Cancer of the Oral Cavity, Pharynx, and Nasopharynx

4

Victor Wünsch Filho

Keywords
Oral cancer • Pharyngeal cancer • Occupation • Asbestos • Diesel engine exhaust • Leather dust • Cotton dust • Occupational risk factors • Formaldehyde • Wood dust • Welding fumes

Overview

Oral Cavity and Pharynx Cancer

Cancer of the oral cavity and pharynx is one of the ten most common in the world. In 2008, the age-standardized incidence rate was 8.7 per 100,000 men and 3.4 per 100,000 women, and mortality rate was 7.0 per 100,000 men and 1.7 per 100,000 women [1]. About 90 % of oral cavity and pharynx tumors are histological squamous cell type. Incidence increases with age and peaks between ages of 50 and 70 years. Incidence is higher in more developed regions for males than less developed regions, while mortality is similar between the more and less developed regions. In women, incidence and mortality are higher in less developed regions [2]. In India, these tumors are a heavy health burden in both urban and rural areas. They are responsible for the highest cancer mortality rates in men and are third after breast and uterine cervix tumors in women [1]. Other high-incidence areas are Eastern, Western, and Southern Europe, Australia and New Zealand, and Melanesia [3]. Latin America and the Caribbean have intermediate incidence rates of oral and pharynx cancers; however, rates vary widely between countries in the region and even within those countries [4, 5]. In Brazil, mortality rates from oral cavity cancer are stable in both men and women; however, pharynx cancer is increasing [6].

V. Wünsch Filho, MD, PhD
Department of Epidemiology,
University of São Paulo School of Public Health,
Av. Dr. Arnaldo, 715, São Paulo, SP 01246-904, Brazil
e-mail: wunsch@usp.br

Increasing incidence of oral and pharynx cancers has been observed in some Western Europe countries [7–10]. Incidence of oral cavity and pharynx tumors in the United States has been decreasing over the last 30 years [11]. However, increasing incidence in cancer of the tongue, base of the tongue, and the tonsils has been observed in patients under 45 years of age [12, 13]. Nordic countries have also shown increasing incidence of tongue cancer in both male and female young adults [14, 15].

Nasopharynx Cancer

Incidence of nasopharynx cancer is higher for those in their 50s. Worldwide incidence rates are about 1.7 per 100,000 in men and 0.8 per 100,000 in women, and mortality rates are 1.1 and 0.4 per 100,000, respectively, in men and women [1]. However, incidence is much higher in Southern China, Southeast Asia, the Middle East, and North Africa. In some regions of Southern China, such as Hong Kong, incidence in men reached levels higher than 20 per 100,000, but there has been a remarkable continuous downward trend for these tumors [16–18]. This can mainly be attributed to changes in environmental risk factors within the Chinese population, such as a diet that has been changing to a more Western style; thus, preserved salted fish is no longer a common food for most Chinese households [16]. This downward trend has also been seen in the United States among Chinese Americans living in California [19, 20]. The World Health Organization classifies nasopharyngeal carcinoma into three types according to histology: squamous cell carcinoma (Type I), nonkeratinizing carcinoma (Type II), and undifferentiated carcinoma (Type III). Nonkeratinizing and undifferentiated

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carcinomas are the most common (>90 %) in high-incidence areas [20–22], and squamous cell carcinoma is the most common (>70 %) in low-incidence regions [20, 21, 23].

