Cancer mortality and morbidity in employees of the United Kingdom Atomic Energy Authority, 1946–86

P. Fraser¹, L. Carpenter¹, N. Maconochie¹, C. Higgins¹, M. Booth¹ & V. Beral²

¹*Epidemiological Monitoring Unit, Department of Epidemiology and Population Sciences, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT*; ²*Imperial Cancer Research Fund Cancer Epidemiology Unit, Gibson Building, Radcliffe Infirmary, Oxford OX2 6HE, UK.*

Summary In further analyses of a cohort of 39,718 United Kingdom Atomic Energy Authority employees after 7 more years follow-up, cancer mortality, based on 1,506 deaths in 1946–86, was 20% below the national average. Prostatic cancer mortality showed a statistically significant association with external radiation exposure, largely confined to men who were also monitored for internal contamination by radionuclides other than plutonium. Prostatic cancer mortality was highest in radiation workers at Winfrith. In women monitored for radiation exposure, mortality from cancer of the uterus (including the cervix uteri) was increased relative to other employees, and, showed a statistically significant association with external radiation exposure. While there were some other statistically significant results, as would be expected by chance alone when multiple comparisons are made, there were no other cancer sites with consistently exceptional findings. Point estimates for risk associated with increasing exposure to radiation suggest a decrease of four deaths per 10⁴ person-years per Sv for leukaemia and an increase of 20 deaths for all cancers except leukaemia, but confidence intervals indicate that a wide range of values are compatible with the data.

Cancer morbidity based on 1,699 registrations in 1971–84 was 12% below the national average. Findings from site-specific analyses largely replicated those of the mortality analyses.

Follow-up data for a further 7 years have accrued since we first described the mortality of employees of the United Kingdom Atomic Energy Authority (UKAEA), 1946–79 (Beral *et al.*, 1985). Cancer mortality then was 21% below the national average and prostatic cancer was the only malignancy with clearly increased mortality in relation to radiation exposure. However, the duration of follow-up to the end of 1979 was only 16 years on average, and small numbers of deaths from some cancers yielded imprecise estimates which were consistent with a wide range of effects. In order to increase precision and allow for longer latency, we have continued to collect follow-up data on the entire UKAEA study population, including employees still in service on 1 January 1980. Analyses of mortality data from 1946 to 1986, and cancer registration data from 1971 to 1984, are reported here with special reference to prostatic cancer, other genital tract cancers, and malignancies such as multiple myeloma which have been associated with radiation exposure in other studies of nuclear industry workers (Smith & Douglas, 1986; Gilbert *et al.*, 1989).

Methods

The design and methods of data collection and validation in the UKAEA mortality study have been described previously (Fraser *et al.*, 1985) and a fully account of the methods used in this report will be published elsewhere (Fraser *et al.*, in preparation).

Study population, personnel data and follow-up

The study population comprised all employees of the UKAEA establishments at Harwell, London, Culham, Dounreay and Winfrith who were ever employed between 1 January 1946 and 31 December 1979. Details of all employees were submitted for tracing to the National Health Service Central Registers (NHSCRs) in Southport and Edinburgh. For subjects recorded as having died, both the underlying and associated causes of death as stated on the death certificate were coded to the eighth (for deaths during 1946–78) and

ninth (for deaths during 1979–86) revisions of the International Classification of Diseases (ICD) by the Office of Population Censuses and Surveys. Coded death certificates and notifications of emigrations and cancers registered since 1971 were obtained. When a subject could not be traced at the NHSCRs, identifying particulars were sent to the Department of Social Security's (DSS) Records Branch in Newcastle for ascertainment of vital status.

The UKAEA's records of deaths in service and among members of their pension scheme provided a cross-check on the completeness of notification of death and sometimes information of assistance in tracing deaths at the NHSCRs. Further checks on the completeness of notification of cancer deaths and random samples of non-cancer deaths were carried out at NHSCR in Southport. Deaths notified in the UKAEA study population were also cross-checked against deaths in radiation workers notified to the National Radiological Protection Board (NRPB) (Kendall *et al.*, 1992a,b). Finally, an extensive computerised check on the vital status of UKAEA study members using National Insurance numbers was carried out by the DSS' Information Technology Services Agency.

Radiation data

Information on employees who had been monitored for exposure to radiation during 1946–85 was obtained from UKAEA records. Data abstracted for each employee included a yearly summary of external whole body radiation exposure (X-rays, gamma rays and neutrons) including exposures accumulated in previous employments when these had been notified to the UKAEA. Annual whole body exposures were cumulated adjusting exposures in 1946–79 for below-threshold measurements as described by Inskip *et al.* (1987). After 1979 no adjustments were made as this source of error became negligible. Adjustments were made throughout the study period for missing values due to lost or damaged films by incorporating an appropriate fraction of the worker's annual recorded exposure in that year. Information on internal exposure from radionuclides was generally limited to noting the years in which subjects were monitored for possible internal contamination by tritium, plutonium, or other unspecified radionuclides. Associated radiation exposures were not included in measures of whole body exposure except from tritium at Harwell from 1977.

Statistical analysis

Person-years at risk were calculated from each worker's first day of employment by the UKAEA (or from 1 January 1946 for workers recruited before that date) to 31 December 1986 or the date of emigration, death, or the last date traced if any of these preceded 1 January 1987. Person-years-at-risk and deaths were stratified by sex, age in 15 groups, calendar year both in single years and in nine groups, establishment in three groups (Harwell with Culham and London, Dounreay and Winfrith), and social class in six groups. Radiation exposure was treated as a time-dependent variable in all analyses. In order to allow for the delayed effects of radiation exposure, the exposures were lagged in some analyses by 2 years for leukaemia and 10 years for other causes of death using the same method as before (Beral *et al.*, 1985). Some analyses were repeated with a 5-year lag.

All mortality analyses were based on the underlying cause of death. Deaths for which an underlying cause could not be ascertained were included in analyses of deaths from all causes but not in cause-specific analyses. Age, sex and single-year specific death rates for England and Wales were used to calculate expected deaths and standardised mortality ratios (SMR). Exact 95% confidence intervals (CI) and statistical significance levels for SMRs were obtained using the Poisson distribution (Bailer & Ederer, 1964) unless the numbers of observed deaths was 200 or more, when approximate significance levels were derived from the standard chi-squared test (Breslow & Day, 1987).

Rate ratios (RR) adjusted for age, sex, calendar period, establishment and social class, and approximate 95% CIs, were estimated by the method of maximum likelihood using the GLIM computer package (Baker & Nelder, 1982). Statistical significance of the RRs was tested using the likelihood ratio statistic and checked using the score statistic (Breslow & Day, 1987). When the total number of deaths contributing to the RR was less than 20, exact confidence intervals and significance levels were generated from the stratum-specific deaths and person-years using the likelihood for binomial data.

For workers with a radiation record, the relation between level of external whole body radiation exposure and mortality was examined without reference to national rates. An overall chi-squared statistic was obtained to test for a linear trend across five levels of exposure stratified by age, sex, calendar period, establishment and social class (Breslow & Day, 1987). When the resultant test statistic was based on a total number of deaths of 20 or less, probability values were checked using 10,000 simulations as described elsewhere (Beral *et al.*, 1988). Changes in cancer risk associated with increasing exposure to radiation were estimated using an additive relative risk model. Excess relative risks and absolute risks (and their 95% CIs) were estimated from this model using maximum likelihood methods described by Gilbert (1989).

The cancer registration data were analysed using methods similar to those employed for mortality. Cancers first identified through a death certificate as the underlying or an associated cause of death were included in all internal (within workforce) comparisons, the date of death being used as a surrogate for the registration date. Where an ill-defined, secondary or unspecified neoplasm was registered but a primary malignant neoplasm was specified on the death certificate, the date of registration was retained but the primary site was substituted in all internal analyses. For comparability with national cancer registration rates in England and Wales, cancers first identified through a death certificate in 1971–73 were not included in calculations of standardised registration ratios (SRR).

