Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ross et al. (1996) North America Not stated ('past 10 years') Case-control	Cases: 84; Cases of infant leukaemia (diagnosed at one year of age or less) from 3 North American case-control studies of childhood leukaemia Controls: 97; Controls had been recruited through RDD, and matched to cases on year of birth, geographical area and race (in 2 of the 3 studies) Exposure assessment method: Questionnaire; A 'supplemental interview' on specific dietary factors (potential DNA topoisomerase II inhibitors) was conducted with the 84 matched sets included in this analysis. These data were combined with data collected in the original 3 studies	Leukaemia (Childhood cancer): Childhood leukaemia	Coffee intake during pregnancy			Year of birth, race, SES (telephone area code and exchange), maternal education	This study involved use of cases and controls from 3 earlier CCG studies; they attempted to contact participating parents for a supplementary interview and were able to find and interview less than 30% of original case mothers. The authors state (p586) that "This was a *very* preliminary investigation ..." and that "The data should be interpreted with extreme caution" Strengths: Presentation of results for infant AL, ALL and AML separately and inclusion of exposure-response. Limitations: Small sample size, and potential for selection bias given the low participation fraction (there were 303 infant cases available in the 3 original studies)
			None	51	1		
			≤ 3 times per week	16	1.5 (0.7–3.3)		
			≥ 4 times per week	17	2.5 (1–6.2)		
			Trend-test p-value: 0.04				
		Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	Coffee intake during pregnancy			Year of birth, race, SES (telephone area code and exchange), maternal education	
			None	36	1		
			≤ 3 times per week	8	1.1 (0.4–3)		
			≥ 4 times per week	10	2.3 (0.7–8.2)		
			Trend-test p-value: 0.2				
		Leukaemia (Childhood cancer): Childhood Leukaemia (AML (Acute myeloid leukaemia))	Coffee intake during pregnancy			Year of birth, race, SES (telephone area code and exchange), maternal education	
			None	15	1		
			≤ 3 times per week	8	2.4 (0.6–9.2)		
			≥ 4 times per week	7	2.6 (0.7–10)		
			Trend-test p-value: 0.1				

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petridou et al. (1997) Greece 1993–94 Case-control	Cases: 153; cases of childhood leukaemia (89% were ALL) diagnosed and confirmed by bone marrow sampling. Ascertained through nationwide oncology network thought to be virtually complete. Controls: 300; Hospital controls (2 per case) selected from children hospitalized at same time as the case, matched on age and sex. Admitted with 'acute conditions' Exposure assessment method: Other; Interviewer-administered questionnaire. Included questions on maternal coffee consumption during pregnancy	Leukaemia: Childhood leukaemia	Coffee drinking during pregnancy: 3+ cups per week			Maternal age at birth, maternal education, sibship size, birth order, persons per room, Day care, maternal smoking, maternal alcohol consumption, breastfeeding, pet ownership, pregnancy radiography, pregnancy ultrasound, residential floor, house heating, hair dryer use, pregnancy anaemia, pregnancy diabetes, birth weight, neonatal jaundice, blood transfusions, allergic disease hospitalized, Total Diphtheria–tetanus–pertussis shots, Bacille Calmette–Guérin vaccination, Total viral vaccination shots	Strengths: Multivariable analysis so control for confounding addressed. Limitations: All leukaemia types combined in the analysis. Lack of detail about control diagnoses. Limited exposure categories so exposure response cannot be assessed
			Yes vs No	93	0.89 (0.55–1.46)		
Menegaux et al. (2005) France (Paris, Lille, Lyon, Nancy) 1995–1999 Case-control	Cases: 280; Incident cases of childhood acute leukaemia from hospitals Controls: 288; Hospital controls – same hospital, mainly orthopaedics	Leukaemia (Childhood cancer): Childhood leukaemia	Coffee intake during pregnancy			Age, sex, ethnic origin, hospital	Results were unchanged with additional adjustment for SES or maternal education, alcohol intake, smoking, early infection, breastfeeding, fetal loss, family history of cancer. Strengths: Standardized
			Never	56	1		
			≤ 3 cups/day	162	1 (0.7–1.5)		
			4–8 cups/day	49	2.1 (1.2–3.8)		