Nonoccupational Risk Factors

Oral Cavity and Pharynx Cancer

For a long time, tobacco smoking and alcohol consumption have been recognized as the main causal factors for oral cavity and pharynx tumors; recent pooled analysis and multicenter studies have confirmed this [24–26]. Tobacco smoking and alcohol intake have a dose-response relationship in the occurrence of these tumors; there is also an evident interaction between these two risk factors [27]. Environmental exposure to tobacco smoke in homes and workplace is also associated with oral cavity and pharynx tumors. A pooled analysis of case-control studies has shown the carcinogenic effect of involuntary smoking on head and neck anatomical sites, particularly the pharynx and larynx [28]. Incidence of oral cavity and pharynx cancer is higher among groups of low socioeconomic status [29]. This can be partly explained by higher prevalence of smoking and alcohol consumption in individuals from socially disadvantaged groups [30]. Other factors related to these tumors have also been reported: for instance, diet, where consumption of fruit and vegetables is inversely associated to the risk of these tumors [31]; being underweight, where individuals with low BMI are at increased risk of head and neck cancer (including oral cavity, pharynx, and larynx) [32, 33]; chewing betel quid with or without tobacco, where products commercially available in India are considered carcinogenic to humans, affecting the oral cavity and pharynx with tobacco and just the oral cavity without tobacco [34–36]; and periodontal disease and regular gum bleeding, as well as daily mouthwash use, which may be independent risk factors for oral cavity and pharynx cancer [37, 38]. Poor mouth condition and missing teeth indicate low mouth health care and limited access to dental assistance, both correlated with low socioeconomic status. Human papillomavirus (HPV), particularly HPV16, is associated with oropharyngeal cancer [39]. Increasing incidence of tongue and tonsil tumors seen among those under 45 has been attributed to increasing prevalence of HPV infection in developing countries, practice of oral sex, and number of sexual partners [2, 40, 41]. In addition to environmental factors, familial clustering of oral cavity and pharynx cancer is related to increased risk of oral cavity and pharynx cancer [42].

Nasopharynx Cancer

Nasopharynx cancer is a complex disease; some environmental factors are involved in its origin, probably interacting, and there is also some type of genetic susceptibility. Consumption of salted fish starting in childhood is an important cause of nasopharyngeal cancer in the Chinese population [35, 36], but in contrast to salted fish and other preserved foods, frequent consumption of fresh fruit and vegetables has been linked to a lower risk [21]. Epstein-Barr virus is associated with nasopharynx cancer, but other cofactors must also be present for the disease to manifest [20, 39, 43]. Other factors also associated with nasopharynx cancer are previous chronic ear or nose diseases, such as chronic rhinitis or otitis media [23, 44]; active and passive smoking [23, 36, 44–47]; and the use of Chinese nasal oil and traditional herbal medicine [45, 48]. Additionally, family history of nasopharynx cancer has also been related to increased risk of nasopharynx cancer [44, 45, 49].

Occupational Risk Factors

Oral Cavity and Pharynx Cancer

Some studies have investigated the relationship between occupation and oral cavity and pharynx cancer considering broad categories; Garrote et al. [50] divided subjects into white-collar and blue-collar workers, farmers and housewives, and others, and Menvielle et al. [51] classified their study population into three groups, manual, nonmanual, and agricultural. Tables 4.1 and 4.2 describe 20 case-control and 24 cohort studies which reported an association between specific occupations and industries and oral cavity and pharynx cancer. Several occupations, work in specific industries, and exposure to specific agents have been screened for their carcinogenic potential.

Formaldehyde

Formaldehyde is widely used to manufacture building materials and household products. Most of formaldehyde production is for manufacture of resins, used to make adhesives for pressed wood products. Formaldehyde is also used as a preservative in medical laboratories and mortuaries.

Three of the four case-control studies in Table 4.1, which examined the effect of exposure to formaldehyde in oral and pharynx cancers, found relative risks (RR) of around 1.0 [52–54], whereas Vlajinac et al. [55] found a high risk (RR 4.4, 95 % confidence interval [95 % CI] 0.6–31.6). In a cohort study of workers from ten formaldehyde-producing or formaldehyde-using plants in the United States, Blair et al. [56] found standardized mortality ratio (SMR) of 443 ($p<0.05$) for oropharynx cancer in those exposed to cumulative doses of 0.5 parts per million-years (ppm-years) or less; however, SMRs were lower than 100 for those exposed to higher cumulative dose levels. Gardner et al. [57] in a cohort study of six formaldehyde-producing companies in the United Kingdom observed increased SMRs for oral and pharynx cancers in those employed before 1965 and for

