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The burden of occupational cancer in Great Britain

Kidney cancer

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

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Kidney 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 cancer of the kidney that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for kidney cancer related to overall occupational exposure is 0.04% (95%Confidence Interval (CI)=0.00-0.15), which equates to 1 (95%CI=0-5) death and 3 (95%CI =0-10) registrations.

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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 cancer of the kidney that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

Coke production has been classified by the IARC as a definite human carcinogen for kidney cancer. Both the production of coke and its use as a fuel, for example in coke-ovens in the iron and steel industry, can lead to exposure to combustion products including as polycyclic aromatic hydrocarbons, ammonia, naphthalene, benzene, creosote oil and toluene. Trichloroethylene has been classified by IARC as a probable human carcinogen for kidney cancer. Occupational exposure to tetrachloroethylene occurred in the dry cleaning industry until the 1950s but has now been largely replaced by other solvents. The widest use of tetrachloroethylene is in metal degreasing in manufacturing industries.

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 in 2005, there were 2145 total deaths in men aged 25+ and 1354 in women aged 25+ from kidney cancer; in 2004 there were 4192 total registrations for kidney cancer in men aged 25+ and 2567 in women aged 25+.

Studies in the UK of coke-oven workers have shown no overall excess risk from kidney cancer. The attributable fraction and numbers of deaths and registrations due to coke production is thus 0.

The estimated total (male and female) attributable fraction for kidney cancer associated with occupational exposure overall and to trichloroethylene is 0.04% (95%Confidence Interval (CI)=0.00-0.15), which equates to 1 (95%CI=0-5) death, and 3 (95%CI =0-10) registrations

CONTENTS

1 INCIDENCE AND TRENDS

The term 'cancer of the kidney' (ICD-10 C64-C66, C68; ICD-9 189) is often limited to cancer of renal cells only, excluding the renal pelvis and other associated tissues (ICD-10 C64; ICD-9 189.0). Cancer of the renal pelvis (ICD-10 C65; ICD-9 189.1), cancer of the ureter (ICD-10 C66; ICD-9 189.2), and cancers of other or unspecified urinary organs including the urethra (ICD-10 C68; ICD-9 189.3 - 189.9) are, however, sometimes also considered in the kidney cancer category (Cancer Research UK, 2007). Wherever possible in this report, information on renal cell cancer (RCC) will be presented separately to data on cancer of the renal pelvis and ureter due to the differences in aetiology and risk factor patterns. However, as many studies do not separate the different types of renal cancer, much of the available data combine all kidney cancers and do not provide analyses by site. When reference is made to "kidney cancer" in this report, it can be considered to include all non-bladder renal/urinary organs as classified by ICD-10 C64-C66, C68; ICD-9 189 (i.e. the widest definition of kidney cancer), unless otherwise specified.

In adults in England and Wales, almost 90% of malignant kidney neoplasms are renal cell carcinoma (RCCs), mainly adenocarcinomas that arise from cells of the proximal convoluted renal tubule (Stewart and Kleihues 2003; Quinn *et al*, 2001). There are five subgroups of RCCs: conventional (clear cell, also called non papillary), which account for 75-80% of RCC tumours; papillary (chromophilic) accounting for 10-15% and chromophobe, collecting duct carcinoma and unclassified renal cell carcinoma which together make up the remainder of RCC tumours. Transitional cell carcinoma (TCC) is a less common tumour type that arises from the transitional cell epithelium in the renal pelvis, ureter and urethra (Lindblad and Adami 2002; Cancer Research UK 2007). Transitional cell epithelium is also found in the bladder, and 50% of patients with renal TCC also develop tumours of the bladder. TCC also serves as a convenient category for the description of non-renal cell kidney cancers. Wilms tumour (nephroblastoma) is an embryonic malignancy that afflicts 1 in 10,000 children and accounts for 2% of all kidney cancers in England and Wales (Quinn *et al*, 2001); it is not a tumour of adults. RCC is common in patients with the genetic disease von Hippel-Lindau (VHL). Both Wilms tumour and VHL disease are characterised by mutations of tumour suppressor genes.

Tables 1 and 2 (ONS 1999-2006) provide an indication of kidney cancer trends over the period from the mid-1990s to the mid-2000s in England and Wales. Generally, registrations of all cancers have increased over the period 1994-2004, as shown in Table 1; rates of kidney cancer reflect this general rise in incidence. However, as a crude rate per 100,000, rates have remained consistent for TCC incidence while RCC rates have increased from 9.8 to 12.5 cases per 100,000 for men and 5.8 to 7.3 cases per 100,000 for women. Mortality rates have also increased for RCC from 1999 to 2005, but the increase has been lower than for incidence (Table 2). Mortality from renal pelvis and ureter cancers have fluctuated but show a small increase, while deaths from unspecified urinary cancers (ICD-10 C68) have shown a rapid increase in recent years. As crude rate per 100,000, the number of male deaths from RCC has increased slightly from 6.26 to 7.03 per 100,000 while for women, the rate increased during the 1999-2005 period from 3.70 deaths to more than 4.00 deaths per 100,000. The increase was greatest for unspecified urinary cancers, which saw an increase from 0.05 to 0.16 male deaths per 100,000 and 0.04 to 0.12 female deaths per 100,000 during the same seven year period. Table 3 clearly shows an increase in all kidney cancers in England and Wales during the period 1971-2000.

Table 1: Number of kidney cancer registrations in England and Wales 1994, England 1995-2004, by ICD-10 category

	Total registrations per kidney cancer category				% Total				Crude rate /100,000			
Year	**C64 (189)**	**C65**	**C66**	**C68**	**C64 (189)**	**C65**	**C66**	**C68**	**C64 (189)**	**C65**	**C66**	**C68**
1994	2985				2.66				11.8			
1995	2351	137	127	73	2.26	0.13	0.12	0.07	9.8	0.6	0.5	0.3
1996	2422	144	116	84	2.33	0.14	0.11	0.08	10.0	0.6	0.5	0.3
1997	2480	151	109	246	2.38	0.14	0.10	0.24	10.2	0.6	0.4	1.0
1998	2628	170	106	68	2.46	0.16	0.10	0.06	10.8	0.7	0.4	0.3
1999	2597	164	127	58	2.39	0.15	0.12	0.05	10.6	0.7	0.5	0.2
2000	2695	201	179	95	2.42	0.18	0.16	0.09	11.3	0.8	0.8	0.4
2001	2701	203	166	83	2.40	0.18	0.15	0.07	11.2	0.8	0.7	0.3
2002	2915	212	172	81	2.59	0.19	0.15	0.07	12.0	0.9	0.7	0.3
2003	2844	220	177	103	2.52	0.20	0.16	0.09	11.6	0.9	0.7	0.4
2004	3059	204	180	124	2.60	0.17	0.15	0.11	12.5	0.8	0.7	0.5
Ave.	**2698**	**181**	**146**	**102**	**2.45**	**0.16**	**0.13**	**0.09**	**11.1**	**0.7**	**0.6**	**0.4**
1994	1781				1.59				6.8			
1995	1435	97	53	44	1.36	0.09	0.05	0.04	5.8	0.4	0.2	0.2
1996	1529	107	62	36	1.45	0.10	0.06	0.03	6.1	0.4	0.2	0.1
1997	1530	116	66	135	1.43	0.11	0.06	0.13	6.1	0.5	0.3	0.5
1998	1567	107	75	28	1.43	0.10	0.07	0.03	6.2	0.4	0.3	0.1
1999	1681	119	69	45	1.50	0.11	0.06	0.04	6.7	0.5	0.3	0.2
2000	1646	131	105	32	1.47	0.12	0.09	0.03	6.5	0.5	0.4	0.1
2001	1648	121	92	28	1.47	0.11	0.08	0.02	6.5	0.5	0.4	0.1
2002	1745	129	83	25	1.57	0.12	0.07	0.02	6.9	0.5	0.3	0.1
2003	1844	157	95	41	1.61	0.14	0.08	0.04	7.2	0.6	0.4	0.2
2004	1877	150	107	44	1.62	0.13	0.09	0.04	7.3	0.6	0.4	0.2
Ave.	**1662**	**123**	**81**	**46**	**1.50**	**0.11**	**0.07**	**0.04**	**6.6**	**0.5**	**0.3**	**0.2**

Source: adapted from ONS (2006a; 2005a,b; 2004a; 2003a; 2002a,b; 2001a; 2000a)

Table 2: Number of kidney cancer deaths in England and Wales 1999-2005, by ICD-10 (and ICD-9) category

	Total deaths per kidney cancer category				% Total				Crude rate /100,000			
Year	**C64 (189.0)**	**C65 (189.1)**	**C66 (189.2)**	**C68 (189.3 - 189.9)**	**C64 (189.0)**	**C65 (189.1)**	**C66 (189.2)**	**C68 (189.3 + 189.9)**	**C64 (189.0)**	**C65 (189.1)**	**C66 (189.2)**	**C68 (189.3 - 189.9)**
1999	1626	8	50	12	0.62	0.00	0.02	0.00	6.26	0.03	0.19	0.05
2000	1580	12	46	11	0.62	0.00	0.02	0.00	5.98	0.05	0.17	0.04
2001	1622	11	53	58	0.64	0.00	0.02	0.02	6.40	0.04	0.21	0.23
2002	1749	8	51	55	0.69	0.00	0.02	0.02	6.82	0.03	0.20	0.21
2003	1713	20	57	43	0.67	0.01	0.02	0.02	6.63	0.08	0.22	0.17
2004	1816	9	51	44	0.74	0.00	0.02	0.02	6.99	0.03	0.20	0.17
2005	1841	15	64	41	0.76	0.01	0.03	0.02	7.03	0.06	0.24	0.16
Ave.	**1707**	**12**	**53**	**38**	**0.68**	**0.00**	**0.02**	**0.02**	**6.59**	**0.05**	**0.21**	**0.15**
1999	988	6	28	11	0.34	0.00	0.01	0.00	3.70	0.02	0.10	0.04
2000	1014	15	30	14	0.36	0.01	0.01	0.00	3.78	0.06	0.11	0.05
2001	1024	11	30	12	0.37	0.00	0.01	0.00	3.83	0.04	0.11	0.04
2002	1035	8	21	27	0.37	0.00	0.01	0.01	3.86	0.03	0.08	0.10
2003	1105	11	34	26	0.39	0.00	0.01	0.01	4.10	0.04	0.13	0.10
2004	1144	6	40	31	0.43	0.00	0.01	0.01	4.23	0.02	0.15	0.11
2005	1089	17	36	32	0.40	0.01	0.01	0.01	4.00	0.06	0.13	0.12
Ave.	**1057**	**11**	**31**	**22**	**0.38**	**0.00**	**0.01**	**0.01**	**3.93**	**0.04**	**0.12**	**0.08**

Source: adapted from ONS (2006b; 2005c; 2004b; 2003b; 2002c; 2001b; 2000b)

Table 3: Cancer mortality trends 1971-2000 in England and Wales and proportions associated with all categories of malignant neoplasms of the kidney (ICD-10 C64-C66, C68; ICD-9 189).