P-values obtained from tests of statistical significance are quoted as two-sided throughout. Separate analyses were performed for many individual anatomical sites – 29 for cancer mortality and 14 for cancer registrations. Some statistically significant results may therefore be expected to occur on the basis of chance alone. In interpreting the findings, those for

which similar results have not been described in other studies are considered as being likely to be due to chance, except when the *P*-value is less than 0.01. Where similar results have been described before, attention is drawn to findings with a *P*-value of less than 0.05 in the expected direction. Confidence intervals for SMRs and RRs are quoted throughout the text, to give an indication of the range of possible values for the true effect, and to examine its consistency with that of other studies.

Results

The total study population numbered 39,869. Of these, 151 lacked essential information such as sex, date of birth, or dates of employment. These individuals could neither be traced nor included in the analyses; only one had a radiation record but no recorded dose. The analyses presented here are therefore based on 39,718 subjects – 172 more than the 39,546 subjects analysed previously (Beral *et al.*, 1985). Of these, 29,085 (73%) were men and 21,545 (54%) had a radiation record, of whom 19,760 (92%) were men. The average length of follow-up was 22 years. Subjects with a radiation record had been followed-up for an average of 23 years and those without for an average of 21 years.

The collective external radiation exposure in the UKAEA study population from 1946–85 was 862 Sv giving an average exposure of 40 mSv per monitored worker. The distribution was highly skewed with half (10,806) of the 21,545 workers with a radiation record having a final cumulative whole body exposure of 10 mSv or more, 10% (2,211) a final exposure exceeding 100 mSv, and less than 1% (150) a final exposure exceeding 500 mSv. Exposures varied between establishments, average exposures at Winfrith (56 mSv) and Dounreay (49 mSv) being higher than at Harwell with Culham and London (32 mSv). Among workers who had a radiation record, 7,480 (35%) were monitored for internal contamination by radionuclides; 1,702 (8%) were monitored for tritium, 3,564 (17%) for plutonium, and 6,412 (30%) for other unspecified radionuclides. Fifty-one percent (3,834) of radionuclide-monitored workers fell into more than one of these categories.

A total of 5,509 deaths (14% of the study population) had occurred by 31 December 1986. The cause of death had been confirmed by necropsy in 781 subjects with radiation records (25.9%) and 655 subjects without (26.3%). There were 1,506 deaths from cancer and 45 deaths for which the underlying cause could not be ascertained. A total of 1,706 ex-employees (4% of the study population) were reported to have emigrated by 31 December 1986. Of the 111 (0.3%) ex-employees who were lost to follow-up after leaving the UKAEA, only ten had a radiation record.

Among the 28,594 study members (72% of the study population) whose records were identified through National Insurance numbers, DSS reported belatedly 82 deaths in the UK during 1970–86 which had not been notified by the NHSCRs, 50 of them in monitored workers. Three more deaths in Dounreay radiation workers came to light in the cross-check against deaths notified to NRPB. The distribution of all 53 missed deaths in radiation workers across dose categories was not dissimilar to the distribution of the 3,021 notified deaths in the study population so their omission from the analyses is unlikely therefore to have resulted in serious bias. An examination of deaths by year suggested a deficit in the numbers of deaths notified by the NHSCRs in 1985, and possibly in 1986. The proportions of missed deaths in 1985 and 1986, 3.5% and 2.9% respectively, whilst above the annual average were not extreme.

Mortality compared with national rates: standardised mortality ratios

The standardised mortality ratio was 78 (95% CI 76–80) for all causes of death combined and 80 (95% CI 76–84) for all malignant neoplasms in the workforce as a whole (Table I).

Table 1 Cause-specific standardised mortality ratios (SMR) by radiation status and rate ratios for employees with a radiation record compared with other employees adjusted for age, sex, calendar period, establishment and social class, 1946–1986

Cause of death (ICD code, (8th revision))	Employees with a radiation record SMR		Other employees SMR (observed/expected deaths)		Rate ratio (95% confidence interval) for employees with a radiation record compared with other employees assuming: 10-year lag	
	All employees SMR (observed/expected deaths)	Employees with a radiation record SMR (observed/expected deaths)	Other employees SMR (observed/expected deaths)		No lag	10-year lag
<i>All malignant neoplasms (140–209)</i>	80 ^a (1506/1881.48)	77 ^a (796/1039.59)	84 ^a (710/841.88)		0.92 (0.82–1.04)	1.00 (0.89–1.13)
Buccal cavity and pharynx (140–149)	85 (23/27.17)	83 (13/15.73)	87 (10/11.44)		1.05 (0.41–2.72)	0.64 (0.23–1.80)
Oesophagus (150)	68 ^a (36/52.99)	61 ^a (19/31.05)	77 (17/21.94)		0.72 (0.34–1.54)	0.99 (0.45–2.16)
Stomach (151)	75 ^a (132/177.11)	72 ^b (73/101.67)	78 (59/75.45)		0.87 (0.60–1.28)	1.14 (0.77–1.69)
Small intestine (152)	107 (43/75)	143 (32/10)	61 (1/1.65)		1.73 (0.13–60.55)	0.69 (0.04–10.82)
Large intestine (153)	90 (111/122.89)	89 (58/65.15)	92 (53/57.74)		0.83 (0.55–1.26)	0.69 (0.44–1.06)
Rectum (154)	71 ^b (59/82.97)	73 (34/46.61)	69 (25/36.35)		0.89 (0.50–1.59)	0.65 (0.36–1.19)
Liver and gall bladder (155–156)	63 (15/23.82)	68 (9/13.24)	57 (6/10.58)		1.32 (0.35–4.36)	1.22 (0.33–4.38)
Pancreas (157)	91 (71/77.88)	73 (32/44.12)	116 (39/33.76)		0.63 (0.38–1.07)	0.65 (0.38–1.12)
Nasal cavities and sinuses (160)	105 (4/3.81)	92 (2/2.18)	123 (2/1.63)		0.48 (0.03–8.11)	1.40 (0.09–30.80)
Larynx (161)	70 (11/15.61)	74 (7/9.48)	65 (4/6.13)		1.58 (0.32–7.00)	0.97 (0.29–4.29)
Bronchus and lung (162)	73 ^a (477/652.77)	70 ^a (280/397.28)	77 ^a (197/255.49)		0.98 (0.80–1.20)	1.10 (0.89–1.35)
Bone (170)	72 (5/6.96)	78 (3/3.83)	64 (2/3.13)		2.15 (0.26–16.72)	2.04 (0.69–6.09)
Connective tissue (171)	64 (4/6.22)	86 (3/3.48)	37 (1/2.74)		1.24 (0.08–69.91)	2.09 (0.09–136.91)
Melanoma and other skin (172–173)	73 (14/19.30)	57 (6/10.59)	92 (8/8.70)		0.35 (0.06–2.27)	0.50 (0.06–4.73)
Breast (174)	95 (84/88.53)	39 ^a (6/15.38)	107 (78/73.15)		0.32 ^b (0.14–0.77)	0.33 ^b (0.13–0.84)
Uterus (180–182)	70 (19/27.32)	184 (8/4.34)	48 ^a (11/22.98)		4.55 ^b (1.20–16.66)	4.28 ^a (1.03–19.97)
Ovary (183)	87 (24/27.46)	113 (5/4.43)	83 (19/23.03)		1.50 (0.54–4.17)	1.90 (0.68–5.33)
Prostate (185)	89 (70/78.91)	87 (42/48.20)	91 (28/30.71)		0.81 (0.48–1.35)	0.92 (0.55–1.54)
Testis (186)	176 (14/7.95)	171 (9/5.27)	187 (5/2.68)		0.92 (0.34–2.07)	0.22 (0.06–4.73)
Bladder and other urinary (188–189 except 189.0)	74 ^a (47/63.82)	85 (32/37.57)	57 ^a (15/26.25)		1.74 (0.89–3.43)	1.98 ^a (0.98–3.97)
Kidney (189.0)	102 (31/30.32)	77 (14/18.10)	139 (17/12.22)		0.49 (0.23–1.05)	0.51 (0.23–1.10)
Brain and other central nervous system (191–192)	65 ^a (32/49.07)	66 (19/28.60)	64 (13/20.47)		1.16 (0.52–2.57)	1.44 (0.60–3.46)
Thyroid (193)	172 (7/4.06)	102 (2/1.96)	238 (5/2.11)		0.34 (0.02–9.96)	1.02 (0.12–9.94)
Ill-defined and secondary (195–199)	89 (73/81.98)	93 (42/45.36)	85 (31/36.63)		1.26 (0.73–2.17)	1.54 (0.90–2.65)
<i>All lymphatic and haematopoietic (200–209)</i>	98 (124/125.92)	92 (66/71.45)	106 (58/54.47)		0.89 (0.59–1.34)	1.13 (0.73–1.75)
Non-Hodgkin's lymphoma (200,202)	109 (38/34.74)	135 (27/19.99)	75 (11/14.75)		1.57 (0.71–3.50)	1.74 (0.80–3.79)
Hodgkin's disease (201)	62 (11/17.72)	39 ^a (4/10.36)	95 (7/7.36)		0.64 (0.15–3.52)	1.28 (0.18–11.82)
Multiple myeloma (203)	76 (15/19.81)	36 ^a (4/11.13)	127 (11/8.68)		0.23 (0.05–1.53)	0.32 (0.06–2.32)
Leukaemia (204–208)	119 (60/50.48)	110 (31/28.19)	130 (29/22.29)		0.97 (0.53–1.78)	1.09 (0.59–2.01)
Leukaemia except CLL (204–208 except 204.1)	– (48/-) ^d	– (24/-) ^d	– (24/-) ^d		1.11 (0.56–2.20)	1.28 (0.65–2.53)
<i>All causes except cancers (0–139, 210–999)</i>	77 ^a (4003/5214.25)	76 ^a (2225/2928.68)	78 ^a (1778/2285.58)		0.94 (0.88–1.01)	1.03 (0.95–1.11)
<i>All causes (0–999)</i>	78 ^a (5509/7095.73)	76 ^a (3021/3968.27)	80 ^a (2488/3127.46)		0.94 ^a (0.88–0.99)	1.02 (0.96–1.09)