Table 4.1 Case-control studies on occupation and cancer of the oral cavity and pharynx

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Decoufle [74], United States, 1956–1965	Oral cavity and pharynx cancer patients from a single New York clinical center	Patients without cancer conditions	Employment in the leather industry	Men			RR adjusted for tobacco smoking	
				Ever	18 (?)	3.22 ($p<0.01$)		
				employed at least for 5 years	12 (?)	3.58 ($p<0.01$)		
Winn et al. [88], United States, 1975–1978	232 women with oral and pharynx cancer residents in certain central North Carolina counties (156 from 5 hospitals and 99 from death certificates)	502 controls matched by admission date, age, race, and county of residence (from the same institutions as cases and from death certificate lists). Controls were not eligible if they had a diagnosis of mental disorder; neoplasms of the oral cavity or pharynx, esophagus, or larynx; or other noninfectious oral or pharyngeal diseases	Employment in textile, apparel, and hosiery industries. It was examined also exposure to dust in textile industry	*Textile*			RR crude. Authors referred that adjusting for smoking and snuff consumption did not appreciably reduce the association	
				No	192 (344)	1.0		
				Yes	40 (66)	1.1 (0.7–1.7)		
				1–4 years	13 (16)	1.5 (0.7–3.1)		
				5–9 years	6 (9)	1.2 (0.4–3.4)		
				10–19 years	6 (18)	0.6 (0.3–1.6)		
				20 years or more	13 (16)	1.5 (0.7–3.1)		
				Apparel				
				No	233 (392)	1.0		
				Yes	9 (18)	0.9 (0.4–2.0)		
				1–4 years	3 (7)	0.8 (0.2–3.0)		
				5–9 years	1 (4)	0.6 (0.1–3.7)		
				10 years or more	4 (5)	1.4 (0.4–5.1)		
				Hosiery				
				No	225 (384)	1.0		
				Yes	7 (26)	0.5 (0.2–1.1)		
				1–4 years	3 (7)	0.8 (0.2–2.9)		
				5–9 years	2 (5)	0.8 (0.2–3.5)		
				10 years or more	1 (11)	0.2 (0.0–1.2)		
				Textile dust				
				Never (work <6 months)	204 (373)	1.0		
				1–4 years	9 (4)	3.9 (1.2–12.0)		
				5–9 years	4 (5)	1.5 (0.4–5.3)		
				10 + years	14 (26)	1.0 (0.5–1.9)		