	Male			Female		
Year	**Total neoplasms**	**All kidney neoplasms**	**% Total**	**Total neoplasms**	**All kidney neoplasms**	**% Total**
1971-1975	326838	4970	1.52	279710	3197	1.14
1976-1980	343180	5580	1.63	298261	3410	1.14
1981-1985	359493	6348	1.77	320635	3861	1.20
1986-1990	374103	7161	1.91	343106	4486	1.31
1991-1995	374029	7874	2.11	342716	5059	1.48
1996-2000	355943	8184	2.30	330414	5229	1.58

Source: ONS (2001b)

In England and Wales since 1971 to 1997, the age-standardised rate in males and females has almost doubled, reaching 11 per 100,000 for men and 5 per 100,000 for women. By the early 1990s, age-standardised mortality had risen by over 85% since 1950 in males (to 6 per 100,000) and females (3 per 100,000). Incidence and mortality from kidney cancer rose for each successive cohort born from the mid-1860s to the mid-1920s; incidence continued rising to the mid 1950s but mortality levelled off for those born between the 1930s and 1950s (Quinn *et al,* 2001). Incidence and mortality in men do not appear to be associated with socioeconomic status but cases of kidney cancers are slightly higher in women from more deprived groups. Rates appear to be higher in Northern England and Wales compared to Southern England.

In the UK, kidney cancer is the eighth most common cancer in men, with 4348 new cases diagnosed (registrations) in 2004 (Cancer Research UK 2007). This compares to 2696 cases in women, giving a male:female ratio of 3:2. In women, it is the fourteenth most common cancer. During the period 1975-1995, rates of RCC cases in the UK have increased for both men and women but rates of cancer of the renal pelvis have remained stable (Cancer Research UK 2007). In Great Britain in 2004, there were 4240 new male registrations and 2617 female cases (ISD 2005; ONS 2006a; WCISU 2008; Table 4). Rates have increased in men by 80% from 7.1 per 100,000 in 1975 to 12.8 per 100,000 in 2004. In women rates have increased over the same period from 3.2 to 6.5 per 100,000, a rise of more than 100%. Most of the increase has occurred in men over 65 and women over 55 (Cancer Research UK 2007). Rates have more than doubled in Great Britain between 1975 and 2004 for both men and women aged over 65. Incidence increases from age 40 years upwards, with the peak number of cases for both men and women in the 70-79 age group and over 45% of cases occurring in those aged 65-79 (Cancer Research UK 2007; Quinn *et al,* 2001). There are a small number of kidney cancer cases in children, most usually Wilm's tumour, which develop at or before birth; rates decline until middle age.

In 2005 there were 3580 deaths from kidney cancer in the UK: kidney cancer is the tenth most common cause of cancer death for males and thirteenth for females in the UK (Cancer Research UK 2007). For Great Britain, mortality rates where 2153 for men and 1342 for women (IDS 2005; ONS 2006b; Table 5). Mortality trends reflect incidence, with deaths increasing from age 40 years and peaking in the 70-79 age group (Cancer Research UK 2007). Death rates increased from 4.3 to 6.1 deaths per 100,000 in men and 2.1 to 2.9 per 100,000 for women between 1971 and 2005.

As kidney cancer commonly causes no obvious symptoms in its early stages, the tumour is often relatively advanced by the time of diagnosis and rates of survival can be low (Stewart and Kleihues 2003). Despite this, the five-year survival rate has increased in England and Wales in the period

1971-2001 from 28% in both men and women, to 50% for men and 49% for women (Cancer Research UK 2007). Survival declines as age at diagnosis increases, particularly after the age of 40, and tends to be lower for women then men, and higher in more affluent groups (Quinn *et al,* 2001).

Rates of kidney cancer incidence and mortality in Europe vary, particularly for men (Cancer Research UK 2007). It is higher in Eastern Europe, especially the Czech Republic and Estonia, and lowest in southern Europe (Zatonski *et al,* 1996). Rates in males are also high in the Bas Rhin area of France and Trieste in Italy. TCC incidence levels are high in rural parts of Bulgaria, Romania and ex-Yogoslavian countries due to a predisposing condition called Balkan neuropathy (Stoyanov *et al,* 1978; McLaughlin *et al,* 2006). Kidney cancer is the sixth most frequently occurring cancer in Europe but the 15th most common globally. Levels are lowest in Africa and Asia, with a ten-fold difference between the highest (Eastern Europe) and lowest rates (Africa/Asia). As well as Europe, incidence is high in North America, Australia and New Zealand. The sex and age patterns identified in the UK are applicable worldwide, such that more men are affected than women in a 1.6-2.5:1 ratio and most cases occur between the ages of 50-70 years (Quinn *et al,* 2001). Globally, there are almost 190,000 cases diagnosed each year, about 2% of all new cancer cases. The annual mortality rate is about 91,000 deaths per year (five-year survival rate is approximately 50%) (Stewart and Kleihues 2003). RCC rates have generally increased in Europe, as have incidence rates in the USA and other developed countries. One suggested reason for this increase is the development of modern imaging procedures and the increased detection of asymptomatic tumours; however, there has also been an increase in late-stage RCC (Mathew *et al,* 2002; McLaughlin *et al,* 2006). The increase in RCC incidence has been more rapid in women than men and in blacks than whites, particularly in young black men and women (McLaughlin *et al,* 2006; Chow *et al,* 1999). Rates among other racial groups tend to be much lower for each sex than the incidences seen in blacks and whites. Incidence of TCC has been more consistent and has not exhibited any global trends, with transitory declines and increases alternating across and within countries; this generally reflects the incidence of bladder cancer rather than RCC (McLaughlin *et al,* 2006). In the US, mortality from kidney cancer increased until the 1990s before stabilising: the increase in men was greater than that seen for women (McLaughlin *et al,* 2006). Globally, the incidence of kidney cancer in England and Wales is in the middle of the range (higher in most of Europe and North America but lower in Africa and Asia; Quinn *et al,* 2001).

The five-year survival rates for RCC have shown general slight increases around the world, from less than 40% in the US in the 1960s to more than 50% by the 1990s (Chow *et al,* 1999; McLaughlin *et al,* 2006). Five-year survival following kidney cancer diagnosis is as low as 20% in Thailand (which also has one of the lowest incidence rates) to 64% in Austria. If caught early enough, five-year survival increases to >80%. RCC and TCC survival rates differ slightly between sexes and racial groups and TCC survival, particularly in the US, does not appear to have increased. Comparison of incidence and mortality figures suggests that survival is better in Italy and the USA, than in England and Wales (Quinn *et al,* 2001).

Mortality and incidence rates for kidney cancer are generally higher in urban than rural areas in the United States, England and Wales, and Scandinavian countries; this is particularly the case for men (Quinn *et al,* 2001; McLaughlin *et al,* 2006). Socioeconomic factors, including education and income levels, have been generally found to have no, weak or even inverse relationships with kidney cancer (McLaughlin *et al,* 2006).

Table 4: Number of new cases and rates of kidney cancer (ICD-10 C64-66 C68; ICD-9 189), 2004.

	England	Wales	Scotland	Total
Males	3567	270	406	4243
Females	2178	169	271	2618
All	5745	439	677	6861

Source: ISD 2005; ONS 2006a; WCISU 2008

Table 5: Number of deaths and mortality rates of kidney cancer (ICD-10 C64-66 C68; ICD-9 189), 2005.

	England & Wales	Scotland	Total
Males	1961	193	2154
Females	1174	168	1342
All	3135	361	3496

Source: ISD 2005; ONS 2006b

2 OVERVIEW OF AETIOLOGY

2.1 INTRODUCTION

The aetiologies of renal cell cancers (RCC) and cancers of the renal pelvis and ureter (usually transitional cell cancers or TCC) are similar. However, the strength of association between the two cancer types and the various causal agents identified do differ. As such, each causal agent that has been identified will be considered separately, where appropriate, for RCC and TCC.

There have been a large number of case-control studies and some recent cohort studies that have evaluated the risk factors associated with RCC and TCC incidence in a number of countries from North America, Europe, Australia and China. Cigarette smoking is the most well established causal risk factor for RCC, and a dose-response relation has been observed among both men and women (Wynder *et al,* 1974; Semenza *et al,* 2001; McLaughlin *et al,* 2006). The studies provide a relative risks range of 1.2 – 2.3, with the relative risk for heavy smokers rising to 2.0 – 2.5. However, all associations are not statistically significant. Population based attributable risks indicate that approximately 20% to 30% of renal cell cancers among men and 10% to 20% among women can be accounted for by cigarette smoking (McLaughlin *et al,* 1995a; 2006; Yuan *et al,* 1998a; Benichou *et al,* 1998; Stewart and Kleihues 2003; Moore *et al,* 2005). A RCC association with cigars, pipes, chewing tobacco and passive smoking has been inconsistently reported (Yu *et al* 1986; Brownson 1988; Kreiger *et al,* 1993; McLaughlin *et al,* 1995a; Yuan *et al,* 1998a). There has also been suggestion that smoking by people of particular genotypes are at higher risk of developing renal cell cancer (Semenza *et al,* 2001). Smoking-related risks are generally higher for TCC than RCC, with attributable risk estimates for cigarette smoking for renal pelvis and ureter cancers as high as 46-82% among men and 35-61% among women (McLaughlin *et al,* 1983; 1992; Jensen *et al,* 1988; McCredie and Stewart 1992). Cigarette smoking is considered to be the strongest risk factor for TCC tumours (McLaughlin *et al,* 2006).

A positive association between RCC and body weight has been reported by a number of case-control and cohort studies (Yu *et al,* 1986; Kreiger *et al,* 1993; Wolk *et al,* 1996a; Heath *et al,* 1997; Yuan *et al,* 1998b). Bergstrom al. (2001) suggested a summary relative risk, irrespective of sex, of 1.07 per unit increase of body mass index. Thus, the rising prevalence of obesity in the US over recent years may explain the increasing incidence of RCC (McLaughlin *et al,* 2006). Various dietary factors have been causally linked to RCC over the years, including consumption of meat, alcohol, coffee and tea, and high fat and high protein diets but evidence is conflicting (Yu *et al,* 1986; Wolk *et al,* 1996a; McLaughlin *et al,* 2006). Similarly evidence of an association between beverage consumption and TCC incidence is limited, although individuals exposed to high levels of arsenic in drinking water demonstrate elevated levels of cancers of the renal pelvis and ureter (Guo *et al,,* 1997; Hopenhayn-Rich *et al,* 1998). The protective effect of fruit and vegetable consumption has been suggested by a number of RCC studies (Wolk *et al,* 1996b; Hu *et al,* 2003; Rashidkhani *et al,* 2005). Hypertension as a causal risk factor for RCC is believed to be independent of obesity. There are a number of epidemiological studies that have reported an association between renal cell cancer and hypertension, rather than antihypertensive medications, and relative risks have been found to be in the region of 1.3 and 2 or greater (McLaughlin *et al,* 1995b; Heath *et al,* 1997; Yuan *et al,* 1998b; Chow *et al,* 2000; Semenza *et al,* 2001). Various hypotheses have been suggested to explain this association, including the presence of early-stage RCC tumours that raise blood pressure (Batty *et al,* 2003) or that diagnosis of RCC is more likely to occur due to better medical surveillance during treatment for hypertension (McLaughlin *et al,* 2006). TCC has also been associated with hypertension (Liaw *et al,* 1997). Diuretics, used to treat hypertension or for the treatment of other disorders, have also been associated with RCC, with relative risks as high as 4 reported (Yu *et al,* 1986; Heath *et al,* 1997) although other studies suggest that adjustment for high blood pressure eliminates excess risk (McLaughlin *et al,* 1995b).

