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 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 Leukaemia (Childhood cancer): Childhood Acute Lymphocytic Leukaemia	None ≤ 3 times per week ≥ 4 times per week Trend-test p-va	during pregnancy 36 8	1 1.5 (0.7–3.3) 2.5 (1–6.2) 1 1.1 (0.4–3) 2.3 (0.7–8.2)	Year of birth, race, SES (telephone area code and exchange), maternal education 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	
	this analysis. These data were combined with data collected in the original 3	Leukaemia (Childhood cancer): Childhood Leukaemia (AML (Acute myeloid leukaemia))		during pregnancy 15 8 7	1 2.4 (0.6–9.2) 2.6 (0.7–10)	Year of birth, race, SES (telephone area code and exchange), maternal education	size, and potential for selection bias given the lov participation fraction (there were 303 infant cases available in the 3 original studies)

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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 drinkin week Yes vs No	g during pregnand 93	cy: 3+ cups per 0.89 (0.55–1.46)	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
Menegaux et al. (2005)	Cases: 280; Incident cases of	Leukaemia (Childhood	Coffee intake of	luring pregnancy		Age, sex, ethnic origin, hospital	Results were unchanged with additional adjustment
France (Paris, Lille, Lyon, Nancy)	childhood acute leukaemia from hospitals	cancer): Childhood	Never	56	1		for SES or maternal education, alcohol intake,
1995–1999 Case-control	Controls: 288; Hospital controls –	leukaemia	≤ 3 cups/day	162	1 (0.7–1.5)		smoking, early infection, breastfeeding, fetal loss,
	same hospital, mainly orthopaedics		4–8 cups/day	49	2.1 (1.2–3.8)		family history of cancer. Strengths: Standardized

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	Exposure assessment method: Questionnaire; Face to face		> 8 cups/day	13	2.8 (0.9–8.1)		interviews, analysis adjusted for range of confounders.
	interview with the mother using standardized questionnaires that included questions on coffee consumption in any period of the pregnancy or breastfeeding. (among other exposures)		Trend-test p-va	alue: 0.05			Limitations: Self-reported exposure
		Leukaemia (Childhood	Coffee intake	during pregnancy		Age, sex, centre, origin	
		cancer): Childhood Acute	Never	50	1	91.g	
		Lymphocytic Leukaemia	≤ 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	Coffee intake	during pregnancy		Age, sex, centre, origin	
		cancer): Childhood	Never	6	1	· ·	
		ANLL	≤ 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)	Cases: 472; Population based,	Leukaemia (Childhood	Coffee intake of	during pregnancy		Age, sex, region, socio-professional	The four regions that provided cases in
France (14 regions in metropolitan areas)		cancer):	None	154	1	category and birth	Menegaux et al. (2005) were excluded from this
1995–98 derived from the National Case-control Registry of Childhood Blood Malignancies (NRCL) Controls: 567; Population based,	leukaemia	Any	298	1.1 (0.9–1.5)		study. Results were unchanged with additional	
	Malignancies (NRCL)		≤ 3 cups/day	245	1.1 (0.8–1.4)	education, ma and smoking	adjustment for parental education, maternal alcohol
			> 3 cups/day	53	1.5 (0.9–2.4)		and smoking during pregnancy, early infectio

