

Table 2.2. Case-control studies of X-ray exposure and cancer

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Bernstein <i>et al.</i> (2006) Northern California, Ontario	2311 cases ascertained via Northern California Family Registry, Ontario Familial Breast Cancer Registry	Recruited via random digit dialling only in Ontario	Interviewer-administered standardized questionnaire	Female breast cancer	Number of diagnostic chest or abdominal X-rays	OR of <i>CHEK2*1100delC</i> positivity among cases with < 2 diagnostic chest or abdominal X-rays 1.0 \geq 2 diagnostic chest or abdominal X-rays (vs < 2) 1.56 (95% CI: 0.65–3.74), OR of <i>CHEK2*1100delC</i> positivity among cases with \geq 2 diagnostic chest or abdominal X-rays (vs < 2) 2.19 (95% CI: 0.91–5.28)	None	Poor ascertainment of radiation exposure and disease (particularly controls); potential for recall bias
Boffetta <i>et al.</i> (2005) 15 areas in Romania, the Russian Federation, Poland, Slovakia, Czech Republic, Hungary 1998–2002	2859 histologically and cytologically confirmed cases	Hospital controls in same area (or in Poland population controls)	Interviewer-administered questionnaire, supplemented by expert assessment of likely exposure by job type	Lung cancer	Number of diagnostic X-rays	OR of 0 exposures 1, OR of 1–10 X-rays 1.21 (95% CI: 0.99–1.48), OR of 11–20 X-rays 1.33 (95% CI: 1.08–1.64), OR of 21–30 X-rays 1.49 (95% CI: 1.18–1.87), OR of 31–40 X-rays 1.52 (95% CI: 1.17–1.99), OR of > 40 X-rays 2.15 (95% CI: 1.50–3.08) (trend $P < 0.0001$)	Adjustment for age, sex, centre, pack years of smoking	Poor ascertainment of radiation exposure; poor ascertainment of cigarette smoking; potential for confounding by indication, potential recall bias
Gilbert <i>et al.</i> (2003) international Hodgkin's disease study	227 cases selected from 19 046 1-year survivors of Hodgkin's disease (HD) 1/1965–12/1994 in US and Netherlands with pathological and clinical confirmation of diagnosis	2 individually matched controls per case (total 455), matched on age at HD diagnosis, calendar year, gender, registry	Clinical data	Lung cancer	> 0–4.9 Gy 5.0–14.9 Gy 15.0–29.9 Gy 30.0–39.9 Gy 40.0+ Gy	Odds ratio 1.64 (0.53–5.2) 4.18 (0.70–21) 2.69 (0.15–15) 8.50 (3.3–24) 6.27 (2.2–19) Excess OR/Gy 0.15 (0.06–0.39)	Adjustment for smoking, chemotherapy	Good ascertainment of radiation + chemotherapy exposure

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Hatcher <i>et al.</i> (2001) cases in Georgia, Michigan, New Jersey, 8/1986–4/1989 aged 30–79	540 cases reported to Georgia Center for Cancer Statistics, Metropolitan Detroit Cancer Surveillance System, New Jersey State Cancer Registry	Frequency matched controls obtained via random digit dialling (ages 30–64) or random sampling from Medicare database listings (ages 65–79)	Interviewer-administered questionnaire	Multiple myeloma	Number of diagnostic X-rays	OR of < 5 exposures 1, OR of 5–9 X-rays 0.9 (95% CI: 0.7–1.2), OR of 10–19 X-rays 1.0 (95% CI: 0.7–1.3), OR of > 20 X-rays 0.9 (95% CI: 0.7–1.2)	Adjustment for education, age, sex, gender, state	Poor ascertainment of radiation exposure, relatively low response rate (63% whites, 67% blacks), possible biases due to control sampling, potential for recall bias
Hung <i>et al.</i> (2006) 15 areas in Romania, the Russian Federation, Poland, Slovakia, Czech Republic, Hungary 1998–2002	2238 histologically and cytologically confirmed cases	2289 frequency matched (by sex, age, centre) hospital controls in same area (or in Warsaw population controls)	Interviewer-administered questionnaire, supplemented by expert assessment of likely exposure by job type	Lung cancer	Ever vs never exposure to diagnostic X-rays, also by number of diagnostic X-rays	<i>CCND1 G870A</i> variant interaction OR (X-ray ever vs never) 1.01 (95% CI: 0.68 – 1.49) trend OR: 1.16 (95% CI: 1.05–1.27); <i>CDKN2A A148T</i> variant interaction OR (X-ray ever vs never) 1.22 (95% CI: 0.62 – 2.40); <i>TP53 R72P</i> variant interaction OR (X-ray ever vs never) of 1.00 (95% CI: 0.72 – 1.38); <i>TP53 intron 3</i> variant interaction OR (X-ray ever vs never) 5.69 (95% CI: 1.33 – 24.3) trend OR: 2.12 (95% CI: 1.12–4.02)	Adjustment for age, sex, country, pack years of smoking	Poor ascertainment of radiation exposure; poor ascertainment of cigarette smoking; potential for confounding by indication, recall bias

