

Table 2.23. Case-control studies of second-hand tobacco smoke and childhood leukaemia & lymphoma

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	(Cases/Controls) Relative risk (95% CI)* * $P < 0.05$, ** $P < 0.01$	Adjustment for potential confounders	Comments
Schüz <i>et al.</i> (1999) Germany	Blood (Leukaemia, NHL) Others: CNS, Neuroblastoma, Nephroblastoma, Bone tumour, Soft tissue sarcoma	2358 cases; 1992–1997; < 15 yrs; German Cancer Registry; from 1992–1997 AL $n = 755$; ALL $n = 650$; ANLL $n = 105$; NHL $n = 172$ Nuclear installations study; cases diagnosed from 1980–1994; lived < 15 km away from nuclear site at date of diagnosis; AL $n = 543$; ALL $n = 481$; ANLL $n = 62$; NHL $n = 91$	2588 population based control matched on age, gender and sampled from district where case lived at date of diagnoses	Structured questionnaire (CCG) Telephone Interview	<i>Maternal cigarettes per day during pregnancy</i> No (reference) 1–10 11–20 > 20 <i>Paternal cigarettes per day before pregnancy</i> No (reference) 1–10 11–20 > 20 No (reference) 1–10 11–20 > 20 No (reference) 1–10 11–20 > 20 No (reference) 1–10 11–20 > 20	Acute leukaemia (Total) Maternal (792/765) 1.0 (159/174) 0.8 (0.6–1.1) (25/39) 0.5 (0.3–0.9)* (6/4) 1.3 (0.4–4.7) Paternal (485/489) 1.0 (112/100) 1.1 (0.8–1.5) (256/259) 1.0 (0.8–1.2) (102/107) 0.9 (0.7–1.2) AL Nationwide Maternal (522/500) 1.0 (111/120) 0.8 (0.6–1.1) (15/26) 0.5 (0.2–1.0)* (2/4) 0.5 (0.1–2.7) Paternal (317/323) 1.0 (78/63) 1.2 (0.9–1.8) (171/170) 1.0 (0.8–1.3) (59/69) 0.8 (0.5–1.2) NHL (combined) Maternal (173/2062) 1.0 (46/426) 1.3 (0.9–1.9) (6/72) 1.0 (0.4–2.5) (3/11) 5.2 (1.2–22.4)* Paternal (107/1336) 1.0 (35/293) 1.6 (1.0–2.5)* (56/647) 1.1 (0.7–1.6) (23/264) 1.1 (0.7–1.8)	1:1 matched analyses overall	The evaluated risk factors during the neonatal and prenatal period account at most for only a small proportion of the childhood cancers.

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Sorahan <i>et al.</i> (2001) UK	Blood (Leukaemia – ALL)	555 children resident in Yorkshire, West Midlands, and North Western Regional Health Authority areas; < 15 yrs; 1980–1983; Not living with biologic mother excluded;	555 controls matched for sex and date of birth; Practice lists of case GPs	Micro-filmed interview	<i>Fathers cigarettes per day before pregnancy</i> (case = 149; controls = 149) < 10 10–19 20–29 30–39 ≥ 40 <i>P</i> for trend (2-tailed) <i>Maternal cigarettes per day during 5th mo of pregnancy</i> (case = 148; controls = 148) < 10 10–19 20–29 >30 <i>P</i> for trend (2-tailed)	(7/9) 0.99 (0.35–2.85) (18/16) 1.34 (0.62–2.91) (36/35) 1.32 (0.72–2.45) (9/5) 2.33 (0.71–7.63) (12/3) 5.29 (1.31–21.30) 0.06 (9/7) 1.34 (0.46–3.87) (24/23) 1.11 (0.59–2.08) (21/22) 0.98 (0.51–1.85) (1/4) 0.26 (0.03–2.38) 0.56	Socioeconomic grouping, ethnic origin, parental age at child's birth	When cases were compared with GP controls there was a statistically insignificant positive trend ($P = 0.06$) between the risk of childhood cancer and paternal daily consumption of cigarettes before the pregnancy; there was no significant trend for maternal smoking habit.

