

Human studies of stillbirth and other adverse pregnancy outcomes: details of epidemiological studies considered in the COMARE Eighth Report (2004)

Reference	Parental study population	Description	Results	Notes
Otake et al (1990) <i>Radiat Res</i> , 122 , 1–11	Atomic-bomb survivors	Cohort study of ARO including early natal death (14 days) in relation to joint parental DS86 dose	<i>Risks per Sv (additive model)</i> Malformation 9.9±18.4 10 ⁻⁴ Stillbirth 15.1±19.9 10 ⁻⁴ Neonatal death 23.7±23.3 10 ⁻⁴ All ARO 42.2±34.3 10 ⁻⁴	Little (1999) (<i>J Radiol Prot</i> , 19 , 361–73) fitted a relative risk model to these data: ARO ERR Sv ⁻¹ = 0.07 (CI -0.14–0.26)
Schull et al (1981) <i>In Population and Biological Aspects of Human Mutation</i> (Hook and Porter, Eds), pp 277–303	Atomic-bomb survivors	Cohort study of ARO including early natal death (30 days) in relation to TD65 dose to mothers and to fathers	<i>Risks per Sv (additive model)</i> Malformation 28.8±5.4 10 ⁻⁴ (paternal) -11.9± 6.8 10 ⁻⁴ (maternal) Stillbirth -9.8±4.3 10 ⁻⁴ (paternal) -60.9±59.7 10 ⁻⁴ (maternal) Neonatal death 35.9±4.5 10 ⁻⁴ (paternal) -26.2±93.6 10 ⁻⁴ (maternal) All ARO 53.4±3.3 10 ⁻⁴ (paternal) -96.4±65.5 10 ⁻⁴ (maternal)	Little (1999) fitted a relative risk model to these data: stillbirth ERR Sv ⁻¹ = -0.11 (CI -0.52–0.25)
Sever et al (1988a) <i>Am J Epidemiol</i> , 127 , 226–42	Residents in two counties near the Hanford plant, 1957–1980	Case-control study of twelve types of congenital abnormality	<i>Association with father's employment at Hanford</i> Tracheoesophageal fistula, congenital dislocation of hip (both p < 0.05) <i>Trend with dose</i> Neural tube defects p = 0.04 (paternal) All major malformations p = 0.14 (paternal) All malformations p = 0.07 (paternal)	672 malformation cases, 977 controls. Individual estimates of occupational exposure. Multiple significance testing
Sever et al (1988b) <i>Am J Epidemiol</i> , 127 , 243–54	Residents in two counties near the Hanford plant, 1957–1980	Study of prevalence, 1968–1980, of congenital abnormalities in the first year of life (determined by hospital and other records). Compared with mean rates at newborn discharge for Washington, Oregon and Idaho. Concentrates on abnormalities recognised at birth	<i>Prevalence per 1000 total births (with CI) of three state mean and p-value for significance of difference</i> Neural tube defects 1.72 (1.22–2.340) cf 0.99, p < 0.001 Spina bifida 0.86 cf 0.42, p = 0.003 Anencephaly 0.74 cf 0.44, p = 0.034 Encephalocele 0.13 cf 0.13 Cleft lip 0.51 (0.26–0.89) cf 0.98 Cleft palate 0.51 (0.26–0.89) cf 0.59 Tracheoesophageal fistula 0.30 (0.12–0.62) cf 0.22 Limb reductions 0.51 (0.26–0.89) cf 0.36	Observed excess of neural tube defects cannot be explained by employment at Hanford or by occupational exposure to radiation
Shields et al (1992) <i>Health Phys</i> , 63 , 542–51	Navajos in uranium mining area	Cohort and (nested) case-control study of ARO and infant death. Main analysis in terms of three groupings of outcomes: (a) chromosomal/gene disorders etc (b) other possible radiation effects including stillbirth (c) conditions unlikely to be due to radiation	38 stillbirths: no association with father's gonadal dose or work in uranium mine. For all outcomes together (n = 266) there is an association with mothers living near mine tailings (OR = 1.83, p = 0.05); more pronounced for the grouping including stillbirth (OR = 2.71, p = 0.03)	Little dosimetric information. Many hypotheses tested. Number of stillbirths small
Roman et al (1996) <i>Occup Environ Med</i> , 53 , 73–9	Medical radiographers who were members of the professional association	Postal questionnaire of reproductive outcome and child health. Comparisons with national rates and case-control analysis	<i>Stillbirths</i> Mothers n = 84 'in line with other studies' Fathers n = 18 'in line with other studies' <i>Congenital abnormalities (with CI)</i> Mothers n = 140, RR = 1.0 (0.8–1.2) Fathers n = 23, RR = 1.0 (0.6–1.5)	No information on radiation exposures