Significance of difference from 100 (SMRs) or 1 (rate ratios): ^a $P < 0.05$; ^b $P < 0.01$; ^c $P < 0.001$. SMRs: All significance probabilities have been calculated using exact methods where observed deaths < 200. Rate ratios: All significance probabilities and confidence intervals have been calculated using exact methods where observed deaths < 20. ^dNational mortality rates unavailable.

At individual cancer sites, SMRs for the oesophagus, stomach, rectum, bronchus and lung, bladder, and brain, were all significantly low. SMRs for testicular cancer, thyroid cancer, leukaemia and non-Hodgkin's lymphoma were above 100 but only that for testicular cancer (SMR = 176, 95% CI 96–295) approached statistical significance ($P = 0.07$). This was largely explained by increased mortality from testicular cancer at Harwell (with Culham and London) (SMR = 192, 95% CI 92–353, $P = 0.08$ based on ten deaths).

For employees with a radiation record, SMRs for all malignant neoplasms and cancers of the oesophagus, stomach, bronchus and lung, were significantly low. Additionally SMRs for breast cancer (SMR = 39, 95% CI 14–85), Hodgkin's disease (SMR = 39, 95% CI 11–99), and multiple myeloma (SMR = 36, 95% CI 10–92) were significantly below 100. While prostatic cancer mortality was not raised overall in employees with a radiation record (SMR = 87, 95% CI 63–118), it was increased in radiation workers at Winfrith (SMR = 245, 95% CI 134–411, $P = 0.005$ based on 14 deaths). By contrast, the SMR for prostatic cancer was 69 (95% CI 44–102) at Harwell (with Culham and London) and 66 (95% CI 21–153) at Dounreay. Mortality from prostatic cancer was higher at younger ages in men with a radiation record; at ages 45–54 years mortality was increased 3-fold relative to national rates (SMR = 354, 95% CI 130–771, $P = 0.02$ based on six deaths). The SMR at ages 55–64 was 83 (95% CI 36–164 based on eight deaths) and 88 (95% CI 52–139 based on 18 deaths) at ages 65–74. The SMR for testicular cancer in all men with a radiation record was 171 (95% CI 78–325 based on nine deaths) and 202 (95% CI 55–217 based on four deaths) at Harwell (with Culham and London) alone.

For employees without a radiation record, no SMR was significantly increased. Significant deficits were apparent however for all malignant neoplasms, cancers of the bronchus and lung, uterus and bladder.

Mortality of employees with radiation records compared with other employees: rate ratios

When death rates for employees with a radiation record were compared with rates for other employees using rate ratios there were few significant differences (Table I). When no lag was assumed, rate ratios were significantly low for all causes of death combined (RR = 0.94, 95% CI 0.88–0.99) and breast cancer (RR = 0.32, 95% CI 0.14–0.77). A 4-fold excess of cancer of the uterus (including the cervix uteri) in women with a radiation record was observed (RR = 4.55, 95% CI 1.20–16.66, $P = 0.008$). Confidence intervals for all other rate ratios embraced 1.00, including those for prostatic cancer (RR = 0.81, 95% CI 0.48–1.35) and testicular cancer (RR = 0.92, 95% CI 0.34–2.07).

Rate ratios were recalculated lagging exposure by 2 years for leukaemia and 10 years for other causes of death (Table I). The 4-fold excess of cancer of the uterus in women with a radiation record persisted (RR = 4.28, 95% CI 1.03–19.97, $P = 0.02$). The deficit of breast cancer was also apparent in the lagged analyses, giving a rate ratio of 0.33 (95% CI 0.13–0.84, $P = 0.008$) for both sexes combined and, for women alone, a rate ratio of 0.36 (95% CI 0.14–0.91, $P = 0.02$). The lagged analyses revealed a 2-fold excess of cancers of the bladder and urinary organs (excluding kidney) or borderline significance (RR = 1.98, 95% CI 0.98–3.97, $P = 0.05$) in employees with a radiation record. The rate ratio for prostatic cancer was 0.84 (95% CI 0.50–1.41) and 0.92 (95% CI 0.55–1.54) with 5 and 10-year lags respectively.

Mortality and level of cumulative external radiation exposure

Table II shows mortality from selected causes of death among workers with a radiation record according to cumulative external whole body radiation exposure. In the unlagged mortality analysis in men, prostatic cancer alone showed a positive trend in mortality with increasing exposure (χ^2 for trend = 6.12, $P = 0.01$), the trend being most evident for

employees at Harwell (with Culham and London) (χ^2 for trend = 5.11, $P = 0.02$). The trends persisted when exposures were lagged by 5 years (χ^2 for trend = 4.39, $P = 0.04$ overall and 6.45, $P = 0.01$ at Harwell) but were less apparent with a 10 year lag (χ^2 for trend = 1.65, $P = 0.20$ overall and 3.70, $P = 0.05$ at Harwell). Contrary to the findings in the previous analysis (Beral *et al.*, 1985), there was no significant trend in prostatic cancer mortality at Winfrith (χ^2 for trend = 0.04, $P = 0.8$).

The unlagged analysis of mortality in women showed a trend for all causes of death (χ^2 for trend = 4.52, $P = 0.03$) and all malignant neoplasms (χ^2 for trend = 5.69, $P = 0.02$), the main components of which were cancer of the uterus (χ^2 for trend = 5.11, $P = 0.02$) and cancer of the bronchus and lung (χ^2 for trend = 4.14, $P = 0.04$). These site-specific trends were based on very few deaths – eight cancers of the uterus (two cervix, five body, one part unspecified) and five cancers of the bronchus and lung. When P -values for these sites were checked by simulation, the values obtained were similar ($P = 0.04$ and $P = 0.01$ respectively). Though the significant trend for all malignant neoplasms was lost in the lagged analysis (χ^2 for trend = 2.66, $P = 0.1$), the trends for the two specific cancer sites persisted when exposures were lagged by 10 years (χ^2 for trend = 5.10, $P = 0.02$ for uterus and $\chi^2 = 8.80$, $P = 0.003$ for bronchus and lung). Again the simulated P -values for these two cancers were similar ($P = 0.04$ and $P = 0.003$ respectively). There were no other statistically significant trends in site-specific cancer mortality with increasing exposure to radiation from either lagged or unlagged analyses.

Mortality and monitoring for internal exposure to radionuclides

Mortality in workers monitored for possible internal exposure to specific radionuclides was examined by calculating SMRs for comparison with national rates and RRs for comparison with other workers who had a radiation record but were not monitored for exposure to that particular radionuclide (Table III). When no lag was assumed, mortality from all malignant neoplasms in workers monitored for exposure to any radionuclide was below national rates (SMR = 80, 95% CI 70–91) but similar to that of workers with a radiation record who were not monitored for radionuclide exposure (RR = 1.05, 95% CI 0.90–1.24).