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Mejía-Aranguré <i>et al.</i> (2003) Mexico	Blood (Leukaemia)	27 children with Down syndrome and AL; 1995; Public institutions that provide care of 95% of the children with cancer in Mexico City	58 children with DS but no AL; Institutions that treat children with DS	In-person interview and questionnaire	<i>Active paternal smoking</i> before during after pregnancy <i>Paternal cigarettes per day before pregnancy</i> None (Ref) < 6 ≥ 6 <i>Active maternal smoking</i> before during after pregnancy <i>SHS during childhood</i> Total > 10 cigarettes per day	90% CI for all in (22/40) 3.57 (0.82–20.27) (14/30) 1.01 (0.36–2.29) (13/33) 0.72 (0.28–1.83) (8/12) 4.86 (1.07–22.00) (14/25) 4.25 (1.02–17.67) (15/31) 1.09 (0.46–2.61) (2/3) 1.53 (0.20–9.39) (6/16) 0.75 (0.26–2.08) (10/13) 2.42 (1.03–5.69) (5/7) 3.39 (1.09–10.48)	Maternal age, socioeconomic level and weight of the child at birth (> median 2 600 g)	

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Pang <i>et al.</i> (2003) UK	Blood (Leukaemia, Lymphoma)	3838 children with cancer; Hospital based; < 15 yrs; 1991–1994 in Scotland; 1992–1995 in England and Wales for NHL; 1992–1996 in England and Wales for leukemias. Cases with paternal smoking information: Leuk = 1 630 cases Lymph = 331 Cases with maternal smoking information: Leuk = 1 732 cases Lymph = 351	7629 control children; matched for sex, date of birth and geographical area of residence at diagnosis; Randomly selected from Family Health Services Authorities in England and Wales and from health boards in Scotland	Face-to-face structured interviews; Computerized self-administered questionnaires	<i>Paternal cigarettes per day preconception</i>	<i>Leukaemia</i>	Deprivation and parental age at birth of index child	There was a significant negative trend for maternal smoking during pregnancy for leukaemia ($P = 0.029$) and a non-significant negative trend for maternal smoking during pregnancy for lymphoma but there was evidence of underreporting of smoking by case mothers.
					1–19	(269/1003) 1.12 (0.96–1.32)		
					>20	(342/1440) 1.01 (0.87–1.17)		
					<i>P for trend</i>	0.743		
					<i>Maternal cigarettes per day during pregnancy</i>			
					1–19	(286/1306) 0.93 (0.80–1.08)		
					>20	(95/528) 0.76 (0.60–0.98)*		
					<i>P for trend</i>	0.029		
					<i>Paternal cigarettes per day preconception</i>	<i>Lymphoma</i>		
					1–19	(55/1003) 1.27 (0.91–1.70)		
					>20	(72/1440) 1.09 (0.80–1.49)		
					<i>P for trend</i>	0.419		
<i>Ex-smoker</i>	(45/827) 1.43 (0.99–2.05)							
<i>Maternal cigarettes per day during pregnancy</i>								
1–19	(60/1306) 0.92 (0.67–1.26)							
>20	(22/528) 0.72 (0.44–1.20)							
<i>P for trend</i>	0.208							

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Menegaux <i>et al.</i> (2005) France	Blood (Leukaemia, ALL, ANLL)	280 incident cases; hospital based; 1995–1999; < 15 yrs; 4 regions of France ALL = 240 cases ANLL = 40 cases	288 hospitalized controls who did not have cancer nor birth defects (mainly orthopaedic dept); matched by age, gender, ethnic origin and centre	Face-to-face interviews Standardized questionnaires	<i>Maternal cigarettes per day during pregnancy</i> Never (Reference) < 5 5–9 ≥ 10 Never (Reference) < 5 5–9 ≥ 10 Paternal smoking during pregnancy Paternal cigarettes per day during childhood from birth to interview 10–19	ALL (177/212) 1.0 (22/23) 0.9 (0.5–1.8) (19/23) 0.8 (0.4–1.6) (20/21) 1.3 (0.7–2.7) ANLL (30/212) 1.0 (4/23) 1.5 (0.4–5.0) (4/23) 1.4 (0.4–4.8) (0/21) NA AL 0.9 (0.6–1.3) AL 1.0 (0.7–1.4) ANLL (8/34) 2.0 (0.8–5.2)	Age, sex centre, origin	