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Infante-Rivard (2003) Quebec 1980–1998	701 cases aged 0–14 derived from hospital and other clinical records	701 age, sex region matched controls selected from family allowance files	Interviewer-administered questionnaire	Acute lymphocytic leukaemia (ICD9 204.0)	Ever vs never exposure to postnatal diagnostic X-rays, also by number of diagnostic X-rays	None OR = 1, 1 X-ray OR = 1.16 (95% CI: 0.87 – 1.55), ≥ 2 X-rays OR = 1.48 (95% CI: 1.11 – 1.97) trend $P = 0.006$	Adjustment for mother's age, education	Poor ascertainment of radiation exposure, potential for recall bias
Millikan <i>et al.</i> (2005) 15 counties in central and eastern North Carolina 1993–2001	1808 invasive cases, 503 in situ cases	2022 cases frequency matched to cases based on age and race, via Division of Motor Vehicles (ages < 65) or US Health care Financing Administration (ages ≥ 65) databases	Interviewer-administered questionnaire	Invasive and in situ female breast cancer	Number of diagnostic X-rays	0–1 variant codons among <i>XRCC3</i> , <i>NBS1</i> , <i>XRCC2</i> , <i>BRCA2</i> Number of mammograms (2 y lag) None OR = 1, 1–2 OR = 1.0 (95% CI: 0.7 – 1.5), 3–5 OR = 0.7 (95% CI: 0.5 – 1.0), 6–10 OR = 0.7 (95% CI: 0.4 – 1.0), ≥ 11 OR = 0.9 (95% CI: 0.6 – 1.4) trend $P = 0.16$; 2–4 variant codons among <i>XRCC3</i> , <i>NBS1</i> , <i>XRCC2</i> , <i>BRCA2</i> Number of mammograms (2 y lag) None OR = 1, 1–2 OR = 0.8 (95% CI: 0.5 – 1.1), 3–5 OR = 1.3 (95% CI: 0.8 – 1.9), 6–10 OR = 1.3 (95% CI: 0.9 – 2.1), ≥ 11 OR = 1.8 (95% CI: 1.2 – 2.8) trend $P = 0.0003$	Adjustment for age, race	Poor ascertainment of radiation exposure, potential for recall bias

