

Table 2.8. Cohort studies of exposure to radium-224, 226 or 228 and their decay products

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Nekolla <i>et al.</i> (2000) Germany Ra-224 TB and ankylosing spondylitis patients	Cohort of 899 patients (278 males, 621 females) treated for tuberculosis or ankylosing spondylitis with injections of Ra-224, mainly during 1948-52. Analysis restricted to 812 patients (204 treated at ages under 21 years) for whom the period of over injections were given is known. Follow-up to 1998, based on collection of morbidity data every 2-3 years since the 1950s; "only a few persons lost to follow-up".	Internal dosimetric calculations based on amount injected. Mean bone surface dose: 30 Gy.	Bone	Dose response analyses based on continuous measure of dose to bone surface.	45 cases	Overall RR = 155. Excess absolute risk modelled as a function of dose, time since first injection, age at first injection and duration of treatment.	Age, gender	Virtually all of the bone tumours in this cohort are attributable to Ra-224 treatment. Excess risk peaked 8 years after exposure and increased with dose to bone surface. Radiation-related risk increased with decreasing age at first injection and – at high doses – with increasing duration of treatment.
Nekolla <i>et al.</i> (1999) Germany Ra-224 TB and ankylosing spondylitis patients	As above	Mean specific activity: 0.66 MBq/kg.	SIRs presented only for selected cancers.	Mostly comparisons of rates for exposed patients with population cancer rates. ERR/Sv was calculated for a few cancers.	<u>Cancer (Lag) Cases</u> Liver (5 y): 7 Lung (5 y): 20 Connective tissue (5 y): 7 Male breast (5 y): 2 Female breast (5 y): 28 Bladder (5 y): 14 Kidney (5 y): 10 Thyroid (5 y): 5 Leukaemia (0 y): 8 Leukaemia (2 y): 7	<u>SIR (95%CI)</u> 3.18 (1.28-6.56) 0.67 (0.41-1.03) 7.78 (3.13-16.0) 10.0 (1.21-36.1) 3.5 (2.33-5.06) 1.94 (1.06-3.26) 2.38 (1.14-4.38) 6.25 (2.03-14.6) 2.11 (0.91-4.15) 1.84 (0.74-3.80)	Age, gender, calendar period	ERR/Sv estimated to be 2.9 for female breast cancer, 0.4 for bladder cancer and 0.6 for kidney cancer. In a control group of 182 unexposed tuberculosis patients, 7 female breast cancers were observed compared with 3.8 expected.

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Wick <i>et al.</i> (2008) Germany Ra-244 ankylosing spondylitis patients	Cohort of 1588 patients (90.5% male) treated for ankylosing spondylitis with injections of Ra-224, during 1948-75. Control group of 1324 ankylosing spondylitis patients (91.8% male) not treated with radioactive drugs or x-rays. Follow-up based on questionnaires sent periodically to patients. Causes of death ascertained from hospital records, death certificates and reports from family doctors.	Internal dosimetric calculations based on amount injected. Average cumulative skeletal dose: 0.56 Gy.	All leukaemia (204-208) Myeloid leukaemia (205), including CML (205.1) and AML (205.0) Lymphatic leukaemia (204)	Incidence in exposed and unexposed groups compared with rates for Saarland (Germany) and Denmark. No dose-response analysis conducted	<u>All leukaemia</u> Exposed: 19 Unexposed: 12 <u>Myeloid leukaemia</u> Exposed: 11 Unexposed: 4 <u>CML</u> Exposed: 3 Unexposed: 1 <u>AML</u> Exposed: 7 Unexposed: 3 <u>Lymphatic leukaemia</u> Exposed: 7 Unexposed: 6	SIR (p-value) 2.8 (<0.001) 1.6 (0.08) 3.8 (<0.001) 1.3 3.0 (0.08) 1.1 3.9 (0.003) 1.5 2.6 (0.02) 2.0 (0.08)	Age, gender, calendar period	End of follow-up period not stated, nor the completeness of follow-up. Exposures generally lower than those in the study of Nekolla <i>et al.</i> (2000).
Wick <i>et al.</i> (1999) Germany Ra-244 ankylosing spondylitis patients	Same as above, except that the exposed group comprised 1577 patients, the control group comprised 1462 patients, and the end of follow-up was earlier (end of 1998).	See above.	Stomach Liver Lung Female genital organs Female breast Urinary system Bone and connective tissue	Incidence in exposed and unexposed groups compared with rates for Saarland (Germany) and Denmark. No dose-response analysis conducted	<u>Stomach</u> Exposed: 18 Unexposed: 16 <u>Liver</u> Exposed: 1 Unexposed: 4 <u>Lung</u> Exposed: 25 Unexposed: 29	SIR (p-value) 1.5 (0.07) 0.9 0.4 1.3 0.7 0.6	Age, gender, calendar period	