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Clavel <i>et al.</i> (2005) France	Blood (Leukaemia, ALL)	280 cases of acute leukaemia (240 ALL, 40 ANLL) 219 cases for blood sampling Hospital-based; 1995–1999; < 15 yrs	288 controls 105 controls for blood sampling Hospital based; Cases for diseases other than cancer or major birth defect (mainly from orthopaedic departments)	In-person interview	<i>Maternal cigarettes per day</i>		Age, sex, hospital/centre, ethnic origin and parental socio-professional category	Interaction observed in case-only analysis with <i>CYP1A1</i> *2A variant allele and with <i>GSTM1</i> deletion GxE, case-control and case-only analyses
					Never (Ref)	(161/81) 1.0		
					≤ 6	(34/11) 1.5 (0.7–3.1)		
					> 6	(23/13) 0.9 (0.4–2.0)		
					Interaction <i>CYP1A1</i> *2A x Smoking (case-only analysis)	2.2 (1.0–4.9) ($P = 0.04$)		
					Interaction ≤ 6 – mps1	1.9 (0.7–5.0)		
					> 6 – mps1 (c-o analysis)	2.8 (0.9–8.0)		
					Interaction <i>GSTM1</i> (null) smoking (c-o analysis)	2.3 (1.2–4.4)		
					Interaction ≤ 6 – null	2.8 (1.2–6.2)		
					> 6 – null (c-o analysis)	1.7 (0.6–4.2)		
					<i>NQO1</i>	ALL		
					*1/1	(122/68) 1.0 (ref)		
					*1/2	(59/33) 0.9 (0.5–1.6)		
*2/2	(10/3) 2.1 (0.5–8.3)							
<i>EPHX1</i> exon 3	ALL							
Tyr113/Tyr113	(103/49) 1.0 (Ref)							
Tyr113/His113	(68/39) 0.8 (0.5–1.4)							
His113/His113	(20/17) 0.5 (0.2–1.0)							
<i>EPHX1</i> exon 4	ALL							
His139/His139	(123/62) 1.0 (ref)							
His 139/Arg139	(59/41) 0.7 (0.4–1.2)							
Arg139/Arg 139	(9/2) 3.7 (0.7–18.9)							

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Chang <i>et al.</i> (2006) USA	Blood (Leukaemia – ALL, AML)	Recruited 1995–2002; 35 counties in No. California; 327 acute childhood leukaemia cases (281 ALL, 46 AML); 40% Hispanic. Case/control eligibility: resident of study area, less than 15yrs of age at the time of case diagnosis (reference date for controls), at least one English or Spanish speaking parent or guardian, and no previous diagnosis of cancer	416 controls obtained from CA birth certificate searches matched on age, sex, Hispanic ethnicity, maternal race	Self administered questionnaires (1995–1999) In-person interviews (1999–2002)	<u>Paternal Smoking</u> Ever/Never (Yes/No) ALL AML Preconception (Y/N) ALL AML Preconception (<i>one cigarette per day</i>) ALL AML <u>Maternal Smoking</u> Ever/Never (Y/N) ALL AML Preconception (Y/N) ALL AML Preconception (<i>one cigarettes per day</i>) ALL AML	(104/119) 1.25 (0.85–1.82) (21/14) 2.64 (0.98–7.12) (74/70) 1.32 (0.86–2.04) (16/8) 3.84 (1.04–14.17) 1.03 (1.00–1.06) 1.05 (0.98–1.13) (92/105) 1.12 (0.79–1.59) (13/14) 1.00 (0.41–2.44) (46/60) 0.88 (0.57–1.36) (6/7) 0.79 (0.21–2.95) 1.02 (0.95–1.06) 1.02 (0.93–1.12)	Household income	Greater risk of ALL observed when risk associated with paternal preconception smoking was combined with maternal postnatal smoking or postnatal passive smoking exposure ($P_{\text{interaction}} = 0.004$) for both

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Chang <i>et al.</i> (2006) (contd) USA					Pregnancy (Y/N)			
					ALL	(36/44) 0.93 (0.58–1.51)		
					AML	(5/7) 0.60 (0.15–2.44)		
					Pregnancy (<i>one cigarettes per day</i>)			
					ALL	1.01 (0.95–1.07)		
					AML	1.01 (0.92–1.11)		
					Postnatal (Y/N)			
					ALL	(52/60) 0.99 (0.64–1.52)		
					AML	(9/9) 0.94 (0.32–2.81)		
					Postnatal (<i>one cigarette per day</i>)			
					ALL	1.02 (0.98–1.06)		
					AML	1.05 (0.94–1.17)		
					<u>Paternal preconception & maternal postnatal smoking</u>			
ALL	(37/23) 3.94 (1.25–12.37)							
Menegaux <i>et al.</i> (2007) France	Blood (Leukaemia)	472 incident cases (407 ALL, 62 AML); 1995–1998; National Registry of Childhood Blood Malignancies; < 15 yrs; Residing in metropolitan France at time of diagnosis; Physicians consent; Mothers ability for interview	567 population controls; Matched on age, gender and region of residence; Random digit dialing	Self-administered questionnaire	<i>Maternal smoking during pregnancy (cigarettes per day)</i>		Age, sex, region, socio-professional category and birth order	
					AL			
					(Yes/No)	(98/97) 1.3 (0.9–1.7)		
					≤ 5	(50/58) 1.1 (0.7–1.7)		
					> 5	(44/37) 1.4 (0.9–2.2)		
					ALL			
					(Yes/No)	(90/97) 1.4 (1.0–1.9)		
					≤ 5	(48/58) 1.3 (0.9–2.0)		
					> 5	(41/37) 1.5 (0.9–2.5)		
					AML			
					(Yes/No)	(8/97) 0.6 (0.3–1.5)		
					≤ 5	(2/58) 0.2 (0.04–1.0)		
					> 5	(3/37) 0.7 (0.2–2.6)		
<i>Paternal smoking before pregnancy (cigarettes per day)</i>								
AL								
No	(207/278) 1.0 (ref.)							
≤ 20	(180/214) 1.2 (0.9–1.6)							
> 20	(28/33) 1.0 (0.6–1.7)							
ALL								
No	(176/278) 1.0 (ref.)							

