

Table 2.9. Cohort studies of exposure to benzene and the risk for non-Hodgkin lymphoma (NHL)

Reference, location	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Wong (1987) USA	4602 men chemical workers from 7 plants occupationally exposed to benzene for at least 6 mo 1947–1975, and 3 074 workers from the same plants not exposed to benzene	Jobs with exposure to benzene classified as continuous and intermittent exposure. Tasks classified by occupational hygienists, with level of exposure assigned from exposure measurements.	NHL 200, 202, 203	Benzene Non-exposed < 180 ppm-mo 180–719 ppm-mo ≥ 720 ppm-mo	2 3 3 1	(SMR) 0.5 (0.0–1.8) 1.2 (0.2–3.4) 1.9 (0.4–5.4) 0.8 (0.0-4.4)		A Mantel-Haenszel analysis of relative risks revealed a non-significant trend with increasing exposure to benzene ($P = 0.7$)
Satin <i>et al.</i> (1996) USA	Cohort of 17844 petroleum refinery workers, employed 1937–1983, followed up to 1987	No exposure assessment was performed.	NHL 200, 202		30	(SMR) 0.7 (0.5–1.0)		
Schnatter <i>et al.</i> (1996) Canada	Cases and controls matched 1:4 with cases derived from a cohort of petroleum distribution workers	Industrial hygienists assigned exposure on the basis of work histories from personnel records.	NHL 200, 202	Benzene ppm-yr 0.0–0.49 0.50–7.99 8.00–19.99 20.0–219.8	4 3 1 0	(OR) 1.0 1.2 (0.2–8.1) 1.1 (0.0–22.1) -		Nested case-control analysis

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Hayes <i>et al.</i> (1997) PR China	74828 exposed and 35805 unexposed workers employed 1972–1987 in 12 cities in China, followed up to 1987	Average occupational exposure to benzene estimated by local industrial hygienists	NHL 200, 202	Benzene cumulative ppm-yr		(SMR)	Age and sex	NCI-CAPM cohort
				None	3	1.0		
				< 40	6	3.3 (0.8–13.1)		
				40–99	1	1.1 (0.1–11.1)		
				≥ 100	9	3.5 (0.9–13.2)		
		p for trend		0.02				
Lynge <i>et al.</i> (1997) Denmark, Norway, Sweden, Finland	Cohort of gasoline service station workers (16524 men, 2445 women), followed for 20 yr by linkage to national cancer registries	Service station occupation identified from the 1970 censuses of each country	NHL 200, 202	Men Women	37 2	(SIR) 1.1 (0.8–1.5) 0.6 (0.0–2.0)		Estimated average level of exposure to benzene below 1 mg/m ³
Nilsson <i>et al.</i> (1998) Sweden	Cohorts of men Swedish seamen, age 20–64, identified through the 1960 (13499) and 1970 (11290) censuses, cases identified by linkage to the Swedish cancer register, 1961–79 and 1971–87, respectively (17 and 20 NHL).	Details of service on ships from the Swedish Registry of Seamen. Ship classified as chemical or product tanker, crude oil tanker, other	NHL 200, 202	1960 cohort		(OR)		Nested case-control analysis. 3–5 controls per case randomly selected among men in the same 5 yr age stratum classified as seamen in the same national census and confirmed to be alive at the time of diagnosis of the case
				Chemical or product tanker	4	4.0 (0.9–18.9)		
				Crude oil tanker	0	-		
				1970 cohort				
Chemical or product tanker	6	3.3 (1.1–10.6)						
Crude oil tanker	3	0.9 (0.2–4.0)						

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Pukkala (1998) Finland	Cohort of 7512 men and 1942 women employed in one group including oil refinery, and chemical manufacturing; follow-up by linkage with the Finnish cancer registry 1971–1994.	No exposure assessment was performed	NHL 200, 202	Employed at least 3 mo during 1967–1982	12	(SIR) 1.2 (0.6–2.2)		

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Consonni <i>et al.</i> (1999) Italy	Cohort of 1583 workers employed 1949–1982 in an oil refinery and followed up to May 1991.	No exposure assessment was performed	NHL 200, 202		5	(SMR) 2.1 (0.7–5.0)		
Divine <i>et al.</i> (1999b) USA	All (28480) employees who worked at selected refinery, petrochemical, and research establishments at least one day between 1947–1977; employed at these for a cumulative total > 5 yr; still employed on the end date of the study	Complete work history of all jobs held at the participating factories (Divine <i>et al.</i> , 1999a)	NHL 200, 202	Employed: Ever Before 1950 After 1950	74 56 18	(SMR) 0.9 (0.7–1.1) 0.9 (0.6–1.1) 1.0 (0.6–1.5)		No estimates of exposure to benzene
Wong <i>et al.</i> (2001a) USA	Cohort of 7543 petroleum refinery workers (91% men) employed for at least 1 yr, 1945–1996, followed up to 1996	No exposure assessment was performed	NHL 200, 202	Men workers hired before 1950 Hired 1950 or later	22 4	(SMR) 1.0 (0.6–1.6) 0.7 (0.2–1.9)		No estimates of exposure to benzene