An association between analgesic use, specifically phenacetin-containing pharmaceuticals, and RCC has been reported (McLaughlin *et al,* 1984; Kreiger *et al,* 1993) but this is lower in magnitude

and less conclusive than the causal link identified between heavy use of phenacetin-containing drugs and TCC of the renal pelvis (IARC 1987). Jensen *et al,* (1989) suggest that relative risk between TCC and phenacetin use is 2.4 among men and 4.2 among women, after adjustments for smoking, occupation and use of other analgesics. Paracetamol and aspirin use have also been examined as causal factors for both RCC and TCC, but epidemiological studies have generally not identified an association (McLaughlin *et al,* 1985; Rosenberg *et al,* 1998; Gago-Dominguez *et al,* 1999). However, this may be due to methodological issues concerning the difficulty in determining levels of over-the-counter use of analgesic medicine (McLaughlin *et al,* 2006). Menopausal oestrogen use and oral contraceptive use, as well as reproductive status, have been inconsistently reported to be associated with RCC incidence, although this is generally not considered to be a causal factor (Kreiger *et al,* 1993; Lindblad *et al,* 1995). There are three major inherited forms of RCC, including von Hippel-Lindau associated, which together account for only a small proportion of total malignancies (Zbar and Lerman 1998). Predisposition to RCC can occur through long-term kidney dialysis and in renal transplant recipients following renal cystic disease (Ishikawa *et al,* 1991; Stewart *et al,* 2003).

There are a number of occupational agents/exposure scenarios associated with RCC and TCC, although neither cancer is considered to be an occupationally associated tumour type. RCC has been linked to asbestos (Selikoff *et al,* 1979; Enterline *et al,* 1987; Yu *et al,* 1986; Brownson *et al,* 1988; Partanen *et al,* 1991; Mandel *et al,* 1995; Pesch *et al,* 2000; Mattioli *et al,* 2002; Sali and Boffetta 2000), trichloroethylene (TCE) (Vamvakas *et al,* 1998; Bruning *et al,* 2003; Blair *et al,* 1998; Boice *et al,* 1999; Raaschou-Nielsen *et al,* 2003) and perchloroethylene (tetrachloroethylene) (Blair *et al,* 1979; Brown and Kaplan 1987; Anttila *et al,* 1995; Mandel *et al,* 1995; Boice *et al,* 1999; Blair *et al,* 2002; Mundt *et al,* 2003) exposure, and to employment in the coke production (Redmond *et al,* 1972; Redmond 1983; Mandel *et al,* 1995; Dosemeci *et al,* 1999) and oil refinery (Wong and Raabe 1989; IARC 1989a; MacFarland *et al,* 1984; McCredie and Stewart 1993; Mandel *et al,* 1995; Gamble *et al,* 1996) industries, as well as with gasoline/diesel delivery (Spirtas *et al,* 1991). Associations with other occupational exposures have been reported, including elevated risks among workers exposed to cadmium, lead and polychlorinated biphenyls (Shalat *et al,* 1989; Pesch *et al,* 2000), and a recent study reported an interaction between self-reported occupational exposure, genotype for glutathione S-transferase M1 and T1, and renal cell cancer (Buzio *et al,* 2003). TCC occupational associations resemble those for bladder cancer (McLaughlin *et al,* 2006) and include links with exposure to dyes or employment in leather and shoe manufacturing (MacAlpine 1947; Poole-Wilson 1969; Armstrong *et al,* 1976). Cancers of the renal pelvis and ureter have also been associated with exposure to coal/coke, natural gas and mineral oils (McLaughlin *et al,* 1983; Jensen *et al,* 1988), or employment in dry cleaning, iron and steel, chemical, and petroleum refining industries (Jensen *et al,* 1988; McCredie and Stewart 1993).

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. IARC have classified one occupational agent and one occupational exposure circumstance, Group 2A and Group 1 carcinogens respectively, as associated with kidney cancer (Table 6; IARC 1984a; 1995). Siemiatycki *et al,* (2004) summarised the evidence used in the classification of these agents and substances as suggestive (see Table 6). Coke production is considered to be a Group 1 exposure circumstance for kidney cancer, with TCE classified as a Group 2A carcinogenic agent. Other chemicals and exposure scenarios have not been considered by IARC due to lack of evidence of causal association with kidney cancer.

Table 6: Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1-88, into Groups 1 and 2A, which have been associated with the kidney. "Strength of evidence" is derived from Siemiatycki *et al,* (2004).

Agents, mixture, circumstance	Main industry, use; or, suspected substance	Evidence of carcinogenicity in humans	Strength of evidence	Target organs
Group 1: carcinogenic to humans				
Agents, groups of agents				
None specified				
Exposure circumstances				
Coke production	Coal-tar fumes	Sufficient	Suggestive	Kidney, Skin (including scrotum), Lung, Bladder
Group 2A: probably carcinogenic to humans				
Agents, groups of agents				
Trichloro-ethylene	Production; dry cleaning; metal degreasing	Limited	Suggestive	Renal cell, Liver and biliary tract, Non-Hodgkin lymphoma
Exposure circumstances				
None specified				

Source: adapted from Siemiatycki *et al.* (2004) and IARC (1984a;1995)

The Occupational Health Decennial Supplement (Drever 1995) examined cancer incidence (1981-1987) in England and cancer mortality (1979-1980, 1982-1990) in England and Wales in men and women aged 20-74 years. Table 7a shows that renal cell carcinoma (RCC) cancer incidence, as shown by significantly high proportional registration risks (PRRs), is related to occupations where elevated exposure to solvents may be likely, such as machine tool operators and compositors in men and laboratory technicians in women. Renal cell cancer mortality, as indicated by high proportional mortality ratios (PMRs), may also be linked to occupational solvent exposure (e.g. male production/maintenance managers and female technicians). For men, exposure to gasoline, diesel and products of their combustion is a possible causal factor for mortality from RCC (bus conductors, sales representatives). Other kidney cancers, especially cancer of the renal pelvis but also ureter cancer, have been included in the urothelial cancer category by Drever (1995). While indistinguishable from bladder cancer, incidence of, and mortality from, cancers of the renal pelvis and ureter may be associated with occupational exposures of gasoline and diesel (driving instructors, railway station workers) or solvents (electrical/electronic engineers, rubber/rubber goods manufacture). Table 7b provides more recent data regarding occupation and mortality from kidney cancer (Coggon *et al*, 2009). For men, the occupations identified for the period 1991-2000 are similar to those shown in Table 7a, with the addition of school teachers. For women, the high level association with laboratory technicians and other technicians is no longer evident, but a possible association is now evident between school teachers and renal cell cancer.

Table 7a: Job codes with significantly high PRRs and PMRs for kidney cancer in men & women aged 20-74 years (England). Job descriptions signified by # correspond to PMRs or PRRs significantly different from 100 for urothelial cancer (ICD-9 188, 189.1-189.8); all other jobs correspond to cancer of the kidney, specifically renal cell cancer (ICD-9 189.0) (Drever 1995).

Job group		Registration	PRR*	95% CI	Deaths	PMR**	95% CI
SIC code	Description	(1981-87)			(1979-1980 and 1982-90)		
Men							
006	Sales managers#	168	117	100-137	206	122	106-140
018	Pharmacists#	35	146	102-203			
023	Driving instructors#	36	161	113-224			
029	Electrical & electronic engineers#				58	152	115-196
038	Production and maintenance managers				378# 265	113# 114	102-125# 100-128
039	Managers in construction				83	143	114-177
046	Caterers#				117	123	102-148
049	Police				73	134	105-169
054	Postal worker#	222	114	100-131	303	131	116-146
057	Sales representatives				208	115	100-132
063	Railway station workers#	90	126	102-156			
085	Rubber manufacture#	58	226	172-293			
093	Plastics goods makers#	19	187	113-293			
094	Compositors	11	238	119-426			
097	Printers#	115	123	102-148			
124	Machine tool operators	735# 210	112# 115#	105-121# 101-132#			
132	Production fitters#				661	111	103-120
133	Motor mechanics#				202	120	104-138
139	Telephone fitters	29	153	103-221			
158	Coach painters#	12	198	103-347			
167	Masons and stonecutters#	23	164	104-247			
175	Face-trained coalminers	54	146	110-191			
184	Other motor drivers#	112	125	103-151			
185	Bus conductors				30	172	116-246
192	Refuse collectors#				63	141	108-180
194	Boiler operators#				99	136	111-166
Women							
017	Nurses#				138	120	101-142
032	Laboratory technicians	9	255	117-486	14	215	117-360
037	Technicians nec				5	357	116-833
041	Office managers#				21	178	110-273
072	Knitters#	14	193	106-324			
077	Brewery workers#	3	589	122-1723			
085	Rubber manufacture#	7	350	141-723			
092	Rubber goods manufacture#				9	457	209-867

*p<0.05 based on at least 3 registrations; adjusted for age, social class and registration region.

**p<0.05 based on at least 3 registrations; adjusted for age and social class.

#Urothelial cancer i.e. cancer of the bladder, renal pelvis, ureter, urethra and other urinary organs/tissues.

Table 7b: Job codes with significantly high PMRs for kidney cancer. Men and women aged 20-74 years, England. Renal cell carcinoma only (ICD-10C64; ICD-9 189.0)

Job group		Observed mortality	Expected mortality	PMR**	95% CI
SIC code	Description	(1991-2000)			
Men					
008	Government administrators	56	39.7	141.0	106.5-183.1
011	School Teachers	157	129.0	121.7	103.4-142.3
038	Production and maintenance managers	276	235.2	117.3	103.9-132.0
049	Police	114	72.7	156.7	129.2-188.3
075	Chemical workers	90	62.7	143.6	115.5-176.5
094	Compositors	19	10.2	186.3	112.1-290.9
105	Cabinet Makers	26	16.9	153.8	100.5-225.4
122	Centre, Capstan, Turret & Other Lathe Setters & Setter-Oper	35	23.3	150.1	104.6-208.8
123	Machine Tool Setter Operators	69	53.6	128.8	100.2-163.0
124	Machine Tool Operatives (including CNC machine tool operati	274	223.0	122.8	108.7-138.3
142	Other Electrical/Electronic Trades nes	86	67.9	126.7	101.4-156.5
Women					
011	School Teachers	161	135.2	119.1	101-138.9

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

2.2 IARC EXPOSURES

2.2.1 AGENTS OR GROUPS OF AGENTS

Trichloroethylene

Trichloroethylene (TCE) has been used as an extraction solvent for natural fats and oils, spices and hops, and the decaffeination of coffee (Linak *et al,* 1992), but recognition of its toxicity led to discontinuation of its use in food stuffs, cosmetics and medicines (US-FDA 1977). TCE was also used in the dry cleaning industry but was largely replaced in the 1950s by tetrachloroethylene (IARC 1995). Since the 1920s, most TCE demand has been for vapour degreasing, with 85% and 95% of TCE produced in the United States and Europe respectively used for metal cleaning. As a metal degreasant, TCE is used in 5 main industrial groups: furniture and fixtures; fabricated metal products; electrical and electronic equipment; transport equipment; and miscellaneous manufacturing industries. As for dry cleaning, TCE has increasingly been replaced by other solvents, such as 1,1,1-trichloroethane, in metal degreasing applications but use continues as many of the replacement solvents are themselves being withdrawn from use. TCE is also used in the manufacture of polyvinyl chloride and as a solvent in the rubber and textile (dyeing and finishing) industries as well as in adhesive formulations, printing inks, paints, lacquers, varnishes and paint strippers. It has been used as both an anaesthetic and analgesic, and in the aerospace industry for flushing liquid oxygen (IARC 1995).

A UK study of 32 plants using TCE for metal degreasing found that 99% of 212 personal air samples detected TCE at levels below 537 mg/m^3, with 91% of samples at less than 161 mg/m^3 (Shipman and Whim 1980). Raaschou-Nielsen and coworkers (2003) evaluated TCE exposure data from Danish health authorities and found that TCE concentration decreased over the four decades between 1947-1989 from a geometric mean of 329 mg/m^3 to a mean measurement of 23 mg/m^3.

