

**Table 2.4 Case-control studies of exposure to formaldehyde and cancer of the the nasal cavity, paranasal sinuses, nasopharynx and hypopharynx**

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Number of Exposed Cases	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Hernberg et al. (1983a), Denmark, Finland, Sweden, 1977–80	167 patients [sex distribution not reported] with primary malignant tumours	167 patients with cancer of the colon and rectum, matched by country, sex and age	Employment in particle-board or plywood industry Painting, lacquering and glazing	Nasal cavity and paranasal sinuses (160.0–160.9; ICD revision not given)	Yes/no Yes/no	0 18	NR NR		Concomitant exposure of 15 cases to wood dust
Brinton et al. (1984), USA, 1970–80	160 (93 men, 67 women), including 86 squamous-cell carcinomas, 24 adenocarcinomas or adenoid cystic carcinomas; 61 in nasal cavity, 71 in maxillary sinus, 28 other sinus or overlapping sites	290 (178 hospital controls, 112 death certificate controls); hospital controls were required to be alive for living cases; death certificate controls were identified for deceased cases; matched on age, sex, race and county of residence	Telephone interviews with subjects or next of kin included a checklist of industries and self-reported exposures including formaldehyde.	Nasal cavity and paranasal sinuses (ICD-8 160.0, 160.2–160.5, 160.8–160.9)	<i>Men and women combined</i> Exposed	2	0.35 (0.1–1.8)	Adjusted for sex; control for tobacco use did not change results.	Formaldehyde exposure assessment was self-reported.; only 33% of cases and 39% of controls were interviewed directly; for the remainder, exposures relied on recall of next of kin.

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Olsen et al. (1984) Olsen & Asnaes (1986), Denmark, 1970–82	754 incident patients [sex distribution not reported] selected from the Danish Cancer Registry including 488 carcinomas of the nasal cavity and sinuses and 266 carcinomas of the nasopharynx	2465 patients with cancers of the colon, rectum, prostate and breast; frequency-matched by sex, age ( $\pm 5$ years) and year of diagnosis ( $\pm 5$ years); 4.2% of men and 0.1% of women exposed to formaldehyde	Record linkage with pension fund with compulsory membership; job title from Central Pension Registry; exposure assessed blindly as certain, probable, unlikely, unknown	Nasal cavity and nasal sinuses (160.0, 160.2, 160.9)	<b>Industries and occupations with certain exposure to formaldehyde</b>	<i>Ever exposed</i>	33	<i>Sinonasal</i> 2.8 (1.8–4.3)	Unadjusted	Data for sinonasal cancer reported for men only	
						Unexposed to wood dust	5				1.8 (0.7–4.9)
						Exposed to wood dust	28				3.5 (2.2–5.6)
						<i>Exposure for &gt; 10 years before diagnosis</i>	23				3.1 (1.8–5.4)
						Unexposed to wood dust	3				1.5 (0.4–5.3)
				Exposed to wood dust	20	4.1 (2.3–7.3)					
				Adjusted for wood dust	23	1.6 (0.7–3.6)	Adjusted for exposure to wood dust	Data presented for men for cancer of the nasal cavity and paranasal sinuses			
				Nasal cavity and paranasal sinuses (160.0, 160.2–160.9)	<i>Likely or possible exposure to formaldehyde &gt; 10 years before diagnosis</i>	Squamous-cell carcinoma (215)			6	2.4 (0.8–7.4)	
						Adenocarcinoma (39)			11	1.8 (0.5–6.0)	

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Hayes et al. (1986), Netherlands, 1978–81	91 male patients histologically confirmed, alive or deceased	195 age-stratified random sample of living men resident in the Netherlands in 1982 or deceased in the Netherlands in 1980	Taking into account job history, time period and potential frequency of exposure, exposure was classified into 10 groups independently by two occupational hygienists (assessment A and B)	Nasal cavity and accessory sinuses (ICD-9 160.0, 160.2–160.5)	<i>Any exposure to formaldehyde</i>		2.5 (1.5–4.3) <sup>a</sup>	Standardized for age in 10-year groups; control for usual number of cigarettes smoked did not modify the results.	Relative risk for adenocarcinoma for those ever employed in the wood and paper industry, 11.3 (90% CI, 4.0–35.1); moderate increase associated with increase in level of exposure to formaldehyde with no concomitant exposure to wood dust
					Assessment A		1.9 (1.2–3.0) <sup>a</sup>		
					Assessment B				
					<i>No or little exposure to wood dust</i>				
					Assessment A	15	2.5 [1.0–5.9]		
					Assessment B	24	1.6 [0.8–3.1]		
<i>Moderate to high exposure to wood dust</i>									
Assessment A	16	1.9 [0.6–6.5]							
Assessment B	26	NR							
					<i>Squamous-cell carcinoma only</i>			No or little exposure to wood dust	
					Assessment A	12	3.0 [1.2–7.8]		
					Assessment B	19	1.9 [0.9–4.1]		