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Källén et al (1998) <i>Radiat Res</i> , 149 , 202–8	Women treated with radiation for skin haemangioma in childhood	Cohort study of ARO and infant death (early natal death 7 days), plus other endpoints	<p><i>Comparison with national rates (with CI)</i></p> <p>Stillbirths O = 114, E = 93, RR = 1.23 (1.02–1.47)</p> <p>Early natal death O = 97, E = 81, RR = 1.20 (0.98–1.46)</p> <p>Perinatal death O = 211, E = 174, RR = 1.21 (1.06–1.39)</p> <p>Malformation O = 960, E = 887, RR = 1.08 (1.02–1.15)</p> <p>Neural tube defects O = 25, E = 22.8</p> <p><i>Tests for trend with ovarian dose</i></p> <p>Perinatal deaths p = 0.28</p> <p>All malformations p = 0.52</p> <p>Neural tube defects p = 0.02</p>	–
Parker et al (1999) <i>Lancet</i> , 354 , 1407–14	Male radiation workers at Sellafield	Cohort study with nested case–control	<p><i>Cohort study: odds ratio for stillbirth (adjusted) (with CI)</i></p> <p>1950–1989: ASD_{tot}, 100 mSv all stillbirth 1.24 (1.04–1.45), p = 0.009</p> <p>1950–1989: ASD₉₀, 10 mSv all stillbirth 1.86 (1.21–2.76), p = 0.003</p> <p>1961–1989: ASD_{tot}, 100 mSv all stillbirth 1.26 (1.02–1.51), p = 0.018</p> <p>All congenital abnormalities 1.43 (0.93–1.94), p = 0.047</p> <p>Neural tube defects 1.69 (1.10–2.32), p = 0.011</p> <p><i>Case–control study: odds ratio for stillbirth (adjusted) (with CI)</i></p> <p>FB_{tot}, 100 mSv all stillbirth 1.30 (1.03–1.66), p = 0.014</p> <p>FB₉₀, 10 mSv all stillbirth 1.08 (0.68–1.74), p = 0.37</p>	Cohort study uses 90-day doses ('ASD ₉₀ ') estimated from annual totals ('ASD _{tot} '). Case–control uses more precise doses ('FB ₉₀ '). Cumbrian stillbirth rate fell five-fold 1950–1989; this and other factors were modelled using non-Sellafield births
Doyle et al (2000) <i>Lancet</i> , 356 , 1293–9	Nuclear industry workers from AEA, AWE, BNFL (NIFS cohort)	Questionnaire-based study of a number of endpoints. Outcomes in offspring are examined according to parental monitoring at any time prior to conception. Validation study of a sample of stillbirths and malformations conducted	<p><i>Birth outcomes: odds ratio (with 95% CI)</i></p> <p>Father monitored miscarriage <13 weeks 1.0 (0.9–1.1), ≥13 weeks 0.9 (0.7–1.0)</p> <p>stillbirth 1.1 (0.8–1.4)</p> <p>Mother monitored miscarriage <13 weeks 1.3 (1.0–1.6), ≥13 weeks 0.8 (0.5–1.4)</p> <p>stillbirth 2.2 (1.0–4.6)</p> <p><i>Congenital abnormality: odds ratio (with 95% CI)</i></p> <p>Father monitored major malformation 1.0 (0.8–1.2)</p> <p>neural tube defects 1.1 (0.3–3.5)</p> <p>Mother monitored major malformation 1.4 (0.9–2.1)</p> <p>central nervous system defects 1.2 (0.3–4.8)</p>	–
Green et al (1997) <i>Occup Environ Med</i> , 54 , 629–35	Employees of a large Canadian company supplying electrical power	Case–control study of congenital abnormalities in offspring of the workers, ascertained by linkage to the Canadian surveillance scheme	<p><i>Comparison of relative risks in offspring of parents monitored before conception to offspring of parents who had not been monitored (with CI)</i></p> <p>Fathers RR = 0.84 (0.68–1.05)</p> <p>Mothers RR = 1.75 (0.85–3.55)</p> <p><i>Comparison of relative risk in offspring of fathers with recorded preconceptional dose to offspring of fathers without recorded preconceptional dose (with CI)</i></p> <p>Fathers RR = 0.72 (0.55–0.95)</p> <p>(Too few mothers had preconceptional dose for analysis)</p>	–
<p><i>Notes</i></p> <p>ARO = adverse reproductive outcomes – these comprise congenital malformation, stillbirth and early natal death. Perinatal death = early natal death + stillbirth</p> <p>RR = relative risk, ERR = excess relative risk</p> <p>O = observed deaths, E = deaths expected based on mortality rates in reference population</p>				