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Wong <i>et al.</i> (2001b) USA	Cohort of 3328 petroleum refinery workers employed for at least 1 yr, 1959–1997, followed up to 1997	No exposure assessment was performed	NHL 200, 202	Length of employment: < 10 yr 10–29 yr 30+ yr	4 5 0	(SMR) 2.3 (0.6–5.8) 1.2 (0.4–2.8) -		No estimates of exposure to benzene
Rinsky <i>et al.</i> (2002) USA	Cohort of 1291 men employed at one of three rubber hydrochloride plants for at least 1 d 1940–1976, followed 1960 to 1981.	Job exposure matrices were based on available air sampling data. Cumulative exposures (ppm-yr) were derived from the matrices by summing daily exposure values using detailed work histories.	NHL 200, 202	Exposed to at least 1ppm-d of Benzene	5	(SMR) 1.0 (0.3–2.3)		
Sorahan <i>et al.</i> (2002) United Kingdom	Cohorts of 29630 oil refinery and 16480 petroleum distribution workers, first employed after 1 January 1946 who had worked for at least a yr, followed 1951–1998 by linkage with national files	No exposure assessment was performed	NHL 200, 202	Refinery workers Distribution workers	84 37	(SMR) 1.2 (1.0–1.5) 0.9 (0.6–1.2)		NHL was described as Lymphosarcoma ICD 9 200, 202

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Collins <i>et al.</i> (2003) USA	Hourly workers (4172 men and 245 women) employed at a chemical manufacturing plant from 1940–1977 and followed up to 1997	Work histories, sampling measurements and industrial hygienists assessments	NHL 200 202	Benzene cumulative exposure ppm-yr		(SMR)		The SMR for peak benzene exposure > 40 ppm was 1.8 (95%CI: 0.4–5.1) based on 3 deaths.
				0	14	1.5 (0.8–2.5)		
				< 1	3	1.1 (0.2–3.4)		
				1–6	4	1.5 (0.4–3.8)		
				> 6	4	1.2 (0.3–3.2)		
Glass <i>et al.</i> (2003) Australia	Australian petroleum workers cohort in which 46 cases of NHL and multiple myeloma were identified.	Benzene exposure based on task-based algorithm involving the subject's occupational history; previously measured exposures for particular tasks in the Australian petroleum industry; and task-, site-, and period-specific data.	NHL and multiple myeloma 200, 202, 203	Cumulative lifetime Benzene exposure (ppm-yr)				Nested case-control analysis 5 controls per case randomly selected and matched by age and availability at time of diagnosis of the case 15 of the cases had multiple myeloma
				≤ 1	15	1.0		
				1–2	6	1.1 (0.4–2.9)		
				2–4	8	1.2 (0.5–3.0)		
				4–8	9	1.3 (0.5–3.2)		
				8–16	5	0.8 (0.3–2.6)		
				> 16	3	1.1 (0.3–4.5)		

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Lewis <i>et al.</i> (2003) Canada	Cohort of 17230 men and 8062 women employed for at least a yr for a petroleum company hired between 1964 and 1994 linked to national mortality and cancer incidence databases to 1994.	Estimates of similar exposure groups based upon job title and location by industrial hygienists	NHL 200, 202	Men	20	(SIR) 1.0 (0.5–1.9)		No specific estimates of benzene exposure
				Women	7	1.2 (0.5–2.5)		
				Hydrocarbons/solvents/fuels (Men)				
				Unexposed	8	1.0		
				< 2.5	9	2.1 (0.8–5.4)		
≥ 2.5- < 30	2	0.3 (0.1–1.3)	Smoking					
≥ 30	0	-						
Bloemen <i>et al.</i> (2004) USA	Workers exposed to benzene at a chemical plant; 2 266 workers (94% men). 68% were followed for at least 30 yr.	Job-titles were assigned to exposure categories by an industrial hygienist, based on industrial hygiene measurements.	NHL 200, 202	Benzene exposed workers	10	(SMR) 1.1 (0.5–2.0)		

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Huebner <i>et al.</i> (2004) USA	All employees of two refinery/petrochemical plants (Baton Rouge 6941 men, Baytown 6241 men) active in 1970 or hired between 1970–1982 with at least 1 mo of employment at the facility and followed up to 1997	No exposure determination performed	NHL 200, 202	Hired before 1950	23	(SMR) 1.6 (1.0–2.4)		
				Baton Rouge	13	1.0 (0.5–1.6)		
				Baytown				
				Hired in 1950 or later				
Baton Rouge	6	1.2 (0.4–2.6)						
Baytown	2	0.5 (0.1–1.7)						
Sorahan <i>et al.</i> (2005) United Kingdom	Cohort of 5130 men and 384 women followed for mortality, 1968–2002, and incidence 1971–2001 by linkage to national files.	Occupational exposure to benzene 1966/67 or earlier as reported by 233 employers	NHL 200, 202	All benzene exposed workers	15	(SMR) 0.9 (0.5–1.6)		
					24	(SIR) 1.0 (0.6–1.5)		

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Gun <i>et al.</i> (2006) Australia	Australian petroleum workers cohort, 16547 men and 1356 women, followed 1981–1999	None	NHL 200, 202		48	(SIR) 0.9 (0.7–1.2)		Overlap with Glass <i>et al.</i> (2003)
Kirkeleit <i>et al.</i> (2008) Norway	Cohort of 27919 offshore petroleum workers registered to the Norwegian registry of employers and employees and 366 114 matched referents from the general working population	Location of work and job category	NHL 200, 202	Exposed upstream offshore workers	14	1.0 (0.6–1.8)	Sex, age, yr of first exposure and education	Cases identified by linkage to the Norwegian cancer registry.

D, day or days, m, month or months; NHL, non-Hodgkin lymphoma; ppm, parts per million; yr, year or years