyb AF, Stepanenko VF, Orlov MY, Kopecky KJ, Davis S (2003) Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents in the Bryansk region of Russia following the Chernobyl power station accident. *International Journal of Epidemiology* **32(4):** 584-591

Siemiatycki J, Richardson L, Straif K, Latreille B, Lakhani R, Campbell S, Rousseau M, Boffetta P (2004) Listing occupational carcinogens. *Environmental Health Perspectives* **112:** 1447-1459

Sigurdson AJ, Doody MM, Rao RS, Freedman DM, Alexander BH, Hauptmann M, Mohan AK, Yoshinaga S, Hill DA, Tarone R, Mabuchi K, Ron E, Linet MS (2003) Cancer incidence in the US radiologic technologists health study, 1983-1998. *Cancer* **97(12):** 3080-9

Smith PG, Douglas AJ (1986) Mortality of workers at the Sellafield plant of British Nuclear Fuels. *Br Med J* **293(6551):** 845-54

Sont WN, Zielinski JM, Ashmore JP, Jiang H, Krewski D, Fair ME, Band PR, Letourneau EG (2001) First analysis of cancer incidence and occupational radiation exposure based on the National Dose Registry of Canada. *Am J Epidemiol* **153(4):** 309-18

Telle-Lamberton M, Samson E, Caer S, Bergot D, Bard D, Bermann F, Gelas JM, Giraud JM, Hubert P, Metz-Flamant C, Neron MO, Quesne B, Tirmarche M, Hill C (2007) External radiation exposure and mortality in a cohort of French nuclear workers. *Occup Environ Med* **64(10):** 694-700

United Nations Scientific Committee on the Effects of Atomic Radiation, 2006. Effects of ionising radiation: UNSCEAR 2006, Volume 1, Report to the General Assembly, Annex A

Wang JX, Boice JD, Jr, Li BX, Zhang JY, Fraumeni, JF Jr (1988) Cancer among medical diagnostic x-ray workers in China. *J Natl Cancer Inst* **80(5):** 344-50

Wang JX, Zhang LA, Li BX, Zhao YC, Wang ZQ, Zhang JY, Aoyama T (2002) Cancer incidence and risk estimation among medical x-ray workers in China, 1950-1995. *Health Physics* **82(4):** 455-466

WCISU, 2008. *Cancer Incidence in Wales.* Available at http://www.wales.nhs.uk

6. STATISTICAL APPENDIX

Formulae used in the estimation of AF

Levin's equation

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

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

A common denominator is used across exposure levels and industries for each exposure

Miettinen's equation

$$AF = Pr(E|D)*(RR-1)/RR \quad (2)$$

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

Turnover equation to estimate numbers ever employed during the REP

$$N_{e(REP)} = \sum_{i=a}^{i=b} l_{(adj15)i} * n_0/(R-15)\} + \sum_{k=0}^{k=(age(u)-age(1))} \sum_{j=c+k}^{j=d+k} \{l_{(adj15)j} * n_0 * TO /(age(u)-age(l)+1)\} \quad (3)$$

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) (e.g. 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, available on the HSE website. 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 below.

Equation to estimate the proportion of the population exposed

$$Pr(E) = N_{e(REP)} / N_{p(REP)} \quad (4)$$

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

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

$$AF_{overall} = 1- \Pi_k(1-AF_k) \text{ for the k exposures in the set} \quad (5)$$

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

		Main Industry Sector	Adjustment factor for change in employment levels*	Turnover per year
Men	A-B	Agriculture, hunting and forestry; fishing	1	7%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.4	9%
	F	Construction	1	12%
	G-Q	Service industries	0.9	11%
		Total	1	10%
Women	A-B	Agriculture, hunting and forestry; fishing	0.75	10%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.5	14%
	F	Construction	0.67	15%
	G-Q	Service industries	0.8	15%
		Total	**0.9**	**14%**

* Applied to CAREX data for the solid tumour REP 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).

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The burden of occupational cancer in Great Britain

Bone cancer and thyroid cancer

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for cancers of the bone and thyroid derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for bone cancer related to overall occupational exposure to ionising radiation is 0.02% (no 95%Confidence Interval available), which equates to 0 attributable deaths and 0 attributable registrations. The estimated total (male and female) attributable fraction for thyroid cancer associated with occupational exposure overall and to ionising radiation is 0.05% (no 95%Confidence Interval available), which equates to 0 attributable deaths and 1 attributable registration.

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