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Menegaux <i>et al.</i> (2007) (contd)					≤ 20 > 20 No ≤ 20 > 20	(156/214) 1.2 (0.9–1.6) (27/33) 1.2 (0.7–2.0) AML (29/278) 1.0 (ref) (23/214) 0.9 (0.5–1.7) (1/33) 0.2 (0.02–1.7)		
MacArthur <i>et al.</i> (2008) Canada	Blood (Leukaemia)	399 Cases; 1990–1994; < 15 yrs; 100 km within the five designated regions across Canada; Paediatric Oncology Centers; Population-based cancer registry; No Downs syndrome	399 Controls; Provincial health insurance rolls matched on age, gender, and area; Within three months of case birth date for children less than 2 years; Within six months for children greater than 2 years	In home interviews with parents	<i>Maternal smoking during pregnancy</i> No Yes No Yes <i>Maternal smoking Cigarettes/day during pregnancy</i> No < 10 10–19 ≥ 20 P for trend No < 10 10–19 ≥ 20 P for trend No < 10 10–19 ≥ 20 P for trend	AL (241/272) ref (154/121) 1.26 (0.90–1.76) ALL cases (218/272) ref (130/121) 1.25 (0.89–1.77) AML cases (18/272) ref (20/121) 2.17 (0.93–5.09) AL (241/272) ref (68/54) 1.29 (0.84–1.98) (62/38) 1.54 (0.95–2.51) (24/28) 0.88 (0.46–1.68) 0.233 ALL (218/272) ref (58/54) 1.30 (0.83–2.03) (50/38) 1.41 (0.85–2.35) (22/28) 0.98 (0.50–1.89) 0.373 AML (18/272) ref. (8/54) 2.24 (0.71–7.04) (10/38) 3.89 (1.31–11.58) (2/28) 0.40 (0.04–3.80) 0.287	Maternal age at birth, maternal education, household income, ethnicity and number of residences since birth	

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MacArthur <i>et al.</i> (2008) (contd)					<i>Paternal smoking Cigarettes/day in year before birth</i>			
					No	AL (201/224) ref.		
					< 10	(35/23) 1.29 (0.70–2.39)		
					10–19	(47/38) 1.01 (0.60–1.70)		
					≥ 20	(102/90) 1.13 (0.78–1.64)		
					<i>P for trend</i>	0.817		
						ALL (186/224) ref.		
					No	(186/224) ref.		
					< 10	(15/23) 0.62 (0.29–1.33)		
					10–19	(43/38) 1.18 (0.68–2.05)		
					≥ 20	(96/90) 1.11 (0.76–1.61)		
					<i>P for trend</i>	0.509		
						AML (21/224) ref.		
					< 10	(4/23) 3.43 (0.82–14.38)		
					10–19	(4/38) 0.98 (0.27–3.56)		
					≥ 20	(10/90) 0.69 (0.26–1.88)		
					<i>P for trend</i>	0.437		
Rudant <i>et al.</i> (2008) France	Blood (Leukaemia & Lymphoma)	765 AL cases; 130 HL cases; 165 NHL cases; National registry based; 2003–2004; < 15 years; resident of France; no adoptions	1681 controls; French national telephone directory;	Telephone interviews with biological mothers using structured questionnaires	<i>Maternal smoking during pregnancy (cigarettes per day)</i>		Age, sex, parental professional category, and maternal age at the time of birth. Analyses restricted to children aged more than 4 yrs for HL and more than 1 yr for NHL	
					(Yes/No)	ALL 1.2 (0.9–1.5)		
					≤ 10	1.3 (1.0–1.6)		
					> 10	1.0 (0.6–1.4)		
					(Yes/No)	AML 1.3 (0.8–2.1)		
					≤ 10	1.5 (0.9–2.5)		
					> 10	0.9 (0.4–2.2)		
					(Yes/No)	HL (27/172) 0.9 (0.6–1.4)		
					≤ 10	(16/112) 0.9 (0.5–1.6)		
					> 10	(10/56) 0.8 (0.4–1.8)		
					(Yes/No)	NHL (45/265) 1.5 (1.0–1.8)		
					≤ 10	(33/177) 1.6 (1.1–2.5)		
					> 10	(10/82) 1.0 (0.5–1.9)		