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
	Exposure assessment method: Questionnaire; Face to face interview with the mother using standardized questionnaires that included questions on coffee consumption in any period of the pregnancy or breastfeeding. (among other exposures)		> 8 cups/day	13	2.8 (0.9–8.1)		interviews, analysis adjusted for range of confounders. Limitations: Self-reported exposure
			Trend-test p-value: 0.05				
		Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	Coffee intake during pregnancy			Age, sex, centre, origin	
			Never	50	1		
			≤ 3 cups/day	137	1.1 (0.7–1.8)		
			4–8 cups/day	41	2.4 (1.3–4.7)		
			> 8 cups/day	12	3.1 (1–9.5)		
		Leukaemia (Childhood cancer): Childhood ANLL	Coffee intake during pregnancy			Age, sex, centre, origin	
			Never	6	1		
			≤ 3 cups/day	25	1.6 (0.6–4.3)		
			4–8 cups/day	8	2.8 (0.7–10.4)		
			> 8 cups/day	1	3 (0.3–35.1)		
Menegaux et al. (2007) France (14 regions in metropolitan areas) 1995–98 Case-control	Cases: 472; Population based, incident cases of ALL (n = 407) and AML (n = 62) derived from the National Registry of Childhood Blood Malignancies (NRCL) Controls: 567; Population based,	Leukaemia (Childhood cancer): Childhood leukaemia	Coffee intake during pregnancy			Age, sex, region, socio-professional category and birth order	The four regions that provided cases in Menegaux et al. (2005) were excluded from this study. Results were unchanged with additional adjustment for parental education, maternal alcohol and smoking during pregnancy, early infections,
			None	154	1		
			Any	298	1.1 (0.9–1.5)		
			≤ 3 cups/day	245	1.1 (0.8–1.4)		
			> 3 cups/day	53	1.5 (0.9–2.4)		

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
	RDD, frequency matched on age, sex and region, quotas determined a priori on the basis of expected distribution of cases Exposure assessment method: Questionnaire; Comprehensive self-administered standardized questionnaire	Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	Coffee intake during pregnancy			Age, sex, region, socio-professional category and birth order	day care attendance and family history of cancer. Strengths: Population-based, standardized questionnaire, adjustment for a range of confounders, presentation of results for ALL and AML separately. Limitations: Self-reported exposure and modest sample size for AML
			None	134	1		
			Any	255	1.1 (0.8–1.4)		
			≤ 3 cups/day	208	1.1 (0.8–1.4)		
			> 3 cups/day	47	1.4 (0.9–2.4)		
		Leukaemia (Childhood cancer): Childhood Leukaemia (AML (Acute myeloid leukaemia))	Coffee intake during pregnancy			Age, sex, region, socio-professional category and birth order	
			None	20	1		
			Any	40	1.6 (0.8–2.9)		
			≤ 3 cups/day	35	1.6 (0.8–3)		
			> 3 cups/day	5	1.4 (0.5–4.4)		
Milne et al. (2011) Australia 2003–2007 Case-control	Cases: 337; Incident cases of acute lymphoblastic leukaemia in children treated at all paediatric oncology centres in Australia Controls: 697; Whole population, random digit dialling Exposure assessment method: Food frequency questionnaire	Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	Coffee intake during last 6 months of pregnancy			Age, sex, state, maternal age, mother's country of birth, parent education	Strengths: Population-based cases and controls, standardized questionnaires, adjustment for a range of confounders, assessment of exposure-response. Limitations: Low response fractions; self-reported exposure
			No coffee or tea	63	1		
			Any coffee	180	0.89 (0.61–1.3)		
			< 2 cups per day	96	0.77 (0.51–1.16)		
			2+ cups per day	84	1.12 (0.72–1.74)		
			Trend-test p-value: 0.5				