High TCE concentrations occurred in the iron and metal industry compared to other TCE-using industries, and men were exposed to twice the concentrations of women employed in similar plants (Raaschou-Nielsen *et al,* 2003). TCE exposure can also be identified from urinary measurements of the biomarker trichloroacetic acid although high exposure will saturate TCE metabolism and hence obscure peak exposures (Harth *et al,* 2005), and the biomarker is also a metabolite of tetrachloroethylene (Wartenberg *et al,* 2000). Occupational exposure limits for TCE in the UK were revised from 535 mg/m^3 TWA and 805 mg/m^3 STEL set in 1993 to the current limits of 550 mg/m^3 TWA and 820 mg/m^3 STEL (HSE 2007).

The most recent IARC monograph concerned with trichloroethylene (IARC 1995) states that there is limited evidence of carcinogenicity in humans but sufficient evidence in experimental animals for classification as a Group 2A carcinogen – probably carcinogenic to humans. Harth and co-workers (2005) report that trichloroethylene preferentially induces clear-cell renal carcinoma through homozygous inactivation of the von Hippel-Landau tumour suppressor gene. The IARC Working Group found that the association between kidney cancer and trichloroethylene exposure was unclear based on the results of number of cohort studies and one case-control study (Garabrant *et al,* 1988; Sharpe *et al,* 1989; Spirtas *et al,* 1991; Axelson *et al,* 1994; Anttila *et al,* 1995; Henschler *et al,* 1995; Blair *et al,* 1998; Morgan *et al,* 1998; Boice *et al,* 1999; Hansen *et al,* 2001; Raaschou-Nielsen *et al,* 2003; Charbotel *et al,* 2006), a conclusion supported by McLaughlin *et al,* (2006). The main studies are included in Table 8. Exposure to TCE rarely occurs in isolation and there is likely to be confounding from exposures to other solvents, as well as other risk factors including lifestyle effects (smoking and obesity).

The majority of cohort studies report small, usually non-significant, elevations or deficits in kidney cancer (Garabrant *et al,* 1988; Spirtas *et al,* 1991; Axelson *et al,* 1994; Anttila *et al,* 1995; Blair *et al,* 1998; Morgan *et al,* 1998; Boice *et al,* 1999; Hansen *et al,* 2001; Raaschou-Nielsen *et al,* 2003) after exposure to trichloroethylene; there is no clear evidence of exposure-response or exposure period relationships. All studies note that it is not always possible to evaluate risks from exposure to individual chemicals while controlling for other, often non-occupational, exposures. The exception is the retrospective cohort study reported by Henschler *et al.* (1995), with four cases of RCC and one case of urothelial cancer of the renal pelvis in cardboard manufacture workers employed for at least one year during 1956-1975. These cases resulted in two deaths, generating a standardised mortality ratio (SMR) of 3.3 (95% CI, 0.4-12) in comparison with the local population. However, the IARC Working Group noted that the study appeared to originate from the observation of a cluster of renal cancer cases and, hence, must be treated with caution (IARC 1995). Vamvakas *et al.* (1998) and Bruning *et al.* (2003) also reported elevated relative risks for RCC associated with TCE exposure but methodological short-comings in both studies have been identified (McLaughlin *et al,* 2006). Furthermore, Bruning and coworkers (2003) determined TCE exposure for occupations likely to involve metal degreasing as opposed to other TCE uses, generating an odds ratio of 5.57 (95% CI 2.33-13.32). Harth *et al,* (2005) suggest that the difference between the three German studies with high relatives risks (Henschler *et al,* 1995; Vamvakas *et al,* 1998; Bruning *et al* 2003) and the predominantly Scandinavian evidence of no association between TCE and renal cell cancer, was the historical difference in working conditions with no precautionary measures adopted in the small German metal manufacturing plants to limit exposure.

Table 8: Studies of trichloroethylene and kidney cancer.

Reference	Industry/ product	Country	Design	Study size	Results#
Garabrant *et al.* (1988)	Aircraft manufacture	USA	Cohort	14,067 men & women	SMR=0.93 (95% CI 0.48-1.6, 12 obs.)
Spirtas *et al.* (1991)	Aircraft manufacture	USA	Cohort	7282 men & women	SMR=1.1 (95% CI 0.46-2.1, 8 obs.)
Axelson *et al.* (1994)	TCE use – biological monitoring	Sweden	Cohort	1421 men	SIR=1.2 (95%CI 0.42-2.5, 6 obs.)
Anttila *et al.* (1995)	TCE use – biological monitoring	Finland	Cohort	3089 men & women	SIR=0.87 (95% CI 0.32-1.9, 6 obs.)
Blair *et al.* (1998) (update of Spirtas *et al.* 1991)	Aircraft maintenance	USA	Cohort	14,457 men & women	RR=1.6 (95% CI 0.5-5.1) * SMR=1.22 (95% CI 0.85-1.74, 30 obs.)
Morgan *et al.* (1998)	Aerospace workers	USA	Cohort	20,508 men & women [4733]	SMR=1.14 (95% CI 0.78 – 1.61, 32 obs.) [SMR=1.32 (95% CI 0.57-2.6, 8 obs)] *RCC and TCC*
Boice *et al.* (1999)	Aircraft manufacture	USA	Cohort	77,965 men & women	SMR=0.99 (95% CI 0.4-2.04, 7 obs) *SMR=0.92 (95% CI nr, 125 obs.) *RCC and TCC*
Hansen *et al.* (2001)	TCE use – biological monitoring	Denmark	Cohort	803 men & women	SIR(male)=0.9 (95% CI 0.2-2.6, 3 obs.) SIR(female)=2.4 (95% CI 0.03-14, 1 obs.)
Raaschou-Nielsen *et al.* (2003)	Industries using TCE	Denmark	Cohort [subcoh't of higher exposure]	40,049 men & women [14,360 subcohort]	SIR=1.2 (95% CI 0.94-1.50, 76 obs.) – RCC only SIR=1.2 (95% CI 0.8-1.8, 27 obs.) – TCC only [SIR=1.4 (95% CI 1.0-1.8, 53 obs.)]
Vamvakas *et al.* (1998)	Exposure derived from work history	Germany	Population Case-control	58 cases; 84 controls	OR=10.8 (95% CI 3.36-34.75) all exposures$
Bruning *et al.* (2003)	Exposure derived from work history	Germany	PopulationCase-control	134 cases; 401 controls	OR=2.47 (95% CI 1.36-4.49)
Henschler *et al.* (1995)	Cardboard manufacture	Germany	Retrospective cohort	169 men	SMR=3.3 (95% CI 0.40-12, 2 deaths)
Sharpe *et al.* (1989)	Work history (undefined degreasing solvents)	Canada	Case-control	164 cases, 161 controls	OR=3.4 (95% CI 0.92-13)
Charbotel *et al.* (2006)	Work history	France	Case-control	86 cases; 316 controls	OR=1.64 (95% CI 0.95-2.84) ever exposed OR=2.73 (95% CI 1.06-7.07) peak

#Considered to be RCC only unless otherwise specified

*Only workers with job descriptions indicating TCE exposure; all other workers included in second figure provided

nr = not reported

$TCE and tetrachloroethylene combined

The difference between cancer incidence and cancer mortality has also been cited as a possible explanation of the contrasting risk estimates (Hansen *et al,* 2001; Vamvakas *et al,* 1998). However, it should be noted that the three German studies were initiated in response to reports of apparent clusters of disease. It is further suggested that only high doses may be carcinogenic, with a threshold of 250 ppm (Harth *et al,* 2005). Despite the absence of a clear exposure-response gradient, intermittent or continuous low levels of exposure to TCE are non-significantly associated with increased incidence and mortality from kidney cancer whilst higher exposures result in lower cancer rates in some studies (Blair *et al,* 1998). Morgan and coworkers (1998) provide a low exposure SMR of 0.47 (95% CI 0.01-2.62) and high exposure (>50 ppm) SMR of 1.78 (95% CI 0.72-3.66). Hansen and colleagues (2001) identify a sex difference in kidney cancer incidence associated with TCE exposure (Table 8). Raaschou-Nielsen and coworkers (2003) conclude that TCE exposure leads to elevated risk for non-Hodgkin's lymphoma but not other cancers. Dosemeci and coworkers (1999) report sex differences with regard to kidney cancer and TCE exposure, with a significantly elevated association among women (OR=1.96, 95% CI 1.0-4.0) and a very small risk among men (OR=1.04, 95% CI 0.6-1.7).

A case-control study of 164 patients diagnosed with RCC identified exposure to degreasing solvents (including trichloroethylene, tetrachloroethylene, 1,1,1-trichloroethane and dichloromethane) as a potential causal factor (OR, 3.4; 95% CI, 0.92-13) (Sharpe *et al,* 1989). Charbotel *et al.* (2007) reported a significant dose-response relationship between RCC and TCE exposure taking into account confounding factors such as tobacco smoking and body mass index. High cumulative doses provided an adjusted OR of 2.16 (95% CI 1.02-4.60), which, with the inclusion of peak exposures, produced an OR = 2.73 (95% CI 1.06-7.07) However, adjusting for exposure to cutting fluids resulted in a non-significant but still high OR of 1.64 (95% CI 0.95-2.84).

TCE is also used in the nuclear industry for the processing of uranium. Total cancer mortality for uranium processers has been determined by Ritz (1999) who derived a SMR of 1.1 (95% CI 1.0-1.2). Bruning and coworkers (2003) also identified plastic product manufacture (OR 3.53, 95% CI 1.37-9.12), textile/clothing manufacturing (OR 2.12, 95% CI 0.76-5.89), transport (OR 3.16, 95% CI 1.59-6.29) and cleaning and waste disposal (OR 3.69, 95% CI 1.28-10.61) as being associated with the development of RCC.

Wartenberg *et al.* (2000) reviewed evidence for an association between TCE, as a degreasing agent and solvent, and cancer, based on all cohort and case-control studies up to the year 2000. The studies are predominantly in the iron and steel industry and dry cleaning. The review divides the cohort studies across three tiers, with Tier I studies providing the best characterisation of TCE-only exposure and Tier III the least. Citing the pre-2000 cohort and case-control studies in Table 8, the combined risk of kidney cancer is elevated in Tier 1 studies for incidence (RR=1.7, 95% CI 1.1-2.7) and mortality (RR=1.2, 95% CI 0.8-1.7) despite the lack of association reported by the authors of most of the individual studies (Axelson *et al,* 1994; Anttila *et al,* 1995; Henschler *et al,* 1995; Blair *et al,* 1998; Morgan *et al,* 1998; Boice *et al,* 1999; Ritz 1999). Tier II and Tier III incidence and mortality findings are also elevated, and support Tier I results (Blair *et al,*1980, 1989; Katz and Jowett 1981; Duh and Asal 1984; Dubrow and Gute 1987; McLaughlin *et al,* 1987; Garabrant *et al,* 1988; Blair *et al,* 1990; Lynge and Thygesen 1990; Sinks *et al,* 1992; Ruder *et al,* 1994). Wartenberg and co-workers report that the case-control studies provide further support of an association but are less robust due to limited exposure definition and potential biases. Two of the case-control studies are further discussed due to the high relative risks determined for occupations where high exposure to TCE is likely (RR=16.6, 95% CI 1.7-452.1; Sinks *et al,* 1992) or from hospital-based accident victims (OR=10.8, 95% CI 3.4-34.8; Vamvakas *et al,* 1998). However, failure to adjust for confounding and effect modification are problems associated with all the studies; direct causality cannot be assessed and exposure-response data are frequently not available. The review also notes the controversy concerning the carcinogenic status of TCE and the debate concerning the validity of the work by Henschler and co-workers (1995) and subsequent studies.