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	RDD, frequency matched on age, sex and region, quotas determined a priori	Leukaemia (Childhood		during pregnancy		Age, sex, region, socio-professional	day care attendance and family history of cancer. Strengths: Population-
	on the basis of expected distribution of cases	cancer): Childhood Acute	None	134	1	category and birth order	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
	Exposure assessment method:	Lymphocytic Leukaemia	Any	255	1.1 (0.8–1.4)		
	Questionnaire; Comprehensive self-		≤ 3 cups/day	208	1.1 (0.8–1.4)		
	administered standardized questionnaire		> 3 cups/day	47	1.4 (0.9–2.4)		
		Leukaemia (Childhood	Coffee intake of	during pregnancy		Age, sex, region, socio-professional	
		cancer): Childhood	None	20	1	category and birth order	
		Leukaemia (AML (Acute	Any	40	1.6 (0.8–2.9)		
		myeloid leukaemia))	≤ 3 cups/day	35	1.6 (0.8–3)		
			> 3 cups/day	5	1.4 (0.5–4.4)		
Milne et al. (2011) Australia	Cases: 337; Incident cases of acute	Leukaemia (Childhood	Coffee intake during last 6 month		hs of pregnancy	Age, sex, state, maternal age,	Strengths: Population-based cases and controls,
2003–2007 lymphoblastic Case-control children treate paediatric one Australia Controls: 697; Whole por random digit of	lymphoblastic leukaemia in children treated at all	ymphoblastic leukaemia in cancer): hildren treated at all Childhood Acute aediatric oncology centres in Lymphocytic kustralia Leukaemia	No coffee or tea	63	1	mother's country of birth, parent education	standardized questionnaires, adjustment for a range of confounders, assessment of exposure-response. Limitations: Low response fractions; self-reported exposure
	Australia		Any coffee	180	0.89 (0.61–1.3)		
	697; Whole population, random digit dialling		< 2 cups per day	96	0.77 (0.51–1.16)		
	Exposure assessment method: Food frequency questionnaire		2+ cups per day	84	1.12 (0.72–1.74)		
			Trend-test p-va	alue: 0.5			

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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	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.	764 (648 ALL, 101 AML); (Childhood cancer): with AL, identified through the National Registry of Childhood Haematopoietic Malignancies Controls: 1681; selected contemporaneously from French households with landline telephones using		Never/ occasionally Regular (≥ 1 cup/week) < 1 cup/day 1 or 2 cups/day > 2 cups/day	273 487 203	1 1.2 (1–1.5) 1 (0.8–1.3) 1.3 (1–1.7) 1.6 (1.2–2.1)	breastfeeding, with admaternal education, parental socioprofessional category, ancestry exposur family lasted based, society interviee range or presental ALL an Limitati	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
	controls was similar to that		Trend-test p-val	lue: 0.001			exposure	
	of all ESCALE cases (all childhood cancers) and to the French population for	Leukaemia (Childhood	Coffee intake du	uring pregnancy		Sex, age, birth order, breastfeeding,		
	the number of children < 15 y/o in the household. Exposure assessment	cancer): Childhood Acute Lymphocytic	Never/ occasionally	238	1	maternal education, parental socio- professional category,		
	method: Questionnaire; Standardized telephone interview,	Leukaemia	Regular (≥ 1 cup/week)	406	1.2 (1–1.4)	ancestry		
	including questions on maternal consumption of		< 1 cup/day	174	1 (0.8–1.3)			
	coffee and other beverages during the pregnancy or		1 or 2 cups/day	108	1.3 (1–1.7)			
	breastfeeding		> 2 cups/day	124	1.5 (1.1–2)			
			Trend-test p-val	lue: 0.0027				

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		Leukaemia (Childhood cancer): Childhood Leukaemia (AML (Acute myeloid leukaemia))	Never/ occasionally Regular (≥ 1 cup/week) < 1 cup/day 1 or 2 cups/day > 2 cups/day	25	1 1.6 (1–2.6) 1.3 (0.7–2.1) 1.8 (1–3.3) 2.4 (1.3–4.3)	Sex, age, birth order, breastfeeding, maternal education, parental socioprofessional category, ancestry	
			Trend-test p-va	lue: 0.002			
Orsi et al. (2015) France 2010–2011 Case-control	100 AML cases	Childhood leukaemia Never occasi Regul (≥ 1 cu > 1 cu > 1 cu to 2 cu	Coffee intake d Never/ occasionally	uring pregnancy 351	1	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
			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)		

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		Leukaemia: Childhood Acute	Coffee intake d	uring pregnancy		Age, sex, mother's education, mother's	
		Lymphocytic Leukaemia	Never/ occasionally	298	1	age at child's birth, birth order	
			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 d	uring pregnancy		Age, sex, mother's education, mother's	
			Never/ occasionally	46	1	age at child's birth, birth order	
			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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