Mortality from prostatic cancer was raised nearly 3-fold in men monitored for exposure to tritium (SMR = 282, 95% CI 113–580, $P = 0.03$; RR = 2.85, 95% CI 1.17–6.95). At Winfrith, the SMR of 689 (95% CI 188–1763) though based on only four deaths from prostatic cancer in tritium-monitored workers was highly significant ($P = 0.006$) as was the SMR of 345 (95% CI 139–710) associated with other unspecified radionuclides ($P = 0.01$ based on seven deaths). The rate ratio for prostatic cancer in tritium-monitored workers remained elevated when exposures were lagged by 5 years (RR = 3.39, 95% CI 1.40–8.24) but not with a 10-year lag (RR = 1.75, 95% CI 0.50–6.10).

Mortality from cancer of the uterus was raised in women monitored for exposure to any radionuclide by comparison with other radiation workers (RR = 17.99, 95% CI 2.14–290.14) but based on only two deaths. There were no deaths from cancers of the bronchus or lung in women monitored for radionuclide exposure. A 2-fold excess mortality from cancers of ill-defined and secondary sites was observed in radiation workers monitored for radionuclide exposure compared to other radiation workers (RR = 1.95, 95% CI 1.01–3.77). This was largely confined to workers monitored for radionuclides other than tritium or plutonium (RR = 2.39, 95% CI 1.22–4.69).

In order to investigate further the effects of internal and external radiation exposure, the trends in prostatic cancer mortality were re-examined after stratification for radionuclide exposure (Table IV). Rate ratios for prostatic cancer mortality increased with increasing cumulative whole body exposure in men monitored for exposure to any radionuclide

Table II Relation of mortality from selected causes of death to cumulative whole body exposure adjusted for age, sex, calendar period, establishment and social class. Results expressed as ratio of observed to expected deaths (observed and expected numbers of deaths in parentheses; expected numbers based on rates in all subjects with a radiation record)

Cause of death (ICD code (8th revision))	<10	10–	Cumulative whole body exposure (mSv)		Total deaths	Chi-squared test for trend on 1 d.f. (direction of trend)	
			20–	50–		No lag	10-year lag
<i>All malignant neoplasms (140–209)</i>	M 0.95 (283/299.13) F 0.92 (29/31.44)	0.97 (112/115.62) 0.51 (3/5.84)	1.07 (172/161.25) 1.39 (8/5.76)	1.05 (89/84.66) 2.79 (3/1.08)	751	1.05 (95/90.34) 2.27 (2/0.88)	0.93 (+) 2.66 (+) ^a
Oesophagus (150)	1.10 (7/6.37)	1.13 (3/2.66)	1.75 (6/3.43)	0.82 (2/2.44)	45	0.24 (1/4.10)	3.26 (–)
Stomach (151)	0.86 (24/27.89)	0.90 (10/11.12)	1.34 (22/16.47)	0.79 (7/8.85)	19	1.16 (10/8.66)	1.75 (+)
Large intestine (153)	1.14 (28/24.47)	0.90 (8/8.91)	0.83 (10/12.08)	0.90 (6/6.67)	73	1.02 (6/5.87)	0.69 (–)
Rectum (154)	0.78 (10/12.76)	1.22 (7/5.76)	1.42 (11/7.77)	0.83 (3/3.61)	58	0.73 (3/4.11)	0.11 (–)
Pancreas (157)	1.35 (16/11.89)	0.94 (5/5.34)	0.85 (6/7.10)	0.52 (2/3.81)	34	0.78 (3/3.86)	0.40 (–)
Bronchus and lung (162)	M 0.98 (111/113.22) F 0.91 (3/3.30)	0.77 (32/41.49) 0.0 (0/0.65)	1.02 (60/58.60) 0.0 (0/0.48)	1.20 (35/29.24) 3.96 (1/0.25)	32	1.14 (37/32.46) 3.15 (1/0.32)	1.08 (–) 1.68 (+)
Bone and connective tissue (170–171)	1.32 (4/3.04)	1.28 (1/0.78)	0.0 (0/1.12)	0.0 (0/0.55)	275	1.99 (1/0.50)	4.14 (+) ^a
Breast (174)	0.81 (3/3.72)	2.22 (2/0.90)	0.0 (0/0.87)	0.0 (0/0.14)	5	2.69 (1/0.37)	0.03 (+)
Uterus (180–182)	0.67 (4/5.95)	0.0 (0/1.04)	1.67 (3/1.80)	4.71 (1/0.21)	6	0.0 (0/0.0)	1.00 (+)
Ovary (183)	0.55 (2/3.65)	0.0 (0/0.68)	4.64 (2/0.43)	7.05 (1/0.14)	8	0.0 (0/0.10)	5.11 (+) ^a
Prostate (185)	0.86 (14/16.36)	0.79 (5/6.32)	0.92 (9/9.77)	0.85 (4/4.69)	5	2.01 (+)	2.01 (+)
Testis (186)	0.96 (5/5.23)	0.78 (1/1.28)	1.33 (2/1.50)	0.0 (0/0.61)	42	2.06 (10/4.86)	6.12 (+) ^a
Bladder and other urinary (188–189 except 189.0)	1.08 (13/12.02)	1.29 (7/5.45)	0.56 (4/7.18)	0.80 (3/3.73)	9	2.59 (1/0.39)	0.51 (+)
Kidney (189.0)	0.91 (5/5.51)	1.48 (3/2.03)	1.11 (3/2.71)	0.56 (1/1.79)	32	1.38 (5/3.62)	0.18 (+)
Brain and nervous system (191–192, 225, 238) ^c	0.99 (11/11.12)	1.14 (4/3.52)	0.66 (3/4.53)	1.19 (3/2.52)	14	1.02 (2/1.96)	0.01 (–)
Thyroid (193)	0.0 (0/0.48)	0.0 (0/0.19)	2.47 (1/0.40)	3.20 (1/0.31)	24	1.29 (3/2.32)	0.22 (+)
Ill-defined and secondary (195–199)	0.66 (11/16.57)	1.30 (8/6.18)	1.51 (14/9.28)	1.04 (5/4.81)	2	0.0 (0/0.61)	0.23 (–)
<i>All lymphatic and haematopoietic (200–209)</i>	0.81 (22/27.29)	1.26 (14/11.07)	1.12 (15/13.37)	1.53 (11/7.20)	42	0.78 (4.5.16)	0.01 (–)
Non-Hodgkin's lymphoma (200, 202)	0.63 (7/11.05)	1.24 (5/4.03)	1.38 (8/5.78)	1.38 (4/2.91)	66	0.57 (4/7.08)	0.26 (–)
Multiple myeloma (203)	0.62 (1/1.61)	2.06 (1/0.49)	0.0 (0/1.00)	3.58 (2/0.56)	27	0.93 (3/3.23)	0.16 (+)
Leukaemia (204–208)	1.07 (13/12.14)	0.98 (6/6.14)	1.16 (7/6.06)	1.16 (4/3.45)	4	0.0 (0/0.35)	0.01 (+)
Leukaemia except CLL (204–208 except 204.1)	1.27 (13/10.23)	0.47 (2/4.22)	1.30 (6/4.60)	0.77 (2/2.60)	31	0.31 (1/3.21)	1.42 (–)
<i>All causes except cancers (0–139, 210–999)</i>	0.98 (906/926.65)	0.98 (339/344.74)	1.12 (519/463.98)	0.98 (236/240.66)	24	0.43 (1/2.35)	1.22 (–)
<i>All causes (0–999)</i>	M 0.97 (1149/1180.90) F 0.90 (69/76.31)	0.98 (436/447.34) 0.96 (18/18.86)	1.10 (682/619.86) 1.53 (17/11.13)	1.00 (324/323.83) 1.55 (4/2.58)	2225	0.90 (225/248.98) 0.94 (320/339.07)	1.58 (–)
Person-years at risk	241536	67195	77631	40030	2911	1.78 (2/1.12)	0.36 (–)
Median cumulative exposure (mSv)	2.55	14.12	30.88	66.98	110	37192	4.52 (+) ^a
						172.98	3.19 (+)

Significance of trend: ^a $P < 0.05$; ^b $P < 0.01$; ^c P -values checked using 10,000 simulations where observed deaths ≤ 20 . ^d Includes benign and unspecified neoplasms of the nervous system.