2.2.2 EXPOSURE CIRCUMSTANCES

Coke oven workers

Coke is a solid carbonaceous residue derived from low-ash, low-sulphur bituminous coal. The volatile constituents of the coal (including water, coal-gas and coal-tar) are driven off by baking in an airless oven at temperatures as high as 1000 °C. Coke is used as a fuel for use in the blast furnace for the production of steel, and has been used for the recovery of gas for use as town-gas (IARC 1984a). Chemical by-products of coke production include ammonia, naphthalene, benzene, creosote oil and toluene (Redmond 1983). Coke production is considered to be a Group 1 carcinogenic occupation (IARC 1984a). Coke-oven workers employed in iron and steel foundries are exposed to extremely high concentrations of coke combustion products, particularly polycyclic aromatic hydrocarbons (PAHs). As a result, "coke production" can be expanded to include all employment involving coke, from production to use in foundries. Considerable overlap can also be expected through consideration of PAHs as carcinogenic agents, as discussed separately below, although IARC and Siemiatycki and coworkers (2004) do not describe definite or probable associations between kidney cancer and PAH exposure. The highest exposures have been reported for workers on the topside of the coke-oven battery (IARC 1984a) and it has been suggested for lung cancer that workers in coke ovens in the iron and steel industry carry an elevated relative risk compared to coke oven workers employed in other industries (Sakabe *et al,* 1975).

Substantial airborne exposure to PAHs has been measured in various occupations associated with coke production (IARC, 1984a). Coke-oven workers in the steel industry were reported to be at an increased risk of kidney cancer by Lloyd (1971) when two cases of kidney cancer were reported in a cohort study of 3530 employees employed in a coke plant compared with an expected number of 0.6. The initial study was included in an expanded cohort of 59,000 steelworkers by Redmond and coworkers (1972) who reported a significant relative risk of kidney cancer of 7.49 in oven workers. A later study by Redmond and co-workers (1976) found a statistically significant excess of kidney cancer for all coke-plant workers (RR=4.5). A 30-year follow-up study for 15,818 individuals from the same cohorts failed to find a significant risk for kidney cancer mortality, although a relative risk cause-specific mortality among all coke oven workers of 2.03 (95% CI 0.89-4.53) was reported (Costantino *et al,* 1995). Redmond *et al.* (1981) found significant levels of kidney cancer mortality in two cohorts employed in a steel foundry (RR=2.55 and 3.68). Mandel *et al.* (1995) reported a significant association between employment in the blast-furnace or the coke-oven industries (OR 1.7, 95% CI 1.1-2.7) and renal cell cancer, and between workers in the iron and steel industry and RCC (OR 1.6, 95% CI 1.2-2.2). All reports are included in Table 9. Occupations in coke, coal, natural gas and mineral oil-related industries have also been associated with cancers of the renal pelvis and ureter (McLaughlin *et al,* 1983; Jensen *et al,* 1988).

Hurley *et al.* (1991) provide an update of earlier work concerning the mortality of two cohorts of coke workers in Britain employed in 1967. One cohort included workers employed at National Smokeless Fuels (NSF) plants (3883 men) and the second cohort were coke-oven workers in the steel industry (2790 men); both cohorts were followed for 20 years. No excess mortality from kidney cancer (defined by ICD-8 189 as other and unspecified urinary organs) was reported for either cohort: the SMR for coke-oven workers in the steel industry was reported to be 1.16 but the SMR for NSF workers showed a deficit of risk of 0.16 (1 death, 6.1 expected). Cherrie *et al.* (2007) reviews exposures of coke oven workers in the UK and USA and identifies differences in exposure levels. Exposures from UK coke ovens ranged from 0.5–2.2 mg/m^3 across job categories; US coke oven workers had higher equivalent exposures in the range 0.9-3.2 mg/m^3.

Table 9: Studies of coke oven workers and kidney cancer, including PAH exposure case-control studies.

Reference	Industry/ product	Country	Design	Study size	Results
Lloyd (1971)	Coke-oven workers	USA	Cohort	3530	2 cases/0.6 expected
Redmond *et al.* (1972)	Coke-oven workers	USA, Canada	Cohort	4661	RR=7.49 (8 cases/2.6 exp) – kidney RR=2.05 (21/13.3) – genitor-urinary
Redmond *et al.* (1976)	Coke-oven workers	USA	Cohort	(update of Lloyd (1971))	RR=4.50 (6/1.6)
Davies (1977)	Coke-oven workers	Wales	Cohort	610	SMR=2.52 (3 deaths)
Redmond *et al.* (1981)	Coke-oven workers	USA	Cohort	(update of Redmond *et al.* (1972))	RR=3.55 (6/1.8)
Hurley *et al.* (1991)	Coke-oven workers	UK	Cohort	2790 3883	SMR=1.16 SMR=0.16 (1/6.1)
Costantino *et al.* (1995)	Coke-oven workers	USA	Cohort	15,818 workers	RR=2.03 (95% CI 0.89-4.53, 12 obs)
Mandel *et al.* (1995)	Blast furnace & coke ovens	Australia, Denmark, Germany, Sweden, USA	Case-control	57/40	RR=1.7 (95% CI 1.1-2.7)

2.3 OTHER EXPOSURES

2.3.1 AGENTS OR GROUPS OF AGENTS

Tetrachloroethylene and other solvents

A number of other solvents have also been suggested as associating with an increased risk of RCC. Tetrachloroethylene is mainly associated with laundry and dry cleaning activities, with about 75% used as a cleaning fluid and the reminder as a chemical intermediate, metal degreasant and other uses such as in paint removers, printing inks, adhesives etc. (Linak *et al*, 1992; McLaughlin *et al*, 2006). Also known as perchloroethylene, tetrachloroethylene (tetraCE) is considered by IARC to be a Group 2A carcinogen – probably carcinogenic to humans (IARC 1995). Identified as one of the degreasing solvents associated with RCC in the case-control study reported by Sharpe *et al*, (1989), several cohort studies also report an association between tetraCE and kidney cancer. Anttila *et al* (1995) and Ruder *et al.* (1994; 2001) evaluated workers predominantly exposed to tetraCE and reported slightly elevated RCC risks with a standardised incidence ratio (SIR) of 1.8 (95% CI 0.22-6.6) and SMR of 1.2 (95% CI 0.03-6.5), respectively. Boice *et al.* (1999) reported a non-significant SMR of 0.69 (95% CI 0.08-2.47) for tetraCE and kidney cancer (cancer of the renal cells and renal pelvis). Blair *et al.* (1990; 2002) reported a SMR of 0.5 (95% CI 0.1-1.8) for occupational exposures to dry cleaning solvents and RCC; although specific exposures were not accounted for, tetraCE was the dominant cleaning agent. Mundt *et al.* (2003) concluded that epidemiological evidence for an association between tetraCE and kidney cancer was inadequate, while Schlehofer and colleagues (1995) reported an elevated risk associated with exposure to tetraCE and carbon tetrachloride (OR 2.52, 95% CI 1.2-5.2).

Sharpe *et al.* (1989) also included 1,1,1-trichloroethane and dichloromethane exposures in the case-control study for RCC (see Table 8). Blair *et al.* (1998) included methylene chloride, chloroform, carbon tetrachloride and other solvents alongside TCE and tetraCE in their study of cancer incidence and mortality of aircraft maintenance workers but did not report incidence/mortality for kidney cancer. Boice *et al.* (1999) considered the exposure of aircraft manufacturing workers to mixed, but undefined, organic solvents other than TCE and tetraCE and mortality from kidney cancer, reporting a SMR of 0.81 (95% CI 0.44-1.36) for this comparison.

Renal cell carcinoma has also been associated with exposure to other industrial solvents such as benzene (Brautbar *et al,* 2006), pentachlorophenol (Friesen *et al,* 2007; Demers *et al,* 2006) and other chlorinated aliphatic hydrocarbons (Dosemeci *et al,* 1999). Dosemeci *et al.* (1999) examined sex differences in renal cell carcinoma and exposure to solvents and chlorinated aliphatic hydrocarbons. They report significantly elevated risks associated with exposure to all organic solvents combined (OR=2.3, 95% CI 1.3-4.2) and all chlorinated aliphatic hydrocarbons (OR=2.1, 95% CI 1.1-3.9); non-significant excess risks are also reported for 1,2-dichloroethane, chloroform, carbon tetrachloride and methyl chloroform. Among men, little or no excess risk of RCC was associated with any or a combination of solvents or chlorinated aliphatic hydrocarbons.

Asbestos

Asbestos is an important occupational lung carcinogen but its use has been increasingly restricted, as its dangers became known. All forms of asbestos, serpentine (chrysotile) and amphiboles (crocidolite, amosite, tremolite, etc.) are carcinogenic to humans, although the potency of chrysotile might be lower than that of other types (IARC, 1977; 1987; IPCS, 1998). Asbestos has been linked to kidney cancer in two cohort studies (Selikoff *et al,* 1979; Enterline *et al,* 1987) and a number of case-control studies (Mandel *et al,* 1995; Pesch *et al,* 2000; Mattioli *et al,* 2002; Bruning *et al,* 2003). However, a meta-analysis of occupational studies of asbestos-exposed workers cohorts revealed no increased risk for kidney cancer (Sali and Boffetta, 2000). This is supported by several other case-control studies (McLaughlin *et al,* 1984; Asal *et al,* 1988; Brownson *et al,* 1988; Partanen *et al,* 1991). Mandel and colleagues (1995) reported a significant association between occupational exposure to asbestos and RCC (OR 1.4, 95% CI 1.1-1.8).

Heavy metals

Among mercury miners, rates of kidney cancer have been found to be lower than expected (Gomez *et al,* 2007). A recent review of seven epidemiological and eleven clinical studies identified a possible association between occupational exposure to cadmium and renal cancer but a meta-analysis could not adjust for cadmium exposure derived from smoking or diet (Il'yasova and Schwartz, 2005). Mandel *et al.*(1995) reported a significant association between RCC and cadmium exposure (OR 2.0, 95% CI 1.0-3.9). Occupational exposure to lead has also been associated with kidney cancer (Fu and Boffetta 1995; Pesch *et al,* 2000). Boice *et al.*(1999) do not report an association between kidney cancer and chromate exposure (SMR 1.19, 95% CI 0.48-2.45). Associations with heavy metal exposure have thus not been consistently seen and most studies have not shown a dose-response relationship where an association has been identified (McLaughlin *et al,* 2006).

Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are formed by the incomplete combustion of carbon-containing fuels such as wood, coal, diesel, fat or tobacco. Workers are exposed by inhalation, ingestion and dermal contact with inhalation the main route of exposure. PAHs are produced in a number of occupational settings, including coal gasification, coke production, coal-tar distillation, chimney sweeping (soots), coal tar and pitches, creosotes, and others (IARC 1984a-c, 1985), most of which have been classified by IARC as Group 1 carcinogenic situations. PAHs are common constituents of many occupational exposures, including soot and tar, untreated and mildly treated

mineral oils, coke or iron steel foundries; findings of an association should be considered to be indirect evidence of the carcinogenic effects of PAHs (IARC 1987; Mastrangelo *et al,* 1996). However, diesel and gasoline engine exhausts are considered separately below, as the carcinogenicity of diesel is associated with the particulate phase rather than PAHs.