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Wick <i>et al.</i> (1999) (Contd.)			(Leukaemia findings have been updated by Wick <i>et al.</i> , 2008)		<u>Female genital organs</u> Exposed: 7 Unexposed: 7 <u>Female breast</u> Exposed: 3 Unexposed: 1 <u>Urinary system</u> Exposed: 19 Unexposed: 16 <u>Bone and connective tissue</u> Exposed: 4 Unexposed: 1	1.7 2.0 0.7 0.3 1.2 0.7 3.0 (0.04) 1.4		
Rowland <i>et al.</i> (1978) United States Radium dial workers	Cohort of 1476 female workers employed in the US radium dial-painting industry before 1930. Measured body burdens due to intakes of Ra-226 were available for 759 of these workers. About 50% of workers employed before 1930 were identified by themselves or by co-workers. Follow-up was to the end of 1976; completeness of follow-up not stated.	Estimates of systemic intake of radium and skeletal dose, based on measured body burden	Bone sarcoma Cancers of the paranasal sinuses and mastoid air cells (head carcinomas)	Dose-response analysis, based primarily on systemic intake.	<u>Bone sarcoma</u> cases: 38 in measured workers, 23 in unmeasured workers <u>Head carcinomas</u> : 17 in measured workers, 4 in unmeasured workers	A dose-squared-exponential dose-response model provided good fit to the bone sarcoma data. A linear dose-response model provided a good fit to the data for head carcinoma.	Age, race, calendar period	A subsidiary analysis showed that exclusion of cases identified through exhumation did not significantly influence the shape of the dose-response relationships.

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Stebbing et al. (1984) United States Radium dial workers	Cohorts of 1285 female workers employed in the US radium dial-painting industry before 1930 (693 with measurements of body burden) – ie. a subset of the workers considered by Rowland <i>et al.</i> (1978)- and 1185 female workers first employed in this industry in 1930-1949 (561 with measurements of body burden).	Estimate of systemic intake of radium, based on measured body burden.	Stomach Colon Rectum Liver Pancreas Lung Breast Cervix uteri Corpus uteri Multiple myeloma Leukaemia	Dose response analyses conducted for certain cancer types, based on systemic intake of radium.	Stomach: 8 Colon: 24 Rectum: 4 Liver: 2 Pancreas: 7 Lung: 12 Breast: 36 Cervix uteri: 2 Corpus uteri: 3 Multiple myeloma: 6 Leukaemia: 3	SMR 1.33 (0.57-2.62) 1.56 (1.00-2.32) 0.96 (0.26-2.46) 0.49 (0.06-1.77) 1.21 (0.49-2.49) 1.46 (0.75-2.56) 1.44 (1.01-1.99) 0.40 (0.05-1.44) 0.64 (0.13-1.87) 2.79 (1.02-6.08) 0.73 (0.15-2.13)	Age, calendar period	Relationships with systemic intake were indicated for cancers of the lung, breast and – to a lesser extent – multiple myeloma - but not for the other cancer types considered. Lung cancer and multiple myeloma were associated with duration of employment as well as with radium body burden.
Spiers et al. (1983) United States Radium dial workers	A combination of the two cohort studies on dial painters in USA. Out of an initial 4532 persons, 3594 were located, of whom more than 2000 had measured radium-226 and radium-228 burdens. The number of women and men whose burdens were measured in 1977 or earlier, survived at least 2 years and alive in 1957 were 2696 and 244, respectively. Follow-up was to the end of 1979.	Estimates of systemic intake of radium and skeletal dose, based on measured body burden.	Leukaemia	Dose-response analysis, based on skeletal dose.	<u>All located persons</u> <u>Female</u> Expected: 7.97 Observed: 9 <u>Male</u> Expected: 1.27 Observed: 1 <u>Persons with burdens measured in 1977 or earlier, survived at least 2 years and alive in 1957</u> <u>Female</u> Expected: 2.33 Observed: 2 <u>Male</u> Expected: 0.25 Observed: 0		Stratified by gender and calendar period	Further analysis based on skeletal dose did not show a significant difference between the observed and expected cases.

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Baverstock & Papworth (1985) United Kingdom Radium dial workers	Cohort of 1110 women who entered luminising work during or after 1939, who were still in the survey in 1961, and whose names appeared on the original Ministry of Labour records. At the time they started luminising, 78% of the women were under the age of 30 years and approximately one-third were less than 20 years of age. Causes of death ascertained from 1961 through 1977.	Estimate of systemic intake of radium, based on measured body burden.	Lung Leukaemia Stomach Breast		7	SMR (<i>p</i>-value) 1.07 (0.48)	Stratified age by absorbed dose from gamma rays.	Body contents of radium were small in relation to those in the US luminisers. Gamma ray doses were recorded with dosimetry films for a part of the study period. The spread of doses was small and the median values were considered representative of the gamma ray doses received by each woman working at relevant periods. <i>p</i> -values were one-sided. Mortality in exposed and unexposed groups compared with rates for England and Wales (1961 to 1970) and national mortality rates (1971 to 1977). No dose-response analysis (for α -emitters) conducted.	
					0	0 (0.33)			
					2	0.65 (0.41)			
					18	1.38 (0.11)			
				Age	Dose				
				< 30 y	< 0.2 Gy	2			1.03 (0.58)
< 30 y	\geq 0.2 Gy	13	1.87 (0.026)						
\geq 30 y	< 0.2 Gy	2	1.23 (0.48)						
\geq 30 y	\geq 0.2 Gy	1	0.39 (0.28)						

* *p*-value for a one-tailed exact test.

NR, not reported; SIR, Standardised Incidence Ratio; SMR, Standardised Mortality Ratio; y, year or years