Table III Standardised mortality ratios (SMR) and rate ratios (RR) for selected causes of death in employees monitored for exposure to radionuclides

Cause of death (ICD code (8th revision))	Tritium			Plutonium			Other			Any radionuclide			No radionuclide	
	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	RR (95% CI) ^d	SMR (Observed deaths)	SMR (Observed deaths)
<i>All malignant neoplasms</i>														
(140–209)	71 ^a (44)	0.98 (0.72–1.34)	79 ^a (108)	0.97 (0.78–1.20)	82 ^b (207)	1.07 (0.90–1.26)	80 ^c (244)	1.05 (0.90–1.24)	80 ^c (244)	1.05 (0.90–1.24)	80 ^c (244)	1.05 (0.90–1.24)	75 ^c (552)	
Oesophagus (150)	96 (2)	1.81 (0.35–18.91)	45 (2)	0.29 (0.09–3.09)	24 ^a (2)	0.17 (0.02–2.40)	41 (4)	0.32 (0.10–1.68)	41 (4)	0.32 (0.10–1.68)	41 (4)	0.32 (0.10–1.68)	69 (15)	
Stomach (151)	36 (2)	0.51 (0.12–2.08)	93 (12)	1.38 (0.72–2.63)	80 (19)	1.13 (0.66–1.94)	80 (23)	1.14 (0.68–1.91)	80 (23)	1.14 (0.68–1.91)	80 (23)	1.14 (0.68–1.91)	69 ^b (50)	
Large intestine (153)	54 (2)	0.64 (0.15–2.67)	84 (7)	0.97 (0.42–2.20)	78 (12)	0.83 (0.43–1.61)	86 (16)	0.93 (0.51–1.70)	86 (16)	0.93 (0.51–1.70)	86 (16)	0.93 (0.51–1.70)	92 (42)	
Rectum (154)	37 (1)	0.54 (0.07–4.08)	49 (3)	0.50 (0.14–1.79)	53 (6)	0.64 (0.25–1.64)	59 (8)	0.74 (0.31–1.75)	59 (8)	0.74 (0.31–1.75)	59 (8)	0.74 (0.31–1.75)	79 (26)	
Pancreas (157)	37 (1)	0.45 (0.06–3.34)	34 (2)	0.44 (0.10–2.03)	36 ^a (4)	0.35 (0.12–1.04)	38 ^a (5)	0.39 ^a (0.14–1.04)	38 ^a (5)	0.39 ^a (0.14–1.04)	38 ^a (5)	0.39 ^a (0.14–1.04)	88 (27)	
Bronchus and lung (162)	62 (15)	0.92 (0.54–1.57)	82 (44)	1.09 (0.77–1.54)	86 (86)	1.30 (0.99–1.71)	81 ^a (97)	1.23 (0.95–1.61)	81 ^a (97)	1.23 (0.95–1.61)	81 ^a (97)	1.23 (0.95–1.61)	67 ^c (183)	
Uterus (180–182)	0 (0)	0 (0–618.75)	575 (1)	14.30 (0.57–978.78)	715 (2)	13.50 (0.75–247.34)	533 (2)	17.99 ^a (2.14–290.14)	533 (2)	17.99 ^a (2.14–290.14)	533 (2)	17.99 ^a (2.14–290.14)	151 (6)	
Prostate (185)	282 ^a (7)	2.82 ^a (1.17–6.95)	81 (5)	0.87 (0.33–2.32)	132 (15)	1.54 (0.78–3.04)	110 (15)	1.16 (0.60–2.27)	110 (15)	1.16 (0.60–2.27)	110 (15)	1.16 (0.60–2.27)	77 (27)	
Testis (186)	337 (1)	3.72 (0.07–82.79)	298 (2)	1.87 (0.17–22.57)	82 (1)	0.49 (0.01–10.74)	196 (3)	1.62 (0.19–13.11)	196 (3)	1.62 (0.19–13.11)	196 (3)	1.62 (0.19–13.11)	158 (6)	
<i>Bladder and other urinary</i>														
(188–189 exc 189.0)	30 (1)	0.67 (0.09–5.02)	40 (3)	0.63 (0.18–2.20)	50 (7)	0.98 (0.40–2.36)	48 ^a (8)	0.88 (0.38–2.03)	48 ^a (8)	0.88 (0.38–2.03)	48 ^a (8)	0.88 (0.38–2.03)	61 ^a (24)	
Kidney (189.0)	80 (1)	0.95 (0.04–19.20)	116 (3)	1.31 (0.31–7.57)	103 (5)	1.60 (0.63–4.17)	103 (6)	1.54 (0.95–2.02)	103 (6)	1.54 (0.95–2.02)	103 (6)	1.54 (0.95–2.02)	64 (8)	
<i>Brain and nervous system</i>														
(191–192, 225, 238) ^f	43 (1)	0.62 (0.08–4.71)	61 (3)	0.87 (0.25–3.04)	77 (7)	1.14 (0.43–3.01)	64 (7)	0.80 (0.30–2.15)	64 (7)	0.80 (0.30–2.15)	64 (7)	0.80 (0.30–2.15)	69 (17)	
III-defined and secondary	69 (2)	0.76 (0.18–3.24)	97 (6)	1.04 (0.41–2.61)	147 (17)	2.39 ^a (1.22–4.69)	131 (18)	1.95 ^a (1.01–3.77)	131 (18)	1.95 ^a (1.01–3.77)	131 (18)	1.95 ^a (1.01–3.77)	78 (24)	
(195–199)	112 (5)	1.46 (0.57–3.72)	51 (5)	0.57 (0.22–1.46)	78 (14)	0.87 (0.47–1.63)	83 (18)	0.94 (0.53–1.67)	83 (18)	0.94 (0.53–1.67)	83 (18)	0.94 (0.53–1.67)	94 (48)	
<i>All lymphatic and haematopoietic</i>														
(200–209)	219 (3)	1.99 (0.58–6.80)	137 (4)	1.10 (0.37–3.32)	111 (6)	0.70 (0.27–1.80)	138 (9)	1.02 (0.45–2.33)	138 (9)	1.02 (0.45–2.33)	138 (9)	1.02 (0.45–2.33)	125 (18)	
Non-Hodgkin's lymphoma	0 (0)	0 (0–52.57)	0 (0)	0 (0–19.82)	67 (2)	3.41 (0.68–17.04)	56 (2)	2.67 (0.54–13.28)	56 (2)	2.67 (0.54–13.28)	56 (2)	2.67 (0.54–13.28)	25 ^a (2)	
Multiple myeloma (203)	120 (2)	1.25 (0.29–5.47)	27 (1)	0.24 (0.03–1.81)	73 (5)	0.75 (0.27–2.07)	72 (6)	0.67 (0.26–1.73)	72 (6)	0.67 (0.26–1.73)	72 (6)	0.67 (0.26–1.73)	124 (25)	
Leukaemia (204–208)	– (2)	1.77 (0.39–8.04)	– (0)	0 (0–10.58)	– (4)	0.83 (0.26–2.63)	– (5)	0.82 (0.29–2.35)	– (5)	0.82 (0.29–2.35)	– (5)	0.82 (0.29–2.35)	– (19)	
Leukaemia except CLL	63 ^c (99)	0.80 ^a (0.65–0.99)	83 ^b (303)	0.95 (0.83–1.08)	75 ^c (504)	0.88 ^a (0.79–0.97)	75 ^c (608)	0.88 ^b (0.79–0.97)	75 ^c (608)	0.88 ^b (0.79–0.97)	75 ^c (608)	0.88 ^b (0.79–0.97)	77 ^c (1617)	
(204–208 except 204.1)	65 ^c (143)	0.85 (0.71–1.01)	82 ^c (411)	0.95 (0.85–1.06)	76 ^c (711)	0.92 (0.84–1.01)	76 ^c (852)	0.92 (0.85–1.00)	76 ^c (852)	0.92 (0.85–1.00)	76 ^c (852)	0.92 (0.85–1.00)	77 ^c (2169)	
<i>All causes except cancers</i>														
(0–139, 210–999)														
<i>All causes (0–999)</i>														
Number of workers ever monitored	1702		3564		6412		7480		14065		14065			

Significance: ^a $P < 0.05$; ^b $P < 0.01$; ^c $P < 0.001$. SMRs: All significance probabilities have been calculated using exact methods where observed death < 200. RRs: All significance probabilities and confidence intervals have been calculated using exact methods where observed death < 20. ^dRelative to other workers with radiation record and adjusted for age, sex, calendar period, establishment and social class.