Boffetta and coworkers (1997) reviewed a number of cohort and case-control studies for associations between PAH exposure, more particularly occupations where PAH exposure is likely, and kidney cancer. Coke production and associated iron/steel foundry employment are considered separately due to specific citation by IARC and Siemiatycki *et al.* (2004) (Tables 9 and 11). They also identified cohort studies reporting slightly elevated levels of kidney cancer in workers in the aluminium industry (Andersen *et al,* 1982; Rockette and Arena 1983; Spinelli *et al,* 1991; Ronneberg *et al,* 1995).

Diesel, gasoline and engine exhausts

Diesel engine exhaust (DEE) is a complex mixture of substances characterised by polycyclic aromatic hydrocarbons (PAHs) surrounding an elemental carbon core. The gas phase includes PAHs but it is the particulate phase of the exhaust that appears to be implicated as the carcinogen. IARC (1989b) consider DEE to be a Group 2A carcinogen. IARC (1989a) classified diesel fuel (marine) as a Group 2B carcinogen, along with gasoline and gasoline engine exhaust. Jet fuels are considered a Group 3 carcinogen – not classifiable as to carcinogenicity to humans. Although associations have been made with lung and bladder cancer, a relationship with kidney cancer mortality has not been reported (IARC 1989b). Professional drivers, mechanics, railway employees, public transport workers and other related occupations are exposed to elevated levels of emissions from combustion engines. One pathway of effect of DEE is provided by the concentration of PAH metabolites in urine and interactions with the urothelium of the urinary bladder (Silverman *et al,*, 1986); it is a suggested mechanism for urinary bladder cancer and hence, by extrapolation of cell type, to the renal pelvis and ureter.

A number of cohort and case-control studies have evaluated the association between kidney cancer and occupations expected to be exposed to diesel exhaust. Siemiatycki *et al.* (1988) did not find a relationship between kidney cancer and diesel exhaust but Bruning *et al.* (2003) do report an association between both PAHs and diesel fuel with RCC (for low exposures: OR=2.60, 95% CI 1.23-5.47; OR=2.23, 95% CI 1.02-4.89 respectively; for high exposures: OR=2.38, 95% CI 1.17-4.82; OR=3.27, 95% CI 1.57-6.81 respectively). Guo *et al.* (2004) followed a cohort of 667,000 male and 513,000 female economically active Finns born between 1906 and 1945. They found a slight elevation of relative risk for kidney cancer in males at the lowest level of cumulative exposure to DEE (RR=1.17, 95% CI 1.05-1.3) attributed to drivers, but found no increase at higher exposure levels (RR=1.06, 95% CI 0.82-1.36).

Experimentally, gasoline was suspected to be a causal factor in renal cell cancer when male rats exposed long-term to unleaded gasoline vapours developed a significant excess of renal cancers (MacFarland *et al,*, 1984). However, a number of case-control and cohort studies have not found an association between gasoline vapour exposure and kidney cancer (Domiano *et al,* 1985; Wong *et al,* 1993; McCredie and Stewart 1993; Lewis *et al,* 2003). The case-control study reported by Siemiatycki *et al.* (1987) reported an adjusted odds ratio of 3.1 (90% CI 1.5-6.5) for kidney cancer among men exposed to aviation gasoline, with indication of a dose-response relationship. A population-based case-control study reported by Siemiatycki *et al.* (1988) involving 3726 cancer patients in Montreal showed a marginally elevated odds ratio of 1.4 (90% CI 1.2-2.5) for kidney cancer with long-term high-level exposure to gasoline engine exhaust. Mandel *et al.*(1995) reported a similar odds ratio of 1.6 (95% CI 1.2-2.0) for RCC and gasoline exposure. Guo *et al,* (2004) did not find an elevated risk ratio for gasoline engine exhaust and kidney cancer. Occupational exposure in petroleum refining and similar employment is also considered below.

Other agents

Kidney cancer has been associated with a range of causal agents but few of the studies beyond the individual agents or groups of agents discussed in the sub-sections above have shown consistent relationships with RCC or even TCC incidence/mortality. Polychlorinated biphenyls, cutting oils, aromatic amines and tar are some of the agents for which associations with kidney cancer have been reported but for which evidence is inconsistent or lacking (Shalat *et al,* 1989; Bruning *et al,* 2003).

2.3.2 EXPOSURE CIRCUMSTANCES

Dry cleaning

As discussed earlier in section 2, a number of organic solvents have been used in the dry cleaning industry (IARC 1995), including trichloroethylene and tetrachloroethylene. As such, there may be some overlap between the cohort and case-control studies reported although studies among dry cleaners are less specific to TCE exposure than other occupational exposures due to the pre-1960 use of TCE. For dry cleaning, there are four cohort and four case-control studies that have evaluated the relationship between kidney cancer and occupational exposure (McLaughlin *et al,* 1987; Asal *et al,* 1988; Blair *et al,* 1990; Lynge and Thygesen 1990; Siemiatycki 1991; McCredie and Stewart 1993; Mellemgaard *et al,* 1994; Ruder *et al,* 1994). Blair *et al.* (1990) report an SMR of 0.5 (95% CI 0.1-1.8) for US dry cleaners while Lynge and Thygesen (1990) and McLaughlin and coworkers (1987) report incidence deficits for kidney cancer in cohorts of Danish (SIR=0.9, 95% CI 0.4-1.6) and Swedish (SIR=0.9, 95% CI 0.7-1.2) launderers/dry cleaners, respectively. Only Ruder *et al.*(1994) report elevated mortality from kidney cancer for a US cohort of 1701 dry cleaners (SMR=1.5, 95% CI 0.4-3.7). The case-control studies (Table 10) indicate an increase in risk associated with a history of work as a dry cleaner; McCredie and Stewart (1993) provide odds ratios for both RCC and cancer of the renal pelvis. A proportional mortality study of dry cleaners and laundry workers in the US reported a SMR of 3.8 (95% CI 1.9-7.6) for renal cancer, although exposure was largely to petroleum-based solvents (Duh and Asal 1984). Furthermore, Mandel *et al.* (1995) report a significant association between RCC and dry-cleaning solvents (OR 1.4, 95% CI 1.1-1.7).

Table 10: Case-control studies for renal cancer and occupational employment as dry cleaners/launderers. All risk estimates adjusted for age and smoking.

Reference	Industry/product	Country	Study size (Cases/controls)	Odds ratio (95% CI)
Asal *et al.* (1988)	Pop-based, predominantly dry cleaning	USA	315 cases (M&F) / 336 controls (M&F)	M: 0.7 (0.2-2.3) F: 2.8 (0.8-9.8)
Siemiatycki (1991)	Pop-based, employment in laundry/dry cleaning	Canada	177 cases / 2481 controls (male)	Any exp: 2.0 (0.8-5.1) High: 2.1 (0.5-9.2)
McCredie & Stewart (1993)	Pop-based, any employment in dry cleaning	USA	F:179/292 M:310/231 F:89/292 M:58/231	F: 2.7 (1.1-6.7) RCC M: 2.5 (0.97-6.4) RCC F: 6.1 (2.0-19) TCC M: 4.7 (1.3-17) TCC
Mellemgaard *et al.* (1994)	Pop-based, any employment	Denmark	M:226/237 F:142/159	M: 2.3 (0.2-27) F: 2.9 (0.3-33)

Iron and steel founding

Several studies have suggested an association between employment in iron/steel founding and kidney cancer. There are a number of foundry operations, each providing exposures to a variety of agents including airborne crystalline silica, metallic fumes, metal dusts, ingredients used in organic binders and PAHs.

Boffetta *et al.* (1997) report four cohort studies that identified slightly elevated relative risks of kidney cancer associated with employment in iron and steel foundries (Breslin 1979; Decoufle 1979; Andjelkovich *et al,* 1990; Sorahan *et al,* 1994). Four case-control studies showing elevated risk of kidney cancer with PAH exposure are also reported (Jensen *et al,* 1988; Sharpe *et al,* 1989; Partanen *et al,* 1991; Mandel *et al,* 1995). However, the authors urge caution as the few strongly positive results reported may lead to reporting bias. The Sorahan *et al.* study (1994) is the larger of the studies reviewed by Boffetta *et al.* including over 10,000 workers from nine steel foundries in the UK employed between 1946 and 1965. Mortality of the workers was followed for the period 1946-1990 inclusive, with 24 cases of kidney cancer observed (described as "other urinary" cancer), generating a relative risk of 1.34 (95% CI 0.86-2.0). The relative risk estimate includes all workers employed at the foundries. Mandel *et al.* (1995) reported a significant association between employment in the iron and steel industry (OR 1.6, 95% CI 1.2-2.2) and renal cell cancer.

Table 11: Studies of foundry workers and kidney cancer, including PAH exposure case-control studies.

Reference	Industry/ product	Country	Design	Study size	Results#
Breslin (1979)	Steel foundries	USA	Cohort	2167 male workers	RR=1.6 (95% CI 0.4-4.1, 4 obs)
Decoufle and Wood (1979)	Iron foundry	USA	Cohort	2861 male workers	RR=1.6 (95% CI 0.3-4.6, 3 obs)
Andjelkovich *et al.* (1990)	Iron foundry	USA	Cohort	8147 male workers	RR=1.1 (95% CI 0.5-2.1, 9 obs)
Sorahan *et al.* (1994)	Steel foundries	UK	Cohort	10,438 male workers	RR=1.34 (95% CI 0.86-2.0, 24 obs)
Jensen *et al.* (1988)*	Asphalt, tar Coke, coal	Denmark	Case-control	60/180	OR=5.5 (95% CI 1.6-20) OR=4.0 (95% CI 1.2-14)
Sharpe *et al.* (1989)	Tar, pitch	Canada	Case-control	164/161	OR=9.3 (95% CI 1.2-74)
Partanen *et al.* (1991)	PAH	Finland	Case-control	338/484	OR= 1.1 (95% CI 0.4-3.1)
Mandel *et al.* (1995)	Iron & steel	Australia, Denmark, Germany, Sweden, USA	Case-control	113/87	RR=1.6 (95% CI 1.2-2.2) – iron & steel

*Renal pelvis and ureter cancer only. All other studies are renal cell cancer or unspecified kidney cancer.

Petroleum industries

As the earlier section concerning exposure to diesel and gasoline exhaust gases describes, there is limited evidence that employment in the petroleum and related industries is associated with elevated risks of kidney cancer. Reports of case-control and cohort studies generally do not reveal

significant associations with RCC (Rushton, 1993; Schnatter *et al,* 1993; McCredie and Stewart 1993; Gamble *et al,* 1996; Lewis *et al,* 2003). Several cohort studies do record elevated SMRs for kidney cancer. Hanis *et al*. (1982) report a SMR of 1.6 in 8666 workers in a US oil refinery and chemical plant, which increases to SMR = 2.1 when only operators, mechanics and labourers are considered. An updated cohort study of 15,437 workers for the same plant plus two further refineries provides an average SMR of 1.2 and directly adjusted death rates for renal cancer were consistently higher than those for the total US population in each of the three plants (Hanis *et al,* 1985; IARC 1989a). Thomas *et al*. (1982) reported a proportionate mortality ratio of 1.4 for kidney cancer in a cohort of 2509 male union members employed at three Texan refineries, and Divine and Barron (1986) calculated a SMR of 1.3 for maintenance workers in a cohort of 18,798 US refinery workers employed >5 years. Wen *et al*. (1983; 1984) report two cohort studies from the same Texan oil refinery, one study including 15,095 men and the second a cohort of 12,526 retired white men, generating SMRs of 1.1 (all workers) and 1.4 (actively employed workers), respectively. Hanis *et al*. (1979) in a cohort study of 5731 male employees at a Canadian refinery, report a combined SMR for bladder and kidney cancer of 1.2; all reported elevated relative risks for kidney cancer were non-significant. Magnani *et al*. (1987) found a significantly elevated odds ratio for an association between kidney cancer and occupational exposure to petroleum refining in a case-control study involving 147 cases and 556 controls: the odds ratio was not provided. IARC (1989a) found that evidence was inadequate for a relationship between kidney cancer and employment in petroleum refining and similar industries. Enterline and Viren (1985) reviewed 12 cohort studies of oil refinery workers and petroleum product distribution employees, and determined that there was evidence of a small excess of kidney cancer in older workers or workers exposed for long periods. Pukkala (1998) found a significant excess of kidney cancer in males, which was highest among men with at least 5 years of employment in oil refineries (SIR 2.8; 95% CI, 1.6-4.7).