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Vaughan et al. (1986a), USA, 1979–83	285 incident cases [sex distribution not reported] identified by the local Cancer Surveillance System, aged 20–74 years, including oro- and hypopharynx (205), nasopharynx (27) and sinuses (53)	552 identified by random-digit dialling	Job–exposure linkage system, resulting in four categories: high, medium, low and background	Nasal cavity (160), pharynx (146–149) (ICD revision not given)	Low exposure	9	<i>Sinonasal</i> 0.8 (0.4–1.7)	Age, sex, cigarette smoking and alcohol consumption		
					Medium or high exposure	3	0.3 (0.0–1.3)			
					Highest exposure score	NR	0.3 (0.0–2.3)			
										<i>Nasopharynx</i>
					Low exposure	7	1.2 (0.5–3.3)			
					Medium or high exposure	4	1.4 (0.4–4.7)			
					Highest exposure score	NR	2.1 (0.6–7.8)			
										<i>Oro-/hypopharynx</i>
					Low exposure	41	0.8 (0.5–1.4)			
					Medium exposure	13	0.8 (0.4–1.7)			
					High exposure	4	0.6 (0.1–2.7)			
					Highest exposure score	NR	1.5 (0.7–3.0)			

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Vaughan et al. (1986b), USA, 1979–83	285 incident cases [sex distribution not reported] identified by the local Cancer Surveillance System, aged 20–74 years, including oro- and hypopharynx (205), nasopharynx (27) and sinuses (53)	552 identified by random-digit dialing	Residential exposure: residential history since 1950	Nasal cavity (160), pharynx, (146–149) (ICD revision not given)	Mobile home	5	<i>Sinonasal</i> 0.6 (0.2–1.7)	Sex, age, cigarette smoking and alcohol consumption	
					Particle-board at home	13	1.8 (0.9–3.8)		
					1–9 years	12	1.5 (0.7–3.2)		
					> 10 years				
					Mobile home	21	<i>Oro-/hypopharynx</i> 0.9 (0.5–1.8)		
					1–9 years	7	0.8 (0.2–2.7)		
					> 10 years				
					Particle-board at home	40	1.1 (0.7–1.9)		
1–9 years	28	0.8 (0.5–1.4)	consumption						
Roush et al. (1987), USA, 1935–75	198 men with sinonasal cancer and 173 with nasopharyngeal cancer registered at the Connecticut Tumor Registry	605 men who died during the same period, selected by random sampling without matching or stratification	Job title, industry, specific employment, year of employment, obtained from death certificates and city directories	Nasal cavity and sinuses, nasopharynx (ICD code not given)	Probably exposed for most of working life	21	<i>Sinonasal</i> 0.8 (0.5–1.3)	Age and calendar period	
					Plus exposure > 20 years before death	16	1.0 (0.5–1.8)		
					Plus exposure to high level for some years	9	1.0 (0.5–2.2)		
					Plus exposure to highlevel > 20 years before death	7	1.5 (0.6–3.9)		

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Luce et al. (1993), France, 1986–88	207 cases (167 men, 40 women): 59 men and 18 women with squamous-cell carcinomas, 82 men and five women with adenocarcinomas and 25 men and 17 women with other histology	409 from two sources: 323 hospital cancer controls (15 sites) frequency-matched by age and sex; 86 proposed by cases, matched by age ( $\pm 10$ years), sex and residence	Industrial hygienist review of structured job interview, classifying exposure by frequency, concentration and duration. Computation of cumulative exposure level and lifetime average level	Nasal cavity and paranasal sinuses (ICD-9 160.0, 160.2–160.9)	<i>Squamous-cell carcinoma</i>		<b>Men</b>			Adjusted for age, exposure to wood dust and exposure to glues and adhesives	Adjustment for usual cigarette use or for smoking history did not change results.					
					Possibly exposed	7	0.96 (0.38–2.42)									
					Probably or definitely											
					Average level < 2	7	0.70 (0.28–1.73)									
					Average level > 2	9	1.32 (0.54–3.24)									
					Duration < 20 years	9	1.09 (0.48–2.50)									
					Duration > 20 years	7	0.76 (0.29–2.01)									
					Cumulative level:											
					< 30	9	1.26 (0.54–2.94)									
					> 30	7	0.68 (0.27–1.75)									
					<i>Adenocarcinoma</i>											Most cases of adenocarcinomas exposed to both formaldehyde wood dust; very large odds ratio (288) for wood dust; therefore, there is concern about the possibility of incomplete adjustment
					Possibly exposed	6	1.28 (0.16–10.42)									
					Probably or definitely											
					Average level < 2	25	4.15 (0.96–17.84)									
					Average level > 2	44	5.33 (1.28–22.20)									
					Duration < 20 years	11	1.03 (0.18–5.77)									
					Duration > 20 years	58	6.86 (1.69–27.80)									
Cumulative level																
< 30	9	1.13 (0.19–6.90)														
30–60	8	2.66 (0.38–18.70)														
> 60	52	6.91 (1.69–28.23)														