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Myles <i>et al.</i> (2008) cases under age 60 diagnosed in two hospitals in United Kingdom	431 cases	409 frequency matched controls (by age to within 5 years), from same GP practice as cases	Postal questionnaire	Prostate cancer	Barium meal (mean dose 0.2–0.4 mGy), barium enema (mean dose 10–25 mGy), intravenous pyelogram (IVP) (mean dose 3–4 mGy), X-ray (hip/pelvic, upper leg) (mean dose 2–5 mGy for hip/pelvic)	Barium meal > 5 years previously OR = 1.21 (95% CI: 0.84 – 1.73); barium enema > 5 years previously OR = 2.06 (95% CI: 1.01 – 4.20); IVP > 5 years previously OR = 1.67 (95% CI: 0.92 – 3.03); hip/pelvic X-ray > 5 years previously OR = 2.23 (95% CI: 1.42 – 3.49); upper leg X-ray > 5 years previously OR = 1.11 (95% CI: 0.65 – 1.89);	Adjustment for age at diagnosis, social class	Poor ascertainment of radiation exposure, potential for recall bias, potential confounding by indication
Neglia <i>et al.</i> (2006) US childhood cancer study	116 cases selected from 14 361 5-year survivors of childhood cancer 1/1970–12/1986 in CCS centres in US, diagnosed with first primary cancer before age 21, with pathological and clinical confirmation of diagnosis	4 individually matched controls per case (total 464), matched on age at original cancer diagnosis (± 2 years), sex	Clinical data records	Central nervous system (ICD-O-2 9 380–9523, 9 530–9539)	< 1 Gy, 1–9.9 Gy, 10.0–19.9 Gy, 20.0–29.9 Gy, 30.0–44.9 Gy, ≥ 45 Gy	OR of < 1 Gy = 1, OR of 1–9.9 Gy 0.00 (95% CI: 0.00 – 2.44), OR of 10.0–19.9 Gy 9.71 (95% CI: 2.73 – 34.5), OR of 20.0 – 29.9 Gy 13.4 (95% CI: 4.30 – 41.79), OR of 30.0 – 44.9 Gy 50.0 (95% CI: 13.3 – 187.4), OR of ≥ 45 Gy 32.8 (95% CI: 8.38 – 128.3) ERR /Gy 0.33 (95% CI: 0.07 – 1.71) (gliomas) ERR /Gy 1.06 (95% CI: 0.21 – 8.15) (meningiomas) ERR /Gy 0.69 (95% CI: 0.25 – 2.23) (all CNS tumours)	Adjusted for type of first cancer	Good ascertainment of radiation + chemotherapy exposure, follow-up

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Ronckers <i>et al.</i> (2006) US childhood cancer study	72 cases selected from 14 361 5-year survivors of childhood cancer 1/1970–12/1986 in CCS centres in US, diagnosed with first primary cancer before age 21, with pathological and clinical confirmation of diagnosis	4 individually matched controls per case (total 288), matched on age at original cancer diagnosis (± 2 years), sex	Clinical data records	Thyroid	0 – 62 Gy (mean cases 24 Gy, mean controls 13 Gy)	ERR /Gy 1.3 (95% CI: 0.4 – 4.1)	Adjusted for quadratic cell killing term	Good ascertainment of radiation + chemotherapy exposure, follow-up
Rubino <i>et al.</i> (2005) cancer after breast cancer	14 cases	28 individually matched controls (by age to within 6 years, by calendar year of treatment) within cohort of 7 711	Dosimetric estimates based on clinical records	Bone & soft tissue sarcoma	Mean case dose (to site of bone/soft tissue sarcoma) 38.8 Gy (range 11.8 – 60.2), mean control dose (at same site) 18.9 Gy (range 0.01 – 79.8)	Excess odds ratio at 1 Gy (linear-quadratic model) 0.05 (95% CI: ? – 1.18)	None	Good ascertainment of radiation exposure

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Stålberg <i>et al.</i> (2007) Swedish prenatal exposure study, 1975–1984	512 cases diagnosed via Swedish Cancer Registry at age < 15	524 frequency matched controls (by sex, year of birth) selected from Medical Birth Register, alive and resident in Sweden to age 15	Hospital records of antenatal diagnostic procedures (X-ray, ultrasound)	Childhood brain cancer (ICD7 193)	None	All brain tumours abdominal X-ray OR: 1.02 (95% CI: 0.64 – 1.62); non-abdominal X-ray OR: 0.78 (95% CI: 0.52 – 1.17) Astrocytoma low grade abdominal X-ray OR: 0.72 (95% CI: 0.36 – 1.42); non-abdominal X-ray OR: 0.96 (95% CI: 0.57 – 1.62) Astrocytoma high grade abdominal X-ray OR: 1.06 (95% CI: 0.39 – 2.86); non-abdominal X-ray OR: 0.36 (95% CI: 0.12 – 1.08) PNET abdominal X-ray OR: 1.88 (95% CI: 0.92 – 3.83); non-abdominal X-ray OR: 0.81 (95% CI: 0.83 – 1.69)	Adjustment for maternal age at birth, parity, multiple birth, mother's country of birth, hypertension during pregnancy, mode of delivery, breech position, gestational age at birth, birth weight, head circumference at birth, hospital level	Limited ascertainment of radiation exposure (only yes vs no), otherwise thorough study