^eIncludes benign and unspecified neoplasms of nervous system.

Table IV Standard mortality ratios (SMR) observed/expected number of deaths, and rate ratios (RR) for prostatic cancer according to level of cumulative whole body exposure and monitoring for exposure to radionuclides

		Cumulative whole body exposure (mSv)			Chi-squared test for trend on 1 d.f. (direction of trend)		
		<10	10-20	20-50	≥100	No lag	10-year lag
Monitored for any radionuclide	SMR	58 (1/1.74)	77 (1/1.29)	83 (3/3.63)	33 (1/3.02)	230 ^a (9/3.91)	
	RR	0.38	0.94	1.07	0.76	3.25	6.46 (+) ^a
Not monitored for any radionuclide	SMR	77 (13/16.99)	60 (4/6.62)	80 (6/7.47)	113 (3/2.64)	71 (1/1.41)	2.18 (+)
	RR	1.0	0.87	0.91	1.49	1.90	0.01 (+)
Monitored for tritium	SMR	- (0/0.22)	- (0/0.05)	- (0/0.31)	- (0/0.59)	531 ^b (7/1.32)	0.09 (+)
	RR	0.0	0.0	0.0	0.0	5.20	4.24 (+) ^a
Not monitored for tritium	SMR	76 (14/18.51)	64 (5/7.86)	83 (9/10.80)	79 (4/5.07)	75 (3/4.01)	1.09 (+)
	RR	1.0	0.85	1.05	1.19	1.85	0.31 (+)
Monitored for plutonium	SMR	- (0/0.51)	- (0/0.44)	106 (2/1.89)	74 (1/1.36)	102 (2/1.97)	0.68 (+)
	RR	0.0	0.0	1.68	1.50	1.71	0.75 (+)
Not monitored for plutonium	SMR	77 (14/18.22)	67 (5/7.48)	76 (7/9.22)	70 (3/4.30)	238 ^a (8/3.36)	1.21 (+)
	RR	1.0	0.90	0.88	0.97	3.55	5.84 (+) ^a
Monitored for other radionuclides	SMR	72 (1/1.39)	90 (1/1.11)	101 (3/2.98)	41 (1/2.46)	264 ^a (9/3.41)	0.37 (+)
	RR	0.40	1.20	1.25	0.97	4.67	5.97 (+) ^a
Not monitored for other radionuclides	SMR	75 (13/17.34)	59 (4/6.80)	74 (6/8.13)	94 (3/3.20)	52 (1/1.92)	2.27 (+)
	RR	1.0	0.84	0.90	1.26	0.53	0.22 (-)

Significance: ^a $P < 0.05$; ^b $P < 0.001$.

(χ^2 for trend = 6.46, $P = 0.01$) but not in radiation workers who were not monitored for radionuclide exposure (χ^2 for trend = 0.01, $P = 0.9$). Prostatic cancer mortality increased with increasing external exposure in men monitored for exposure to tritium (χ^2 for trend = 4.24, $P = 0.04$) but not in radiation workers who were not monitored for this radionuclide (χ^2 for trend = 0.31, $P = 0.6$). The trend in rate ratios for tritium-monitored men was based on only seven deaths all of which occurred in the highest category of external exposure (SMR = 531, 95% CI 214-1094); the P -value for trend obtained by simulation ($P = 0.06$) was similar to that based on the chi-squared statistic. Prostatic cancer mortality also increased with increasing whole body exposure in men monitored for exposure to radionuclides (unspecified) other than tritium or plutonium (χ^2 for trend = 5.97, $P = 0.02$) but not irradiation workers who were not monitored for other radionuclides (χ^2 for trend = 0.22, $P = 0.6$). These trends however are not independent as more than half of the radionuclide-monitored workers were monitored for exposure to more than one radionuclide and thus contribute to more than one category in Table IV.

There was no association between prostatic cancer mortality and monitoring for plutonium exposure. The significant trend in radiation workers who were not monitored for plutonium is due to multiple monitoring; seven of the eight men in the highest exposure category, whilst not monitored for plutonium, were monitored for exposure to tritium and/or other radionuclides. There were no significant trends when these analyses were repeated incorporating a 10-year lag (Table IV).

Only two deaths in radionuclide-monitored women precluded useful analyses of the trends in women for cancer of the uterus after stratification for radionuclide exposure.

Risk estimates

Risk estimates for leukaemia were negative regardless of the lag period assumed (Table V). The estimate of -4 leukaemia deaths per 10⁴ person-years per Sv contrasts with an equivalent figure of +0.4 deaths (95% CI -3.2 to +9.9) found previously (Inskip *et al.*, 1987). For all malignant neoplasms except leukaemia, risk estimates were positive although confidence intervals suggest that a wide range of values, both positive and negative, are compatible with the data. The estimates of +20 deaths per 10⁴ person-years per Sv for all malignant neoplasms except leukaemia compares with a figure of +17 deaths derived from previous analyses (Inskip *et al.*, 1987).

Cancer registrations compared with national rates: standardised registration rates

A total 1,699 neoplasms (ICD 140-239) registered during 1971-84 in 1,657 individuals were analysed. When person-years-at-risk as calculated for the mortality analyses were used the standardised registration ratio (SRR) in the workforce as a whole was 88 (95% CI 84-93) based on 1,632 registrations (i.e. excluding 67 cancers first identified through a death certificate in 1971-73). The SRR was 87 (95% CI 82-93) for workers with a radiation record and 90 (95% CI 83-96) for non-monitored workers. Site-specific SRRs were also calculated by censoring person-years-at-risk and registrations at the date of first registration for cancer at that site. This increased the SRRs by 4% on average, the overall SRR being 92 (95% CI 88-97) based on 1,592 registrations. The latter method for calculating person-year-at-risk was used in all subsequent site-specific analyses on the assumption that an individual diagnosed with cancer is unlikely to be at risk of another primary cancer at the same site.

Registrations for employees with radiation records compared with other employees: rate ratios

Fatal cancers dominated the cancer registrations for most cancer sites and analyses of fatal cancers have been reported

Table V Risk estimates^a (with 95% confidence limits) for leukaemia and all malignant neoplasms except leukaemia obtained from additive relative risk models using lag periods of 2 years for leukaemia and 10 years for all malignant neoplasms except leukaemia

	Excess relative risk (per Sv)	Absolute excess risk (per 10 ⁴ person years per Sv) ^b
Leukaemia (ICD8 204–208)		
Unlagged	–4.1 (–5.7, +2.9)	–3.5 (–5.4, +1.8)
Lagged	–4.2 (–5.7, +2.6)	–3.9 (–5.9, +1.7)
All malignant neoplasms except leukaemia (ICD8 140–203, 209)		
Unlagged	+1.2 (–0.4, +3.1)	+19.9 (–6.4, +48.0)
Lagged	+0.8 (–1.0, +3.1)	+20.3 (–26.0, +71.1)

^aAdjusted for age, sex, calendar period, establishment and social class.^bEquivalent to 10⁶ person-years per 10 mSv used in previous analyses (Inskip *et al.*, 1987).

in detail in Tables I to IV. The registration analyses reported here were restricted therefore to cancer sites where previous analyses have suggested a relationship between mortality or cancer incidence and radiation exposure, and sites which carry a better prognosis where an examination of cancer registrations might be expected to provide additional information. The extent to which fatal cancers dominated the cancer registrations even for these selected sites is shown in Table VI; only 429 (27%) individuals with a malignant neoplasm registered in 1971–84 were alive at the end of the study period in December 1986.