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bonaventure et al. (2013) France (ESCALE study) 2003–04 Case-control	Cases: 764 (648 ALL, 101 AML); Children newly diagnosed with AL, identified through the National Registry of Childhood Haematopoietic Malignancies Controls: 1681; selected contemporaneously from French households with landline telephones using random digit dialing. Quotas were applied to ensure the distribution of controls was similar to that of all ESCALE cases (all childhood cancers) and to the French population for the number of children < 15 y/o in the household. Exposure assessment method: Questionnaire; Standardized telephone interview, including questions on maternal consumption of coffee and other beverages during the pregnancy or breastfeeding	Leukaemia (Childhood cancer): Childhood leukaemia	Coffee intake during pregnancy			Sex, age, birth order, breastfeeding, maternal education, parental socio-professional category, ancestry	Results were unchanged with additional adjustment for type of housing, area of residence, heavy traffic near residence, pesticide exposure, early infections, family history of cancer. Strengths: Population-based, standardized interview, adjustment for a range of confounders, presentation of results for ALL and AML separately. Limitations: Self-reported exposure
			Never/ occasionally	273	1		
			Regular (≥ 1 cup/week)	487	1.2 (1–1.5)		
			< 1 cup/day	203	1 (0.8–1.3)		
			1 or 2 cups/day	130	1.3 (1–1.7)		
			> 2 cups/day	154	1.6 (1.2–2.1)		
			Trend-test p-value: 0.001				
		Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	Coffee intake during pregnancy			Sex, age, birth order, breastfeeding, maternal education, parental socio-professional category, ancestry	
			Never/ occasionally	238	1		
			Regular (≥ 1 cup/week)	406	1.2 (1–1.4)		
			< 1 cup/day	174	1 (0.8–1.3)		
			1 or 2 cups/day	108	1.3 (1–1.7)		
			> 2 cups/day	124	1.5 (1.1–2)		
			Trend-test p-value: 0.0027				

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
		Leukaemia (Childhood cancer): Childhood Leukaemia (AML (Acute myeloid leukaemia))	Coffee intake during pregnancy			Sex, age, birth order, breastfeeding, maternal education, parental socio-professional category, ancestry	
			Never/ occasionally	30	1		
			Regular (≥ 1 cup/week)	71	1.6 (1–2.6)		
			< 1 cup/day	27	1.3 (0.7–2.1)		
			1 or 2 cups/day	19	1.8 (1–3.3)		
			> 2 cups/day	25	2.4 (1.3–4.3)		
			Trend-test p-value: 0.002				
Orsi et al. (2015) France 2010–2011 Case-control	Cases: 747; 636 ALL cases 100 AML cases Cases diagnosed in all paediatric oncology units in France Controls: 1421; Population controls matched on age and sex by quota sampling Exposure assessment method: Questionnaire; Structured computer-assisted telephone questionnaire	Leukaemia: Childhood leukaemia	Coffee intake during pregnancy			Age, sex, mother's education, mother's age at child's birth, birth order	Results were unchanged with additional adjustment for rural vs urban residence, parental SES, ethnic origin, breastfeeding, maternal smoking and alcohol intake. Also presented results for coffee drinking in first trimester, which are virtually the same as those shown here. Strengths: population-based, standardized CATI interview, adjustment for a range of confounders, presentation of results for ALL and AML separately. Limitations: Self-reported exposure
			Never/ occasionally	351	1		
			Regular (≥ 1 cup/week)	389	0.9 (0.8–1.1)		
			≤ 1 cup/day	161	0.8 (0.7–1)		
			> 1 cup /day to 2 cups/day	108	1 (0.7–1.3)		
			> 2 cups/day	120	1.1 (0.9–1.5)		

Table 2.20 Case−control studies on childhood leukaemia and coffee drinking (web only)

Reference, location enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
		Leukaemia: Childhood Acute Lymphocytic Leukaemia	Coffee intake during pregnancy			Age, sex, mother's education, mother's age at child's birth, birth order	
			Never/ occasionally	298	1		
			Regular (≥ 1 cup/week)	334	1 (0.8–1.2)		
			≤ 1 cup/day	135	0.8 (0.6–1.1)		
			> 1 cup /day to 2 cups/day	88	1 (0.7–1.3)		
			> 2 cups/day	111	1.3 (1–1.7)		
		Leukaemia: Childhood Leukaemia (AML (Acute myeloid leukaemia))	Coffee intake during pregnancy			Age, sex, mother's education, mother's age at child's birth, birth order	
			Never/ occasionally	46	1		
			Regular (≥ 1 cup/week)	51	0.9 (0.6–1.3)		
			≤ 1 cup/day	25	0.9 (0.6–1.5)		
			> 1 cup /day to 2 cups/day	18	1.1 (0.6–1.9)		
			> 2 cups/day	8	0.5 (0.2–1.1)		

CI, confidence interval

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