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Travis <i>et al.</i> (2000) international testicular cancer study	36 cases selected from 18 567 1-year survivors of testicular cancer 1/1970–12/1993 in Denmark, Finland, Sweden, Ontario, Iowa, Connecticut, New Jersey, Netherlands diagnosed before age 30 with pathological and clinical confirmation of diagnosis	3 individually matched controls per case (2 per case for New Jersey) (total 106), matched on registry, age at HD diagnosis, year of HD diagnosis	Clinical data records	Leukaemia	0–7.5 Gy, 7.5–9.9 Gy, 10.0–14.9 Gy, 15.0–19.9 Gy, ≥ 20 Gy	OR of 0–7.5 Gy = 1, OR of 7.5–9.9 Gy 3.5 (95% CI: 0.6–27), OR of 10.0–14.9 Gy 2.4 (95% CI: 0.4–20), OR of 15.0–19.9 Gy 4.9 (95% CI: 0.5–57), OR of ≥ 20 Gy 19.7 (95% CI: 1.5–590) ERR /Gy 0.27 (95% CI: 0.02–1.2)	Adjustment for chemotherapy	Good ascertainment of radiation + chemotherapy exposure, follow-up
Travis <i>et al.</i> (2003) international Hodgkin's disease study	105 cases selected from 3 817 female 1-year survivors of Hodgkin's disease (HD) 1/1965–12/1994 in Denmark, Finland, Sweden, Ontario, Iowa, Netherlands diagnosed before age 30 with pathological and clinical confirmation of diagnosis	≥ 2 individually matched controls per case (total 266), matched on registry, age at HD diagnosis, year of HD diagnosis	Clinical data	Female breast cancer	0–3.9 Gy, 4.0–6.9 Gy, 7.0–23.1 Gy, 23.2–27.9 Gy, 28.0–37.1 Gy, 37.2–40.4 Gy, 40.5–61.3 Gy	OR of 0–3.9 Gy = 1, OR of 4.0–6.9 Gy 1.8 (95% CI: 0.7–4.5), OR of 7.0–23.1 Gy 4.1 (95% CI: 1.4–12.3), OR of 23.2–27.9 Gy 2.0 (95% CI: 0.7–5.9), OR of 28.0–37.1 Gy 6.8 (95% CI: 2.3–22.3), OR of 37.2–40.4 Gy 4.0 (95% CI: 1.3–13.4), OR of 40.5–61.3 Gy 8.0 (95% CI: 2.6–26.4) Excess OR /Gy 0.15 (95% CI: 0.04–0.73) for women without CT receiving chest RT; excess OR /Gy 0.049 (95% CI: 0.004–0.34) for women with CT receiving ≥ 5 Gy to ovaries	Adjustment for ovary dose, chemotherapy, number of cycles of treatment with alkylating agents	Good ascertainment of radiation + chemotherapy exposure, follow-up

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van Leeuwen <i>et al.</i> (2003) Netherlands Hodgkin's disease study	48 cases selected from 770 female survivors of Hodgkin's disease (HD) 1/1965–12/1988 in Netherlands diagnosed before age 40 with pathological and clinical confirmation of diagnosis	≥ 4 individually matched controls per case (total 175), matched on age at HD diagnosis (± 3 years), year of HD diagnosis (± 5 years)	Clinical data	Female breast cancer	0.26 – 3.9 Gy, 4.0–23.2 Gy, 24.0–38.2 Gy, 38.5–56 Gy	OR of 0.26 – 3.9 Gy = 1, OR of 4.0–23.2 Gy 1.11 (95% CI: 0.32 – 3.85), OR of 24.0–38.2 Gy 4.20 (95% CI: 0.99 – 17.8), OR of 38.5 – 56 Gy 5.16 (95% CI: 1.27 – 21.0) Total ERR /Gy 0.03 (95% CI: 0.002 – 0.06); RT only women ERR /Gy 0.06 (95% CI: 0.01 – 0.13)	Adjustment for ovary dose, chemotherapy	Good ascertainment of radiation + chemotherapy exposure, follow-up