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Vaughan et al. [114], United States, 1980–1983	285 cases (186 men, 99 women) of oro- and hypopharynx cancer ($n=205$), nasopharynx ($n=27$), sinus, and nasal cavity ($n=53$) selected from a population-based cancer registry	552 controls (327 men, 225 women) were identified via random digit dialing	Occupational formaldehyde exposure was assessed via a job-exposure matrix	*Oro-hypopharynx*			Odds ratio adjusted for age, sex, cigarette smoking, and alcohol consumption	
				Exposure level				
				Background	147 (381)	1.0		
				Low	41 (121)	0.8 (0.5–1.4)		
				Medium	13 (42)	0.8 (0.4–1.7)		
				High	4 (8)	0.6 (0.1–2.7)		
				Number of years exposed				
				0	147 (381)	1.0		
				1–9	32 (127)	0.6 (0.3–1.0)		
				10+	26 (44)	1.3 (0.7–2.5)		
				Exposure score (all years)				
				0–4	170 (464)	1.0		
				5–19	14 (59)	0.6 (0.3–1.2)		
				20+	21 (29)	1.5 (0.7–3.0)		
				Exposure score induction (excluding 15 years before diagnosis)				
				0–4	174 (490)	1.0		
				5–19	16 (40)	0.9 (0.4–1.8)		
				20+	15 (22)	1.3 (0.6–3.1)		
Oreggia et al. [96], Uruguay, 1977–1981	242 cases of men with oral cavity, pharynx, and hypopharynx cancer ($n=236$) and larynx cancer ($n=6$) selected in a single center	322 controls matched by age among patients from the same hospital of cases, excluding those with lung, bladder, pancreas, and kidney cancer	Occupation with the longest duration was codified according to the International Classification of Occupations	*Oro-hypopharynx*			RR adjusted for tobacco smoking and alcohol consumption	Reference category: administrative, commerce, and professional workers
				Farmers	16 (72)	0.9 (0.3–2.2)		
				Baristas	2 (6)	1.0 (0.1–7.0)		
				Mechanics workers	2 (7)	1.5 (0.3–9.3)		
				Agriculture workers	2 (6)	1.9 (0.3–10.7)		
				Butchers	7 (8)	2.0 (0.4–9.5)		
				Blacksmiths	3 (3)	2.8 (0.5–16.0)		
				Bricklayers	18 (23)	2.8 (1.1–7.6)		
				Drivers	6 (13)	3.1 (0.7–14.0)		
				Telephone Operators	3 (2)	4.2 (0.5–34.9)		
				Electricians	2 (2)	5.5 (0.7–40.2)		
				Railwaymen	2 (1)	5.7 (0.6–51.3)		
Franco et al. [75], Brazil, 1986–1988	232 cases (201 men, 31 women) with oral cavity cancer from three clinical centers in three Brazilian cities	Controls selected among patients of the same hospitals of cases or from neighboring general hospitals, matched to cases by sex, age, and period of hospital admission	Never/ever employed in selected occupational settings	Textile	12 (40)	0.5 (0.3–1.1)	Adjusted for tobacco smoking and alcohol consumption	Reference category: never exposed
				Wood	27 (39)	1.2 (0.7–2.2)		
				Paper	6 (5)	2.1 (0.6–7.3)		
				Mining	10 (27)	0.8 (0.3–1.8)		
				Leather	7 (13)	1.3 (0.4–3.7)		
				Metal	23 (70)	0.6 (0.3–1.0)		
				Sugar/alcohol	7 (11)	0.9 (0.3–2.5)		
				Rubber	7 (11)	1.5 (0.5–4.8)		

Vaughan [82], United States, 1980–1983	183 cases (121 men, 62 women) of oro- and hypopharynx squamous cell carcinoma selected from a population-based cancer registry	552 controls (327 men, 225 women) were identified via random digit dialing, matched on age and gender	Jobs were broadly classified into 31 industrial and 59 occupations classified via the US Census Bureau. Never/ever considering all years and induction period (excluding 15 years before diagnosis). Presented here are only the odds ratios equal or higher than 1.5 for both situations "all years" and "induction period"	*OR (all years)*			Adjusted for age, gender, race, and smoking	Induction period = duration in job calculated after excluding the most recent 15 years before reference date (diagnosis for cases, interview for controls)
				Occupation/industry				
				Writers, entertainers, athletes in entertainment and recreation	8 (8)	3.6 (0.9–13.9)		
				Administrative support in personal services	3 (4)	2.2 (0.8–6.0)		
				Food service in transportation and communication	3 (1)	3.8 (0.2–57.2)		
				Food service in retail trade	41 (67)	1.9 (1.0–3.6)		
				Personal service in personal services	4 (10)	2.0 (0.4–9.2)		
				Personal service in professional services	4 (9)	3.5 (0.8–14.5)		
				Vehicle mechanics in repair services	5 (9)	2.5 (0.8–8.3)		
				Industrial mechanics in all industries	4 (1)	31.0 (3.0–315.1)		
				Carpenters in construction	10 (17)	1.5 (0.7–3.4)		
				Painters in all industries	4 (5)	2.3 (0.4–14.4)		
				Painters in construction	3 (4)	2.2 (0.3–14.3)		
				Other construction in construction	6 (10)	1.5 (0.4–5.6)		
				Precision metal workers in all industries	13 (33)	1.7 (0.8–3.7)		
				Precision metal workers in metal product manufacturing	3 (3)	4.6 (1.0–21.8)		
				Precision metal workers in public administration	5 (4)	9.7 (1.6–59.9)		
				Metal working machine operator in metal product manufacturing	3 (3)	3.3 (0.6–19.7)		
				Other machine operators in agriculture, forestry, and fisheries	6 (11)	1.6 (0.5–5.3)		
				Other machine operators in lumber and wood product manufacturing	4 (3)	4.4 (0.7–28.3)		
				Motor vehicle operators in public administration	4 (3)	5.4 (1.0–28.4)		
				Other transportation workers in transportation communication	8 (9)	1.7 (0.7–4.5)		
				Handlers, cleaners, and laborers in lumber and wood product manufacturing	8 (18)	1.6 (0.6–4.7)		