Similarly, exposure to jet fuels and other exhaust agents in the aviation industry did not show an association with risk of kidney cancer (Spirtas *et al,* 1991). Increased risk of TCC (cancers of the renal pelvis and ureter) have been reported for petroleum refining and petrochemical industries among other occupational exposures (Jensen *et al,* 1988; McCredie and Stewart 1993).

Aviation industry

Employment within the aviation industry may lead to exposure to fuels and exhausts as well as organic solvents, substances which have been implicated as causal agents for kidney cancer, especially renal cell adenocarcinoma. Aircraft maintenance workers and mechanics would be expected to be the most likely to be exposed to fuel and exhaust vapours, while certain workers involved in aircraft manufacture will be exposed to organic solvents such as TCE and tetraCE. The preceding sections regarding fuel and solvents, including exposure in the petroleum industry, are therefore applicable and many of the risk estimates provided therein refer to employment within the aviation industry (Blair *et al,* 1998; Morgan *et al,* 1998; Boice *et al,* 1999).

Other employment

Ji *et al*. (2005) found an increased risk of renal cell cancer associated with miners and quarry workers, drivers, sales agents, transport workers, and sex-differentiated associations for public safety workers (men) and dry cleaners/launderers (women). Renal pelvis cancer was associated with male food manufacture workers and female workers in shoe and leather manufacturer industry and journalism. Unspecified kidney cancer was linked to male forestry workers, smelters and metal foundry workers. While smoking may explain the associations identified, exposure to gasoline, diesel, dry-cleaning products and other chemicals cannot be discounted.

Other occupational associations with renal cell cancer include newspaper pressmen (Paganini-Hill *et al,* 1980), physicians (McLaughlin *et al,* 1987), truck drivers (Brownson 1988), architects (Lowery *et al,* 1991), paperboard printing workers (Sinks *et al,* 1992), firefighters (Guidotti 1995), pulp and paper mill workers (Band *et al,* 1997) and commercial airline pilots and navigators (Nicholas *et al,* 1998).

Cancers of the renal pelvis and ureter have frequently been included in cohort studies of renal cell cancer without explicit definition. However, Olsen and Jensen (1987) report elevated risks for cancer of the renal pelvis and ureter in a number of industries including forestry and logging, meat production/preservation, and printing and publishing. McLaughlin *et al*. (1987) report significant excess risk among machinists and plumbers: neither study adjusts for smoking. Elevated risk of TCC has been reported for the leather industry (Schmauz and Cole, 1974) but has not been confirmed by later studies (Armstrong *et al,* 1976). McCredie and Stewart (1993) found associations with iron and steel industries while Jensen *et al*. (1988) reports a relationship with occupation in chemical and plastics industries.

3 ATTRIBUTABLE FRACTION ESTIMATION

3.1 GENERAL CONSIDERATIONS

Substances and Occupations
The substances considered in the estimation of the attributable fraction (AF) for cancer of the kidney are those outlined in Table 12.

Table 12: Substances considered in the estimation of the attributable fraction for kidney cancer (Group 1 and 2A carcinogens only)

Agents, mixture, circumstance	AF calculation	Strength of evidence	Comments
Group 1: carcinogenic to humans			
Agents, groups of agents			
None specified			
Exposure circumstances			
Coke production	No	Suggestive	
Group 2A: probably carcinogenic to humans			
Agents, groups of agents			
Trichloro-ethylene	Yes	Suggestive	Possible co-exposure with tetrachloroethylene and use in iron/metal industry
Exposure circumstances			
None specified			

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 point estimate 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 kidney cancer, Great Britain, 2005 = 2145 for men aged 25+ (1952 in England and Wales, 193 in Scotland), 1354 for women aged 25+ (1168 in England and Wales, 186 in Scotland)

- Total registrations for kidney cancer, Great Britain, 2004 = 4192 for men aged 25+ (3524 in England, 266 Wales, 402 in Scotland), 2567 for women aged 25+ (2134 in England, 165 Wales, 268 in Scotland). 2004 is the most recent year for which data are available. Due to the way incidence and mortality of kidney cancer are reported, it is not possible to separate renal cell cancer from cancer of the renal pelvis and cancers of the ureter and, frequently, the urethra. When a RR for kidney cancer is reported, it is usually, but not always, referring to renal cell cancer only. Hence, there may be a margin of error in the AF calculation.

  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.

3.2 TRICHLOROETHYLENE AND OTHER SOLVENTS

(a) Risk estimate:

A number of cohort and case-control studies have evaluated the association between TCE exposure in occupations involving use of TCE as a dry cleaning agent and as a metal degreasant (in aerospace, cardboard and other industries) and incidence of/mortality from kidney cancer. Wartenberg and coworkers (2000) evaluate many of these studies, including 20 cohort and 40 case-control studies, dividing the cohort studies into three tiers based on the specificity of the exposure

information. Tier 1 studies are those which provide the best characterisation of TCE exposure through the use of biomarkers and job-exposure matrices. Across the Tier 1 studies, an average standardised incidence ratio (SIR) of 1.7 (95% CI 1.1-2.7) and an average standardised mortality ratio (SMR) of 1.2 (95% CI 0.8-1.7) were obtained. As the SIR and SMR were derived from the studies Wartenberg and coworkers identify as the best quality cohort studies with sufficient follow-up periods (17-38 years), the values are particularly suitable for use as estimates of relative risk (RR) for attributable fraction (AF) calculation. It must be noted, however, that the risk estimates have some limitations. Firstly, the calculated risk is dependent upon the selection of cohorts in each tier. As the methodology reported by Wartenberg and colleagues is suitably robust and the studies used are highly regarded, it can be assumed that this limitation has a minimal effect on the reliability of the estimate. It must be noted that the risk estimates obtained through case-control studies are much higher than the risks from cohort studies, a point recognised by Wartenberg and colleagues. Secondly, there is no adjustment for confounders. This is common to the majority of epidemiologic studies evaluating the association between TCE exposure and kidney cancer due to the difficulty in separating TCE exposure from exposures to other organic solvents including tertrachloroethylene. As such, it is perhaps more accurate to define the exposure as being to organic solvents including TCE. Other confounding variable such as smoking, alcohol consumption and other 'lifestyle' confounders are rarely considered by any of the studies, making the Wartenberg. risk estimate no better or worse than other risk estimates. Few studies provide any indication of a dose-response relationship between TCE-dominated organic solvent exposure and kidney cancer, so the Wartenberg and co worker estimates do not simplify what would otherwise be more complex data.

Another important factor to note is that the Tier 1 studies used to derive a SMR of 1.2 are derived from cohort studies of occupations using TCE as a metal degreasant (in the aerospace/aviation industry, cardboard manufacture, etc.) and in uranium processing (Ritz, 1999). Whilst use of TCE in dry cleaning declined from the late 1950s, it remains an important exposure scenario. The results obtained from cohort and case-control studies vary quite considerably, with most cohort studies showing a deficit of kidney cancer for workers in dry cleaning services (McLaughlin *et al*, 1987; Blair *et al*, 1990; Lynge and Thygesen 1990) and all case-control studies showing an excess of kidney cancer (Asal *et al*, 1988; Siemiatycki 1991; McCredie and Stewart 1993; Mellemgaard *et al*, 1994; Mandel *et al*, 1995). Only Ruder *et al*. (1994) reports an elevated risk of kidney cancer for a US cohort of 1701 dry cleaners (SMR=1.5, 95% CI 0.4-3.7). As all the studies include exposure to a combination of organic solvents, of which TCE may be a component, it is difficult to determine whether TCE is the causal factor. Based on the uncertainty of exposures and the significant variation in relative risk estimates, it is advisable that the SMR calculated by Wartenberg and coworkers also be applied to dry cleaners and launderers.

Renal cell carcinoma due to occupation is most usually associated with exposures to TCE (IARC 1995; Siemiatycki *et al*, 2004) but there are reports of transitional cell carcinoma in the renal pelvis and ureter (Henschler *et al*, 1995). As there is some uncertainty regarding the definition of kidney cancer, the wider definition of cancer of the kidney (ICD-10 C64-C66, C68; ICD-9 189) will be used for attributable risk estimation. The 'higher exposures' group can thus be assigned a relative risk of 1.2 (95% CI 0.8-1.7), based on the average SMR calculated by Wartenberg *et al*. (2000). 'Low exposures' have been set to 1 based on the study by Morgan *et al*. (1998), which gave a low exposure SMR of 0.47 (95% CI 0.01-2.62).

(b) Numbers exposed:

The numbers of workers exposed to TCE in various industries according to CAREX for 1990-93 are given in Table 13. Exposures in the manufacture of finished metal products were allocated to the 'higher' category, as it was assumed that these occupations were where use of TCE as a metal degreasant was more likely. The textile industry may also have been exposed to TCE as a 'spot cleaning' agent, along with dry cleaners who were considered to fall in the personal and household services category. TCE used in dry cleaning until 1950s/1960s when predominant use was as a metal degreasant. Use as a solvent for oils/resins is less common. Despite declining popularity

during early part of current burden assessment (1956-1996), the classification 'high' has been allocated to dry cleaners.

Workers in the metal manufacturing industries can be expected to be predominantly male but clothing manufacture will include a high proportion of women. However, as only 117 workers were recorded as being exposed to TCE in clothing manufacture, it can be assumed that 99% of workers in the manufacturing industries are male. It has been assumed that 25% of service workers were male, based on numbers of drycleaners/launderers provided in the LFS 1979-2003 (19% male workers in 1979, 25% in 1991 and increasing to 38% in 2003). These data were used to estimate Pr(E) for Levin's calculation of AF.

Table 13: Numbers of workers exposed to trichloroethylene according to CAREX in 1990-1993

Main sector industry	Industry		CAREX Data 1990-1993		% Exposed	Exposure Level
			Number Exposed	Number in Industry		
C-E	Beverage industries		92	88,100	0.104	L
	Tobacco manufacture		40	9,950	0.402	L
	Manufacture of wearing apparel, except footwear		117	189,500	0.062	H
	Manufacture of leather and products of leather or of its		8	16,825	0.048	L
	Manufacture of glass and glass products		130	43,275	0.300	L
	Manufacture of other non-metallic mineral products		50	70,875	0.071	L
	Manufacture of fabricated metal products, except machinery and equipment		2139	292,200	0.732	H
	Manufacture of machinery except electrical		3041	692,275	0.439	H
	Manufacture of electrical machinery, apparatus, appliances		1852	473,750	0.391	H
	Manufacture of transport equipment		2949	456,900	0.645	H
G-Q	Sanitary and similar services		117	274,225	0.043	L
	Education services		122	1,455,875	0.008	L
	Research and scientific institutes		88	91,100	0.097	L
	Recreational and cultural services		74	534,600	0.014	L
	Personal and household services		5517	686,750	0.803	H
	Total		**16,336**	**5,376,200**		
	Main Industry Sector			**Male %**		
A-B	Agriculture, hunting and forestry; fishing		0	0		
C-E	Mining/quarrying, electricity/gas/steam, manufacturing industry	High Low	10,098 320	99 99		
F	Construction		0	0		
G-Q	Service industries	High Low	5517 401	25 25		

(c) AF calculation:

The estimated total (male and female) attributable fraction for kidney cancer associated with occupational exposure to trichloroethylene is 0.04% (95%Confidence Interval (CI)=0.00-0.15), which equates to 1 (95%CI=0-5) death, and 3 (95%CI =0-10) registrations. The estimated AF for men is 0.04% (95%CI=0.00-0.16) resulting in 1 (95%CI=0-3) attributable death and 2 (95%CI=0-7) attributable registrations and for women is 0.04% (95%CI=0.00-0.14) resulting in 1 (95%CI=0-2) attributable death and 1 (95%CI=0-4) attributable registration (Table 14).

