

Table 2.1 Cohort studies of industrial workers exposed to formaldehyde

Reference, location, years of study	Cohort description Type of analysis (cohort size)	Exposure assessment	Organ site (ICD code) ^a	Exposure Categories	No. of cases/deaths	Relative Risk (95% CI)	Adjustment for potential confounders	Comments
Coggon et al. (2003), United Kingdom, 1941–2000 (update of Acheson et al., 1984a; Gardner et al., 1993)	Chemical factories that used or produced formaldehyde Standardized mortality (14 014 men)	Level of exposure (background, low, moderate, high); among highly exposed, time period and duration of exposure	All cancers	Overall	1511 deaths	SMR 1.10 (1.04–1.16)		
			Nasopharynx	Overall	1 death	NR		2.0 expected
			Nose and nasal sinuses	Overall	2 deaths	0.87 (0.11–3.14)		Two additional cases identified from registry that could not be used in the analysis
			Lymphohaematopoietic	Overall	NR	NR		
			Leukaemia	Overall	31 deaths	0.91 (0.47–1.59)		
				Highest exposed category	8 deaths	0.71 (0.31–1.39)		
			Hodgkin lymphoma	Overall	6 deaths	0.70 (0.26–1.53)		
				Highest exposed category	1 death	0.36 (0.01–2.01)		
			Multiple myeloma	Overall	15 deaths	0.86 (0.48–1.41)		
				Highest exposed category	9 deaths	0.89 (0.41–1.70)		
			Non-Hodgkin lymphoma	Overall	31 deaths	0.98 (0.67–1.39)		
				Highest exposed category	7 deaths	1.18 (0.48–2.44)		
			Mouth (ICD-9, 143–145)	Overall	6 deaths	1.28 (0.47–2.78)		

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Coggon et al. (2003) Contd.			Lung	Overall <i>Average Intensity</i>	594 deaths	1.22 (1.12–1.32)		Compared with local rates. Increased risk among highly exposed (1.58; 95% CI, 1.40–1.78); inverse trend with duration of exposure
				<0.1 ppm	123 deaths	1.12 (0.93-1.33)		
				0.1-0.5 ppm	128 deaths	1.15 (0.96-1.36)		
				0.6-2.0 ppm	52 deaths	0.99 (0.4-1.30)		
				>2.0 ppm	272 deaths	1.28 (1.13-1.44)		
				Unknown	19 deaths	0.62 (0.37-0.97)		
			Brain and central nervous system		30 deaths	0.85 (0.57–1.21)		
Hauptmann et al. (2004) for solid tumors, USA, 1966–94 (update of Blair et al., 1986)	Manufacturer of formaldehyde, formaldehyde resins, moulding compounds, moulded plastic products, photographic films and plywood Standardized mortality (25 619 workers; 22 493 men, 3126 women);	Duration; quantitative estimates of cumulative, average and highest peak exposure	All cancers	Overall	1723 deaths	SMR 0.90 (0.86–0.95)		15-year lag for solid cancers; 2-year lag for lymphohaematopoietic cancers. The authors noted that the exact CI is 0.91–4.14; statistically significant trend with highest peak exposure; weaker trends observed with duration of, cumulative and average exposures
			Nasopharynx	Overall	8 deaths	2.10 (1.05–4.21)		
				Peak exposure (ppm)		RR	Adjusted for calendar year, age, sex, race and pay category (wage/salary)	
				0	2	1.0 (REF)		
				>0-<2.0	0	NA		
				2.0-<4.0	0	NA		
				≥4.0	7	1.8		
						p-trend <0.001		

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Hauptmann <i>et al.</i> (2004) Contd.	Exposure assessment through 1980; death for solid tumors through 1994;through 2004 for lymphohemato-poietic malignancies		Nose and nasal sinuses			SMR		
				Overall	3 deaths	1.19 (0.38–3.68)		
				Peak exposure (ppm)		RR		
				0	0 deaths	NA		
				>0-<2.0	1 death	1.0 (Ref)		
				2.0-<4.0	1 death	1.55		
				≥4.0	1 death	1.47		
					p-trend 0.779			
					SMR			
			Buccal cavity					
			Overall	49 deaths	1.01 (0.77-1.34)			
			Peak exposure (ppm)		RR			
			0	13 deaths	2.08			
			>0-<2.0	15 deaths	1.0			
2.0-<4.0	11 deaths	1.07						
≥4.0	23 deaths	1.83						
		p-trend=0.072						