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Rudant <i>et al.</i> (2008) (contd)					<i>Paternal smoking from the year before the child's birth to the interview (cigarettes per day)</i>			
					ALL			
					Yes/No	1.4 (1.1–1.7)**		
					< 20	1.2 (0.9–1.6)		
					≥ 20	1.7 (1.3–2.1)		
					<i>P</i> for trend	< 0.0001		
					AML			
					Yes/No	1.5 (1.0–2.3)		
					< 20	1.3 (0.7–2.4)		
					≥ 20	1.7 (1.0–2.9)		
					<i>P</i> for trend	0.045		
					HL			
					Yes/No	(67/392) 1.2 (0.8–1.7)		
					< 20	(14/120) 0.8 (0.4–1.6)		
					≥ 20	(35/182) 1.2 (0.7–2.0)		
					NHL			
					Yes/No	(94/604) 1.6 (1.1–2.3)**		
					< 20	(32/203) 1.7 (1.1–2.7)		
					≥ 20	(44/259) 1.7 (1.1–2.6)		
					<i>P</i> for trend	0.01		
					Paternal smoking from the year before the child's birth to the interview (cigarettes per day)			Non-Hodgkin's Lymphoma Burkitt ($n = 77$)
					No	(ref)		
					Yes	2.0 (1.2–3.2)**		
					< 20	1.8 (1.0–3.2)		
					≥ 20	2.3 (1.3–4.0)		
					<i>P</i> for trend	0.004		
					Anaplastic large cell ($n = 21$)			
					No	(ref)		
					Yes	3.2 (1.2–9.1)*		
					< 20	2.5 (0.8–8.5)		
					≥ 20	4.2 (1.4–13.2)		
					<i>P</i> for trend	0.011		

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Lee <i>et al.</i> (2009) Republic of Korea	Blood (Leukaemia)	164 cases (of 176); Hospital based; Histologically confirmed; 0–18 yrs; 2003–2005	164 controls (of 298); Hospital based; No history of cancer; matched on age and sex	In person interviews	<i>Paternal smoking</i> (Ever/Never)	1.4 (0.8–2.4) All Leukaemia	Father's education and birth weight	
						1.3 (0.7–2.4) ALL		
					<i>Smoking at home</i> (No/Yes)	1.8 (1.1–2.8) All Leukaemia		
						2.0 (1.2–3.4) ALL		
					<i>Smoking at home during pregnancy</i> (Yes/No)	1.6 (0.8–3.0) All Leukaemia		
						1.8 (0.9–3.7) ALL		
					<i>Pack Years after birth</i>	All Leukaemia		
					≤ 10	1.5 (0.9–2.5)		
					> 10	2.2 (0.8–5.5)		
					<i>P for trend</i>	0.06		
						ALL		
					≤ 10	1.7 (0.9–3.1)		
					> 10	3.0 (1.0–8.8)		
					<i>P for trend</i>	0.02		
					Interaction with <i>CYP1A1</i> Diplotypes			
					<i>Smoking at home</i> (No/Yes)	All Leukaemia		
	0.8 (0.3–2.3) CGACC (+)							
	2.1 (1.2–3.7) CGACC (-)							
<i>P for trend</i>	0.12							
<i>Smokers at home</i> ≥1 person	0.8 (0.3–2.3) CGACC (+)							
	1.8 (1.0–3.2) CGACC (-)							
<i>P for trend</i>	0.12							
<i>Smoking at home</i> (No/Yes)	ALL							
	0.6 (0.2–2.1) CGACC (+)							
	2.8 (1.5–5.3) CGACC (-)							
<i>P for trend</i>	0.03							
<i>Smokers at home</i> ≥1 person	0.5 (0.1–1.7) CGACC (+)							
	2.3 (1.2–4.4) CGACC (-)							
<i>P for trend</i>	0.02							