Table 14 Summary results for occupational exposure to trichloroethylene

				Data		Calculations				Attributable Fraction (Levins[8]) and Monte Carlo Confidence Interval			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	Wartenberg *et al*. 2000)	H	C-E	1.2	7674	1.4	0.09	37122	0.0019	0.0004	0.0000	0.0014	1	0	3	2	0	6
		H	G-Q	1.2	1379	0.9	0.11	5186	0.0003	0.0001	0.0000	0.0002	0	0	0	0	0	1
		H	All		9054			42308	0.0022	0.0004	0.0000	0.0016	1	0	3	2	0	7
	Morgan *et al*. (1998)	L	C-E	1	243	1.4	0.09	1176	0.0001	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	G-Q	1	100	0.9	0.11	377	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		343			1553	0.0001	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		9397			43861	0.0023	0.0004	0.0000	0.0016	1	0	3	2	0	7
Women	Wartenberg *et al*. (2000)	H	C-E	1.2	2424	1.5	0.14	20388	0.0010	0.0002	0.0000	0.0007	0	0	1	1	0	2
		H	G-Q	1.2	4138	0.8	0.15	19813	0.0009	0.0002	0.0000	0.0007	0	0	1	0	0	2
		H	All		6561			40201	0.0019	0.0004	0.0000	0.0014	1	0	2	1	0	4
	Morgan *et al*. (1998)	L	C-E	1	77	1.5	0.14	646	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	G-Q	1	301	0.8	0.15	1440	0.0001	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		378			2086	0.0001	0.0000	0.0000	0.0000	0	0	0	0	0	0
		All	All		6939			42288	0.0020	0.0004	0.0000	0.0014	1	0	2	1	0	4

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 equation 1

3.3 COKE OVEN WORKERS

(a) Risk estimate:

Siemiatycki and coworkers (2004) report the association between employment in the coke production industry and kidney cancer incidence and mortality. It can be presumed that the causal agents that may be associated with kidney cancer are present at both coke production and evolved during its use. Polycyclic aromatic hydrocarbons (PAHs), a diverse group of organic chemicals with carcinogenicity classifications varying from Group 1 to Group 3, are emitted during coke production and combustion in iron/steel foundries. However, as there are few reports of a direct association between PAH exposure and kidney cancer, it is not possible to derive a relative risk estimate for PAH as a causal factor.

There is considerable variation in the risk estimates provided by the different cohort studies summarised in Table 9. The highest relative risks for kidney cancer are provided by a number of studies that assessed coke oven workers in US/Canadian steel foundries, with SMRs from 2.03 to 7.49 (Lloyd 1971; Redmond *et al,* 1972, 1976, 1981; Costantino *et al,* 1995). Costantino and coworkers (1995) provide an update of all earlier US/Canadian steel industry studies and obtained a non-significant relative risk for kidney cancer mortality of 2.03 (95% CI 0.89-4.53) for coke oven workers employed at ten steel foundries in the USA from a cohort of 15,818 workers employed from 1951 to 1955, followed through to 1982. The two UK-based studies provide very different relative risk estimates, with Davies (1977) reporting a SMR for kidney cancer in coke-oven workers of 2.52 and Hurley *et al*. (1991) providing a SMR for each of the two cohorts (covering most of the UK industry) included in their report - a risk of 1.16 for coke-oven workers employed in the steel industry and a risk of 0.16 for coke oven workers at National Smokeless Fuels plants. It is preferable to adopt a UK-derived risk estimate due to the different working practice existing in the UK compared to other countries such as the USA and, as a consequence, the different levels of exposure experienced by UK and US workers (Cherrie *et al*, 2007; Hurley *et al*, 1983). Therefore, either the Davies (1977) or Hurley *et al*. (1991) studies are the most relevant. The Davies (1977) study is based on a small cohort of 610 employees of two Welsh steel plants employed between 1954 and 1965, while the Hurley *et al* (1991) study evaluates mortality in two large cohorts of 2790 and 3883 coke oven workers employed in 1967 and followed for 20 years. Based on cohort size and period of follow-up, it is more accurate to adopt the risk estimate provided by the Hurley *et al* (1991) study. However, two risk estimates are provided, one showing a slight elevation of risk of kidney cancer (SMR = 1.16) and one showing a considerable deficit (SMR = 0.16); 95% confidence intervals are not reported. If the two cohorts are combined, there is no overall indication of an excess of kidney cancer (SMR = 0.58). As the combined SMR is less than 1, it is not necessary to carry out an AF calculation for coke oven workers.

(b) Numbers exposed:

The numbers of workers employed in coke ovens in 1979 according to the LFS are provided in Table 15. This number differs from the numbers reported by Cherrie *et al*. (2007) shown in Table 16 who estimate 9500 workers in 1970 and 500 in 1993. However, the coke production industry went into steep decline in the 1970s and it is very likely that the LFS figure (Table 15) can be used interchangeably with the numbers provided in Table 16. The current burden exposure period is from 1956 to 1996, during which time there has been a considerable fall in the numbers of workers employed in coke production industries from approximately 20,000 in 1956 to less than 500 in 1996. Currently, there are only a few coke plants operating in the UK, mostly associated with the steel industry (Coke Oven Managers Association, 2008). All employees are male (Table 14).

(c) AF calculation:

An AF calculation is not provided as the relative risk for coke oven workers is less than 1.

Table 15: Numbers of workers employed in coke ovens according to the Labour Force Survey

SIC or SOC	Description	Men	Women	Total
1979				
159.3	Foremen of labourers and other unskilled workers in coke ovens and gas works	0	0	0
160.3	Labourers and other unskilled workers in coke ovens and gas works	802	0	802
Total		**802**	**0**	**802**

Table 16: Numbers of workers employed in coke ovens 1924-1993 (after Cherrie *et al,* 2007)

Year	Workers
1924	19100
1930	15600
1935	13800
1948	17200
1949	17600
1950	17200
1951	17300
1954	18300
1958	19900
1963	15400
1968	14500
1970	9500
1993	500

4 OVERALL ATTRIBUTABLE FRACTION

4.1 EXPOSURE MAP

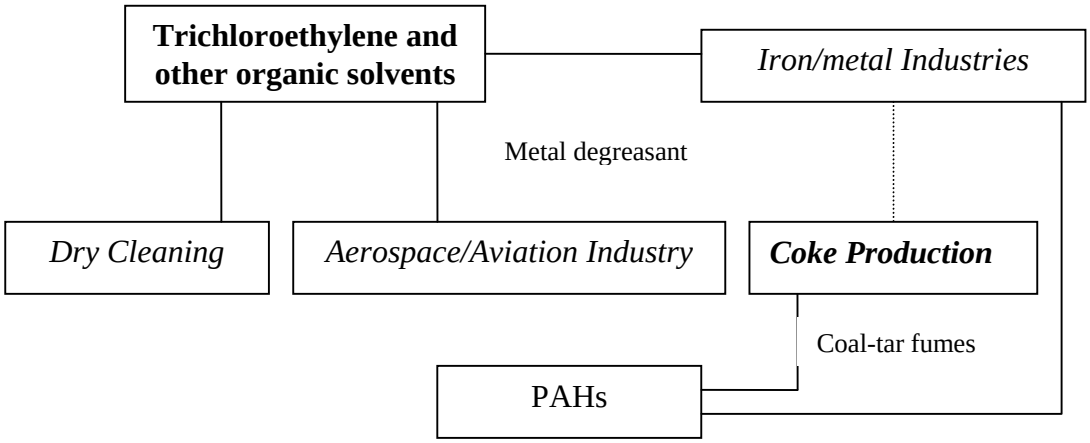

Figure 1: Kidney cancer exposure map

The exposure map (Figure 1) gives an indication of how exposures overlap in the working population. It illustrates the potential for double counting of the exposed population to occur when an overall AF is calculated, and facilitates strategies to avoid this. For a given cancer, the map entries consist of either an agent (or group of agents such as PAHs), or an exposure scenario (i.e. an industry or occupation in which such exposure occurs). Agents are in plain type, exposure scenarios in italics, expanded from Table 6; entries from Table 6 are in bold type to distinguish from extrapolated occupations/agents. Lines joining boxes then indicate where overlap would occur were all the entries in the map simply considered separately – for example, if PAHs and organic solvents were considered separately overlap would occur in both the iron/metal and the aerospace/aviation industries (Section 2.3). Certain exposures, such as asbestos and DEE, have not been included in the exposure map due to uncertainty of the link between exposure and kidney cancer. AF has been calculated for the agent and exposure scenario shown in Figure 1.

Dotted lines in the exposure map would indicate the potential for overlap in the exposed populations. In the iron/metal industries, there is the potential for overlap exposure to PAHs (coal tar/coke fumes) and organic solvents such as TCE and tetrachloroethyne. However, as different groups of workers within the industry, namely coke oven workers and metal finishers, would be exposed to the different agents, the potential for overlap is considered to be low. Exposure scenarios may be excluded entirely, if they wholly overlap with another dominant exposure.

4.2 SUMMARY OF RESULTS

The results are summarised in Table 17 and Table 18

Table 17 Summary of RR used to calculate AF

Agent	Exposure	RR	LL	UL
Trichloroethylene	H	1.2	0.8	1.7
Trichloroethylene	L	1	1	1

Table 18 Results

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)
Trichloroethylene	43861	42288	0.0023	0.0020	0.0004	0.0000	0.0016	0.0004	0.0000	0.0014	1	1	2	1

4.3 EXPOSURES BY INDUSTRY/JOB

Table 19 shows for industry categories from CAREX and job categories from LFS, attributable registrations in 2004 and attributable deaths in 2005 by agent.

Table 19 Industry/occupation codes by agent

Agent	Industry	Numbers Ever Exposed over REP (Men)	Number Ever Exposed over REP (Women)	Attributable Registrations (Men) (2004)	Attributable Deaths (Men) (2005)	Attributable Registrations (Women) (2004)	Attributable Deaths (Women) (2005)
Trichloroethylene	Manufacture of wearing apparel, except footwear	430	236	0	0	0	0
Trichloroethylene	Manufacture of machinery except electrical	11179	6140	0	0	0	0
Trichloroethylene	Manufacture of electrical machinery, apparatus, appliances and supplies	6808	3739	0	0	0	0
Trichloroethylene	Manufacture of fabricated metal products, except machinery and equipment	7863	4319	0	0	0	0
Trichloroethylene	Manufacture of transport equipment	10841	5954	0	0	0	0
Trichloroethylene	Personal and household services	5186	19813	0	0	0	0
Trichloroethylene	Total	43861	42288	2	1	1	1

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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

Kidney 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 cancer of the kidney that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF for kidney cancer related to overall occupational exposure is 0.04% (95%Confidence Interval (CI)=0.00-0.15), which equates to 1 (95%CI=0-5) death and 3 (95%CI =0-10) registrations.

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