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Hauptmann <i>et al.</i> (2004) Contd.			Lung			SMR			
				Overall	641 deaths	0.97 (0.9-1.05)			
				Peak exposure (ppm)		RR			
				0	103 deaths	1.08			
				>0-<2.0	237 deaths	1.0			
				2.0-<4.0	227 deaths	1.45			
				≥4.0	177 deaths	0.94			
					p-trend= 0.669				
					SMR				
					Overall	43 deaths	0.92 (0.68-1.23)		
					Peak exposure (ppm)		RR		
					0		1.64		
					>0-<2.0		1.0		
					2.0-<4.0		1.06		
		≥4.0		0.74					
				p-trend=-0.405					

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Beane Freeman <i>et al.</i> (2009) for lymphohemato poietic , USA 1966-2004 (Update of Blair <i>et al.</i> , 1986, 1987, Hauptmann <i>et</i> <i>al.</i> 2003)			Leukemia	<i>Peak exposure (ppm)</i>		RR	Adjusted for calendar year, age, sex, race and pay category (wage/salary)	Includes deaths through 1994. When additional 10 years of mortality included, associations diminished. Last known exposure in 1980.			
				0	4	0.52 (0.17-1.57)					
				>0-<2.0	23	1.0					
				2.0-<4.0	20	1.36 (0.73-2.51)					
				≥4.0	29	1.60 (0.9-2.82)					
									<i>Average Intensity</i>		
				0	4	0.44 (0.15-1.29)					
				0.1-0.4	12	1.0					
				0.5-0.9	17	1.12 (0.62-2.04)					
				≥1.0	17	1.34 (0.74-2.41)					
											<i>p-trend=0.0942</i>
											<i>p-trend>0.50</i>
			Myeloid leukaemia	<i>Peak exposure (ppm)</i>							
				0	2	0.60 (0.11-3.11)					
				>0-<2.0	7	1.0					
				2.0-<4.0	8	1.98 (0.7-5.64)					
				≥4.0	14	2.79 (1.08-7.21)					
					<i>p-trend=0.0237</i>						

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Beane Freeman <i>et al.</i> (2009) Contd.			Myeloid leukaemia	<i>Average Intensity</i>				
				0	2	0.40 (0.08-1.90)		
				0.1-0.4	15	1.0		
				0.5-0.9	5	1.05 (0.38-2.91)		
				≥1.0	9	2.19 (0.92-5.25)		
						<i>p-trend=0.114</i>		
				Lymphatic leukemia	<i>Peak exposure (ppm)</i>			
					0	0	NA	
			>0-<2.0		11	1.0		
			2.0-<4.0		6	0.81 (0.29-2.24)		
			≥4.0		7	0.74 (0.28-1.94)		
						<i>p-trend>0.50</i>		
				<i>Average Intensity</i>				
			0	0	NA			
0.1-0.4	14	1.0						
0.5-0.9	5	1.03 (0.37-2.88)						
≥1.0	5	1.01 (0.35-2.89)						
		<i>p-trend>0.50</i>						