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Luce et al. (1993) Contd.					<i>Other histology</i> Possibly exposed Probably or definitely	2	0.81 (0.15–4.36)		for wood dust in these results.
					Average level < 2	5	1.67 (0.51–5.42)		
					Average level > 2	8	3.04 (0.95–9.70)		
					Duration < 20 years	7	2.82 (0.94–8.43)		
					Duration > 20 years	6	1.62 (0.48–5.51)		
					Cumulative level < 30	5	2.18 (0.65–7.31)		
					> 30	8	2.21 (0.73–6.73)		
Gustavsson et al. (1998), Sweden, 1988–91	545 incident male cases among residents of two regions, aged 40–79 years [including at least 124 cases of pharyngeal cancer]	641 selected by stratified random sampling, frequency-matched to cases by age (10–15-year groups) and region	Work history reviewed by occupational hygienist; occupations coded by intensity and probability of exposure	Oro- and hypopharynx (ICD-9 146, 148)	Ever exposed	13	1.01 (0.49–2.07)	Age, region, alcohol, consumption, smoking habits	

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Laforest et al. (2000), France, 1989–91	201 men with confirmed histology from 15 hospitals [no information on age]	296 male patients with other (selected) primary tumours selected from the same or nearby hospitals, recruited 1987–91, matched by age	Structured in-person interviews; occupational exposures assessed with a job–exposure matrix earlier developed	Hypopharynx (squamous- cell) (ICD code not given)	Ever exposed	83	1.35 (0.86–2.14)	Age, tobacco smoking, alcohol consumption, coal dust and asbestos		
					<i>Probability of exposure (%)</i>					
					< 10	42	1.08 (0.62–1.88)			
					10–50	15	1.01 (0.44–2.31)			
					> 50	26	3.78 (1.50–9.49)			
					<i>Duration (years)</i>					
					< 7	18	1.09 (0.50–2.38)			
					7–20	37	1.39 (0.74–2.62)			
					20	28	1.51 (0.78–2.92)			
					<i>Cumulative level</i>					
					Low	23	1.03 (0.51–2.07)			
					Medium	32	1.57 (0.81–3.06)			
					High	28	1.51 (0.74–3.10)			
					<i>Exclusion of subjects with exposure probability &lt; 10%</i>					
					Ever exposed	41	1.74 (0.91–3.34)			
<i>Duration (years)</i>										
< 7	6	0.74 (0.20–2.68)								
7–20	19	1.65 (0.67–4.08)								
20	16	2.70 (1.08–6.73)								
<i>Cumulative level</i>										
Low	3	0.78 (0.11–5.45)								
Medium	13	1.77 (0.65–4.78)								
High	25	1.92 (0.86–4.32)								



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Berrino et al. (2003), France, Italy, Spain, Switzerland, 1979–82	100 men, incident cases histologically confirmed from six centres; aged < 55 years	819 men from the general local population of each centre; age- and sex-stratified	Structured in-person interviews; occupational exposures assessed by an expert panel using a previously established job-exposure matrix	Hypopharynx and epilarynx (ICD code not given)	<i>Probability of exposure</i> Possible Probable and certain	NR	1.3 (0.6–2.6) 0.5 (0.1–1.8)	Age, centre, tobacco use, alcohol consumption, diet, socioeconomic status, asbestos, PAHs, chromium, arsenic, wood dust, solvents, other dusts and gases	[The credibility of the negative finding is limited because formaldehyde was the agent for which the validity of the job–exposure matrix was lowest.]
Pesch et al. (2008), Germany, 2003–2005	86 cases among males of histopathologically confirmed adenocarcinoma of nasal cavity and paranasal sinuses identified from woodworking liability insurance association	204 male workers in German woodworking industries, matched on year of birth	Structured interview with cases (n=56) and controls (n=135) and next of kin for some (n=29 cases and n=69 controls). Structured interview on occupational history, expert team rating of none, low, medium, high.	Adenocarcinoma of nasal cavity and paranasal sinus (ICD code not given)	<1985 ≥1985	8 39	0.46 (0.14–1.54) 0.94 (0.47–1.90)	Smoking, age, region, interviewee, and average exposure to wood dust	Conducted within woodworking industry; wood dust exposure significantly elevated with outcome. Next of kin interviews for 1/3 of participants.