When registration rates for employees with a radiation record were compared with rates for other employees there were no significantly raised ratios in either lagged or unlagged analyses (Table VI). In the latter, the rate ratio of 0.38 (95% CI 0.15–0.98) for testicular cancer was significantly low ($P = 0.05$). There was no evidence of excess registrations

Discussion

Cancer mortality

This report describes mortality from all causes, and cancer in particular, among 39,718 employees of the UKAEA over a 41-year period from 1946 to 1986. The analyses are based on a total of 5,509 deaths, representing an increase of 63% over

the number of deaths included in our first report which covered 34 years from 1946 to 1979 (Beral *et al.*, 1985). This substantial increase in material permitted more detailed analyses to be carried out for site-specific cancer sites than previously. Comparisons have been made with mortality in the general population of England and Wales, between employees with a radiation record and other employees, and between groups of radiation workers accumulating different levels of external radiation exposure. Mortality has also been examined in workers monitored for internal exposure to tritium, plutonium and other unspecified radionuclides. The of non-fatal breast cancer among women with a radiation record (not shown) as had been the case in the analysis reported in our previous paper (Inskip *et al.*, 1987).

Cancer registrations and level of cumulative external radiation exposure

In unlagged but not lagged analyses there was a significant trend in prostatic cancer registrations with increasing exposure overall (χ^2 for trend = 6.34, $P = 0.01$) and at Winfrith alone (χ^2 for trend = 5.52, $P = 0.02$). These trends are based on 74 and 23 registrations respectively. In women the unlagged analyses showed trends for all malignant neoplasms (χ^2 for trend = 5.43, $P = 0.02$ based on 61 registrations) and for invasive cancer of the uterus (χ^2 for trend = 4.83, $P = 0.03$ based on eight registrations) which persisted in the lagged analyses. The uterine cancers were all fatal and thus the findings largely replicate those of the mortality analysis.

In our previous analysis of non-fatal cancers in relation to cumulative whole body exposure (Inskip *et al.*, 1987) the trends for skin cancer and bladder cancer were suggestive of an association ($\chi^2 = 3.65$, $P = 0.06$ and $\chi^2 = 3.57$, $P = 0.06$ respectively). These findings were not replicated when the trends for these two sites were re-examined in subjects registered in 1971–84 who were still alive at the end of the study period in December 1986. The chi-squared trend statistic for skin cancer was 0.12 ($P = 0.7$) in unlagged analyses and 0.03 ($P = 0.9$) in lagged analyses based on 71 registrations. The corresponding statistics for bladder cancer were 1.92 ($P = 0.2$) and 0.97 ($P = 0.3$) based on 25 registrations. Non-fatal cancers of the prostate were also examined in relation to cumulative whole body exposure but there was no evidence of an association (χ^2 (unlagged) = 1.91, $P = 0.3$ and χ^2 (lagged) = 0.17, $P = 0.7$, based on 21 registrations).

Table VI Percentage survival at end of study period and registration rate ratios for selected sites for employees with a radiation record compared with other employees, adjusted for age, sex, calendar period, establishment and social class, 1971–1984

Cancer site (ICD code (8th revision))	All registrations	Survival % (No.)	Rate ratio (95% confidence interval)	
			No lag	10-year lag
<i>All malignant neoplasms</i> (140–209)	1594	27 (429)	1.01 (0.90–1.13)	1.07 (0.95–1.20)
Skin (172–173)	178	72 (128)	1.05 (0.75–1.47)	1.14 (0.82–1.59)
Breast (174)	135	42 (57)	1.02 (0.64–1.64)	0.97 (0.58–1.62)
Uterus (180–182)	37	49 (18)	1.44 (0.62–3.37)	1.82 (0.77–4.26)
Cervix <i>in situ</i> (234.0)	25	96 (24)	0.74 (0.17–3.30)	0.97 (0.22–4.35)
Ovary (183)	28	32 (9)	0.82 (0.27–2.47)	1.00 (0.33–3.03)
Prostate (185)	105	25 (26)	1.34 (0.85–2.10)	1.43 (0.92–2.22)
Testis (186)	20	65 (13)	0.38 ^a (0.15–0.98)	0.39 (0.14–1.11)
Bladder (188, 223.3)	94	50 (47)	1.14 (0.73–1.79)	1.15 (0.74–1.78)
Brain and nervous system (191–192, 225, 238) ^b	35	20 (7)	0.89 (0.41–1.92)	0.80 (0.38–1.71)
Thyroid (193)	7	43 (3)	0.36 (0.06–3.93)	0.54 (0.11–4.21)
<i>All lymphatic and haematopoietic</i> (200–209)	119	25 (30)	0.79 (0.53–1.20)	0.85 (0.57–1.29)
Non-Hodgkin's lymphoma (200, 202)	45	33 (15)	0.91 (0.45–1.83)	0.85 (0.43–1.67)
Multiple myeloma (203)	13	8 (1)	0.28 (0.06–1.72)	0.36 (0.08–2.08)
Leukaemia (204–208)	49	16 (8)	0.77 (0.41–1.46)	0.79 (0.42–1.51)
Leukaemia except CLL (204–208 except 204.1)	36	11 (4)	0.63 (0.29–1.34)	0.65 (0.31–1.40)
All neoplasms (140–239)	1657	29 (475)	1.00 (0.90–1.12)	1.06 (0.95–1.18)

Significance: ^a $P < 0.05$. All significance probabilities and confidence intervals have been calculated using exact methods where observed registrations < 20 . ^bIncludes benign and unspecified neoplasms of the nervous system.

results will be discussed here within the context of the previous findings, which have been described fully elsewhere (Beral *et al.*, 1985; Inskip *et al.*, 1987; Carpenter *et al.*, 1988; Carpenter *et al.*, 1990).

As previously, overall mortality in the UKAEA workforce was lower than the national average in England and Wales as a consequence of health-related selection and other differences between employed people and the general population (Carpenter *et al.*, 1990). Cancer mortality remained about 20% below national rates and rate ratios for all malignant neoplasms indicated no overall difference in cancer mortality between workers with a radiation record and other employees. As before, mortality from testicular cancer, thyroid cancer, leukaemia and non-Hodgkin's lymphoma was above average in the workforce as a whole but only that for testicular cancer approached statistical significance. Attention had been drawn previously to increased mortality from testicular cancer, particularly at Harwell (Beral *et al.*, 1985), but there was no evidence in these new analyses that this finding was associated with exposure to radiation.

As in previous analyses, prostatic cancer mortality showed a clear relation with radiation exposure. There was a statistically significant association with increasing cumulative whole body exposure although the trend diminished in strength with longer lags. The pattern of prostatic cancer mortality across age groups suggests, as before, that the highest risk (relative to national rates) is in men aged 45-54. Mortality was significantly raised in men monitored for exposure to tritium, the rates being increased nearly 3-fold in comparison with national rates and other radiation workers who were not monitored for tritium exposure. At Winfrith, where prostatic cancer mortality was significantly increased in employees with a radiation record, mortality was also raised in men monitored for exposure to tritium, and to radionuclides other than tritium and plutonium. Further examination of the dose-response relationships after stratification for radionuclide exposure indicated that the association between prostatic cancer mortality and cumulative whole body exposure was largely confined to radiation workers who had also been monitored for radionuclide exposure, notably tritium and unspecified radionuclides. The highest risks were in radionuclide-monitored workers who had accumulated at least 100 mSv external exposure suggesting as before that men with these dual exposures are most at risk. The findings for prostatic cancer are now being investigated further in a case-control study based on UKAEA records to determine if prostatic cancer can be linked to any particular aspect of the employment history of the individuals concerned. Particular attention is being given to radionuclide exposure and the potential for contamination of the work environment by radionuclides, chemicals and other substances.

Mortality from cancer of the uterus (including the cervix uteri) in women with a radiation record was increased 4-fold by comparison with other employees. As in the previous report (Beral *et al.*, 1985), cancers of the body of the uterus made the major contribution to the excess mortality. The persistent trend in these analyses, whilst based on only eight deaths, is supportive of an association between mortality from cancer of the uterus and external exposure to radiation and warrants further study. Contrary to the findings in the previous analysis, there was no suggestion of increased mortality from ovarian cancer.