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Bertazzi et al. (1986, 1989), Italy, 1959–86	Formaldehyde resin makers Standardized mortality (1332 men)	Duration of exposure, latency, age at employment, year of employment, time since beginning of employment	All cancers Nasopharynx Nasal cavity	Overall	62 deaths	SMR 1.23 [0.94–1.58] ^b		Mortality was close to expected when local rates were used as the referent (1.00 [95% CI, 0.64–1.49])
					NR	NR		
					0 deaths	NA		
					7 deaths	1.77 [0.71–3.65] ^b		
					NR	NR		
					NR	NR		
					NR	NR		
Edling et al. (1987, Sweden, 1955–83)	Abrasives industry Standardized mortality, standardized incidence (521 blue-collar male workers)	None (area measurements)	All cancers Nasopharynx Nasal cavity Lymphohaematopoietic Leukaemia Buccal cavity Lung Brain and central nervous system	Overall	24 inc. cases	SMR 0.84 [0.54–1.25] ^c		All cancer mortality SMR, 0.93 [95% CI, 0.54–1.49]
					1 inc. case	NR		
					0 inc. cases	NA		
					4 inc. cases	NR		
					0 inc. cases	NA		
					0 inc. cases	NA		
					2 inc. cases	0.57 [0.07–2.06]		
					1 inc. case	NR		

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Pinkerton et al. (2004), USA, 1955–98 (update of Stayner et al., 1988)	Garment industry Standardized mortality (11 039 workers; 2015 men, 9024 women)	Duration, time since first exposure, year of first exposure	All cancers	Overall	608 deaths	SMR 0.89 (0.82–0.97)		
			Nasopharynx		0 deaths	NA	0.96 expected	
			Nasal cavity		0 deaths	NA	0.16 expected	
			Lymphohaematopoietic	Overall	59 deaths	0.97 (0.74–1.26)		
			Leukaemia	Overall	24 deaths	1.09 (0.70–1.62)		
				<i>Duration of exposure</i>				All 95C CI include 1.0
				<3 years	7 deaths	0.96		
				3-9 years	5 deaths	0.72		
				10+ years	12 deaths	1.53		
			Myeloid leukaemia	Overall	15 deaths	1.44 (0.80–2.37)		
				<i>Duration of exposure</i>				Excess among workers with both ≥ 10 years of exposure and ≥ 20 years since first exposure (SMR, 2.43; 95% CI, 0.98–5.01)
				<3 years	3 deaths	0.83		
				3-9 years	4 deaths	1.26		
	10+ years	8 deaths	2.19					

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Pinkerton et al. (2004) Contd.			Hodgkin lymphoma		2 deaths	0.55 (0.07-1.98)		
			Multiple myeloma		NR	NR		
			Non-Hodgkin lymphoma		NR	NR		
			Buccal cavity/pharynx		4 deaths	1.33 (0.36–3.41)		
			Lung	Overall	147 deaths	0.98 (0.82–1.15)		
				<i>Duration of exposure</i>				
				<3 years	61 deaths	1.26		
				3-9 years	47 deaths	1.07		
				10+ years	39 deaths	0.67		
			Brain and central nervous system	Overall	19 deaths	1.09 (0.66–1.71)		
				<i>Duration of exposure</i>				
				<3 years	9 deaths	1.45		
				3-9 years	5 deaths	0.94		
			10+ years	5 deaths	0.86			

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Andjelkovich et al. (1995), USA, 1960–89	Foundry workers Standardized mortality (3929 men with potential exposure)	Exposed/ unexposed; none, low, medium and high exposure	All cancers	Overall	127 deaths	SMR 0.99 (0.82–1.17)		
			Nasopharynx		0 deaths	NA		
			Nasal cavity		0 deaths	NA		
			Lymphohaematopoietic		7 deaths	0.59 (0.23–1.21)		
			Leukaemia		2 deaths	0.43 (0.05–1.57)		
			Buccal cavity/pharynx		6 deaths	1.31 (0.48–2.86) 1.16 (0.20–6.51) ^d		
			Lung		51 deaths	1.20 (0.89–1.58) 0.59 (0.28–1.20) ^d		
			Brain and central nervous system		2 deaths	0.62 (0.07–2.23)		