Although the increase in the average duration of follow-up from 16 to 22 years allowed for longer latency and greater statistical power, cancer of the prostate, and possibly the uterus, are the only malignancies which show an association with radiation exposure in the UKAEA workforce. It is noteworthy that mortality from multiple myeloma which has been associated with radiation exposure in the Sellafield (Smith & Douglas, 1986) and Hanford (Gilbert *et al.*, 1989) workforces was not associated with radiation exposure in UKAEA employees. Indeed, the SMR of 36 (95% CI 10-92) based on four deaths from multiple myeloma in employees with a radiation record was significantly low by comparison with national rates ($P = 0.03$).

Despite the additional 7 years of follow-up yielding a substantially increased number of cancer deaths, uncertainty associated with the risk estimates remains large (Table V). For leukaemia, the data are compatible with decreasing risks or increases of up to two deaths per 10^4 person-years per Sv (or an excess RR of 2.6 per Sv). These risk estimates are very similar to those obtained for US nuclear industry workers (Gilbert *et al.*, 1989) but contrast with the positive values recently provided for adult males from A-bomb survivor data of 5.0 deaths per 10^4 person-years per Sv and an excess RR of 3.7 per Sv (UNSCEAR, 1988). Comparing these latter estimates with those relating to nuclear industry workers is questionable because they are likely to be affected by many factors thought to modify the risk of radiation-induced leukaemia. These include the type and duration of exposure and other characteristics of the populations studied. Recent analysis of a much larger population of UK nuclear industry workers (Kendall *et al.*, 1992a,b) (of which the current UKAEA cohorts forms a part) are more appropriate for comparison. This provided an excess RR estimate for leukaemia of 4.3 per Sv (90% CI 0.4 to 13.6).

In contrast with data on US workers, the central risk estimate for all cancers except leukaemia obtained from our data was positive (excess RR per Sv (lagged) = 0.8, 95% CI -1.0 to 3.1). Data from the larger population of UK workers are also suggestive of a generally positive association (excess RR for all malignant neoplasms = 0.5 per Sv, 90% CI -0.1 to 1.2) (Kendall *et al.*, 1992a,b). Estimates of absolute risk from our data ranged from a decrease of 26 deaths per 10^4 person-years per Sv to an increase of about 70. Whilst these include the value recently recommended by the International Commission on Radiological Protection (ICRP) for working populations of approximately 14 deaths per 10^4 person-years per Sv (ICRP, 1990) (assuming a 25-year expression for lifetime risks), our estimates are not sufficiently precise to rule out estimates of up to five times larger than this. To lessen this uncertainty, we have combined the UKAEA, Atomic Weapons Establishment (Beral *et al.*, 1988) and Sellafield (Smith & Douglas, 1986) study populations in a further analysis (the Nuclear Industry Combined Epidemiological Analysis). The combined study population of 75,000 nuclear industry workers will permit the relationship between exposure to low-level ionising radiation and cancer mortality to be estimated with greater precision than was possible in any of the three studies individually.

Cancer morbidity

Because of high case fatality for most cancer sites, the findings for cancer registrations largely replicated those of the mortality analyses. In particular, trends in registrations of prostatic cancer and cancer of the uterus with increasing exposure were apparent. The dose-response relationships reported before for non-fatal skin and bladder cancers (Inskip *et al.*, 1987) were not replicated here. The previous findings were based only on cancer registrations in ex-employees who may not have been typical of the workforce as a whole. These new results based on cancer registrations in all employees suggest that the previous findings may have been biased.

Conclusion

This analysis of a much larger body of material than that reported in our first analysis of the UKAEA workforce generally confirms the robustness of the previous findings for most cancer sites. The association between prostatic cancer and both internal and external exposure to radiation is still evident though the dose-response relationship is diminished in strength. Prostatic cancer is under investigation in a case-control study within the UKAEA workforce. The association between cancer of the uterus and external radiation exposure which has strengthened in this analysis also warrants further study. There are a number of other statistically significant

results, as would be expected by chance alone when such a large number of comparisons are made, but no other cancer sites with consistently exceptional findings. Uncertainty still surrounds estimates of the increase in cancer risk per unit dose. Further combined analyses will provide more precise estimates.

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References

- BAILAR, J.C. & EDERER, F. (1964). Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics*, **20**, 639–643.
- BAKER, R.J. & NELDER, J.A. (1982). The GLIM system. Release 3.77. *Generalised Linear Interactive Modelling*. Oxford: Numerical Algorithms Group.
- BERAL, V., INSKIP, H., FRASER, P., BOOTH, M., COLEMAN, D. & ROSE, G. (1985). Mortality of employees of the United Kingdom Atomic Energy Authority, 1946–79. *Br. Med. J.*, **291**, 440–447.
- BERAL, V., FRASER, P., CARPENTER, L., BOOTH, M., BROWN, A. & ROSE, G. (1988). Mortality of employees of the Atomic Weapons Establishment, 1951–82. *Br. Med. J.*, **297**, 757–770.
- BRESLOW, N.E. & DAY, N.E. (1987). Statistical methods in cancer research. Vol. 2. The design and analysis of cohort studies. *IARC Scientific Publications*, No. 82. Lyon: International Agency for Research on Cancer.
- CARPENTER, L., HARTNELL, J., BROWN, A., BOOTH, M., BERAL, V. & FRASER, P. (1988). United Kingdom Atomic Energy Authority Mortality Study: Supplementary Tables. *Atomic Energy Research Establishment R 13007*.
- CARPENTER, L., BERAL, V., FRASER, P. & BOOTH, M. (1990). Health related selection and death rates in the United Kingdom Atomic Energy Authority workforce. *Br. J. Ind. Med.*, **47**, 248–258.
- FRASER, P., BOOTH, M., BERAL, V., INSKIP, H., FIRSHT, S. & SPEAK, S. (1985). Collection and validation of data in the United Kingdom Atomic Energy Authority mortality study. *Br. Med. J.*, **291**, 435–439.
- FRASER, P., MACONOCHE, N., CARPENTER, L., HIGGINS, C., BOOTH, M. & BERAL, V. (In preparation). Mortality and cancer morbidity in United Kingdom Atomic Energy Authority employees, 1946–86. *Atomic Energy Authority Report*.
- GILBERT, E.S., FRY, S.A., WIGGS, L.D., VOELZ, G.L., CRAGLE, D.L. & PETERSEN, G.R. (1989). Analyses of combined mortality data on workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant. *Radiation Res.*, **120**, 19–35.
- GILBERT, E.S. (1989). Issues in analysing the effects of occupational exposures to low levels of radiation. *Statist. Med.*, **8**, 173–187.
- ICRP (1990). Recommendations of the International Commission on Radiological Protection, Publication 60. *International Commission on Radiological Protection*. Pergamon Press: Oxford.
- INSKIP, H., BERAL, V., FRASER, P., BOOTH, M., COLEMAN, D. & BROWN, A. (1987). Further assessment of the effects of occupational radiation exposure in the United Kingdom Atomic Energy Authority mortality study. *Br. J. Ind. Med.*, **44**, 149–160.
- KENDALL, G.M., MUIRHEAD, C.R., MACGIBBON, B.H., O'HAGAN, J.A., CONQUEST, A.J., GOODHILL, A.A., BUTLAND, B.K., FELL, T.P., JACKSON, D.A., WEBB, M.A., HAYLOCK, R.G.E., THOMAS, J.M. & SILK, T.J. (1992a). *First analysis of the National Registry for Radiation Workers: Occupational exposure to ionising radiation and mortality*. NRPB-R251.
- KENDALL, G.M., MUIRHEAD, C.R., MACGIBBON, B.H., O'HAGAN, J.A., CONQUEST, A.J., GOODHILL, A.A., BUTLAND, B.K., FELL, T.P., JACKSON, D.A., WEBB, M.A., HAYLOCK, R.G.E., THOMAS, J.M. & SILK, T.J. (1992b). Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers. *Br. Med. J.*, **304**, 220–225.
- SMITH, P.G. & DOUGLAS, A.J. (1986). Mortality of workers at the Sellafield plant of British Nuclear Fuels. *Br. Med. J.*, **293**, 845–854.
- UNSCEAR (1988). Sources, effects and risks of ionizing radiation. Annex F. *Radiation Carcinogenesis in Man*. United Nations Scientific Committee on the Effects of Atomic Radiation. E. 88. IX. 7, United Nations New York.