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Hansen & Olsen (1995, 1996), Denmark	Workers from companies with a history of use or manufacture of formaldehyde Standardized proportionate incidence ratio (SPIR) (eligible cancer cases: 2041 men, 1263 women diagnosed in 1970–84)	Low (white-collar) and above baseline (blue-collar)	ICD-7	<i>Overall</i>		SPIR		
			Nasopharynx		<i>Men</i>	4 cases	1.3 (0.3–3.2)	
			Nasal cavity			13 cases	2.3 (1.3–4.0)	Risk increased among more highly exposed workers with (SPIR, 5.0; 95% CI, 0.5–13.4) or without (SPIR, 3.0; 95% CI, 1.4–5.7) exposure to wood dust
			Lymphohaematopoietic Leukaemia			NR	NR	
			Hodgkin lymphoma			39 cases	0.8 (0.6–1.6)	Risk not increased among more highly exposed
			Multiple myeloma			12 cases	0.9 (0.601.2)	
			Non-Hodgkin lymphoma			NR	NR	
			Buccal cavity/pharynx			32 cases	1.0 (0.5-1.7)	
			Lung			23 cases	1.1 (0.7–1.7)	Risk not increased among more highly exposed
			Lung		410 cases	1.0 (0.9–1.1)	Risk not increased among more highly exposed	
			Brain and nervous system		54 cases	1.1 (0.9–1.5)	Risk not increased among more highly exposed	

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Hansen & Olsen (1995, 1996) Contd.			Nasal cavity		4 cases	2.4 (0.6–6.0)		
			Lymphohaematopoietic		NR	NR		
			Leukaemia		21 cases	1.2 (0.7–1.8)		
			Lung		108 cases	1.2 (0.96–1.4)		
			Brain and nervous system		39 cases	1.2 (0.8–1.6)		
Chiazze et al. (1997), USA, 1951–91	Fibreglass manufacturing plant workers Standardized mortality and nested case–control (4631 men and women)	Cumulative exposure	All cancers		96 deaths	0.94 (0.77–1.15) ^b		Analysis restricted to 2933 white men
			Nasopharynx		NR	NR		
			Nasal cavity		NR	NR		
			Lympho haematopoietic		5 deaths	0.46 (0.15–1.08)		
			Leukaemia		1 death	0.24 (0.006–1.36)		
			Buccal cavity/pharynx		2 deaths	0.70 (0.08–2.52)		
			Lung		47 deaths	1.26 (0.93–1.68)		Excess risk for lung cancer reduced when local rates were used (SMR, 1.17; 95% CI, 0.86–1.55); positive trend in case–control study with cumulative exposure to formaldehyde among smokers
			Brain and nervous system		6 deaths	1.48 (0.54–3.23)		

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Stellman et al. (1998), USA, 1982–88	Workers in the American Cancer Society CPS-II study employed in wood-related occupations or who reported exposure to wood dust Retrospective cohort mortality study (45 399 men, of whom 387 reported exposure to formaldehyde)	Dichotomous (yes/no) with and without employment in a wood occupation	All cancers	Formaldehyde alone	367 deaths	RR 0.98 (0.86–1.12)	Age and smoking status	
				Formaldehyde + wood	14 deaths	1.61 (0.95–2.72)		
			Nasopharynx		NR	NR		
				Nasal cavity	NR	NR		
			Lymphohaematopoietic	Formaldehyde alone	28 deaths	1.22 (0.84–1.77)		
				Formaldehyde + wood	3 deaths	3.44 (1.11–10.68)		
			Leukaemia	Formaldehyde alone	12 deaths	0.96 (0.54–1.71)		
				Formaldehyde + wood	2 deaths	5.79 (1.44–23.25)		
			Multiple myeloma	Formaldehyde alone	4 deaths	0.74 (0.27–2.02)		
				Formaldehyde + wood	0	NR		
			Non-Hodgkin lymphoma	Formaldehyde alone	11 deaths	0.92 (0.50–1.68)		
				Formaldehyde + wood	1 death	2.88 (0.40–20.50)		
			Buccal cavity/pharynx		NR	NR		
			Lung	Formaldehyde alone	104 deaths	0.93 (0.73–1.18)		
				Formaldehyde + wood	7 deaths	2.63 (1.25–5.51)		
Brain (ICD-9, 191)		NR	NR					

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Marsh et al. (2001); Youk et al. (2001), USA, 1945–92	Fibreglass workers Standardized mortality and nested case–control (32 000 men and women, 22% of person–years exposed to formaldehyde)	Duration of, cumulative and average exposure	All cancers		2243 deaths	SMR 0.98 (0.94–1.02) ^b		SMR was reduced and no longer significant when local rates were used (SMR, 1.06; 95% CI, 1.00–1.14); a statistically significant excess among formaldehyde-exposed workers observed in the case–control study (smoking-adjusted odds ratio, 1.61; 95% CI, 1.02–2.56); no significant trend with duration or cumulative exposure; some evidence for a trend with average exposure
			Nasopharynx		NR	NR		
			Nasal cavity		NR	NR		
			Lymphohaematopoietic		199 deaths	0.92 (0.80–1.06)		
			Leukaemia		NR	NR		
			Buccal cavity/pharynx		63 deaths	1.07 (0.82–1.37)		
			Lung		838 deaths	1.17 (1.09–1.25)		
			Brain and central nervous system		50 deaths	0.78 (0.58–1.03)		

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Stern et al (1987), USA, 1940-1982	9,365 workers in one of two tanneries	Duration of employment	Buccal cavity and pharynx (140-148)	<1 year employment	3 deaths	0.79 (0.20-2.15)		No significant results when restricted to finishing area, where the formaldehyde levels were highest
			1-9 years employment	3 deaths	1.87 (0.48-5.10)			
			≥10 years employment	2 deaths	0.71 (0.12-2.36)			
			Total 15 years + latency	8 deaths	0.97 (0.42-1.91)			
			Trachea, bronchus and lung (162-163)	<1 year employment	30 deaths	0.78 (0.53-1.12)		
			1-9 years employment	15 deaths	0.93 (0.52-1.54)			
			≥10 years employment	7 deaths	0.27 (0.11-0.57)			
			Total 15 years + latency	52 deaths	0.65 (0.49-0.85)			
			Leukemia and aleukemia (204)	<1 year employment	2 deaths	0.45 (.05-1.68)		
			1-9 years employment	2 deaths	1.00 (0.11-3.61)			
			≥10 years employment	6 deaths	1.70 (0.63-3.73)			
			Total 15 years + latency	10 deaths	1.01 (0.48-1.86)			
			Lymphoma (200-203, 205)	<1 year employment	7 deaths	1.05 (0.42-2.19)		
			1-9 years employment	3 deaths	1.05 (0.21-3.05)			
			≥10 years employment	2 deaths	0.48 (0.05-1.73)			
			Total 15 years + latency	12 deaths	0.87 (0.45-1.53)			

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Tarvainen et al. (2008), Finland, 1971-1995	Incident cases of mouth and pharynx (excluding nasopharynx) in people born 1906-1945 identified through the Finnish Cancer Registry; 1971-1995	National job exposure matrix	Mouth and pharynx (excluding nasopharynx)	0-1 ppm yrs	59 cases	SIR 0.79 (0.60-1.03)	Age, calendar period and SES	10-year lag period
				>1-<5 ppm yrs	8 cases	1.01 (0.43-1.98)		
				≥5 ppm yrs	6 cases	0.73 (0.27-1.59)		
				Overall				
Ambroise et al., (2005), France, 1979-2000	181 municipal pest control workers (all male), employed between 1979 and 1994, mortality follow-up from 1979-2000.	Job exposure matrix developed from administrative records, interviews with employees and historical description of activities	All malignant neoplasms	Overall	21 deaths	SMR 2.24 (1.39-3.43)	Used regional rates, rather than national rates. Co-exposed to insecticides and rodenticides. Significantly elevated SMR in highest cumulative dose of formaldehyde for cancer overall.	
				Buccal cavity/pharynx	2 deaths	2.47 (0.30-8.92)		
				Larynx	0 deaths	NR		
				Lung, bronchus	1 death	0.39 (0.01-2.19)		
				Pleura	1 death	11.19 (0.28-62.36)		
				Leukaemia	1 death	4.42 (0.11-24.64)		