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
				OR (induction period)				
				Occupation/industry				
				Writers, entertainers, and athletes in entertainment and recreation	8 (8)	4.0 (1.0–16.1)		
				Administrative support in personal services	3 (4)	3.0 (1.1–7.9)		
				Food service in transportation and communication	3 (1)	3.8 (0.2–57.2)		
				Food service in retail trade	41 (67)	2.1 (1.1–4.0)		
				Personal service in personal services	4 (10)	2.2 (0.5–10.4)		
				Personal service in professional services	4 (9)	9.1 (1.9–44.8)		
				Vehicle mechanics in repair services	5 (9)	2.6 (0.8–8.8)		
				Industrial mechanics in all industries	4 (1)	31.0 (3.0–315.1)		
				Carpenters in construction	10 (17)	1.8 (0.7–4.8)		
				Painters in all industries	4 (5)	2.3 (0.4–14.4)		
				Painters in construction	3 (4)	2.2 (0.3–14.3)		
				Other construction in construction	6 (10)	1.7 (0.4–6.4)		
				Precision metal workers in all industries	13 (33)	1.7 (0.8–3.7)		
				Precision metal workers in metal product manufacturing	3 (3)	4.6 (1.0–21.8)		
				Precision metal workers in public administration	5 (4)	7.6 (1.1–54.0)		
				Metal working machine operator in metal product manufacturing	3 (3)	3.3 (0.6–19.7)		
				Other machine operators in agriculture, forestry, and fisheries	6 (11)	1.6 (0.5–5.4)		
				Other machine operators in lumber and wood product manufacturing	4 (3)	2.8 (0.3–24.0)		
				Motor vehicle operators in public administration	4 (3)	5.4 (1.0–28.4)		
				Handlers, cleaners, and laborers in lumber and wood product manufacturing	8 (9) 8 (18)	1.5 (0.6–4.0) 1.6 (0.6–4.7)		

Haguenoer et al. [78], France, 1983	283 men with nose ($n=14$), lips ($n=16$), oral cavity ($n=64$), pharynx ($n=114$) and larynx ($n=54$), and other and multiple site ($n=21$) cancer diagnosed in the 1st semester of 1983 in a regional cancer center in North of France	Two controls per case were chosen from patients without cancer in general hospitals in the same geographical area, matched by age, gender, ethnic group, area of residence, and smoking and alcohol drinking history	Types of occupation classified in 11 groups	*Oral cavity*		
				Mining	11 (11)	3.5 ($p<0.5$)
				Building industry	12 (14)	1.9 ($p>0.5$)
				Metal work and mechanics	13 (22)	1.2 ($p>0.5$)
				Agriculture	1 (7)	0.3 ($p>0.5$)
				Road transport	4 (10)	0.8 ($p>0.5$)
				Shipping and seamen	3 (9)	0.5 ($p>0.5$)
				Textile industry	2 (5)	0.7 ($p>0.5$)
				Woodwork	2 (3)	1.3 ($p>0.5$)
				Road works	5 (5)	2.2 ($p>0.5$)
				Service	11 (39)	0.5 ($p>0.5$)
				Others	1 (3)	0.7 ($p>0.5$)
				Pharynx		
				Mining	17 (28)	1.4 ($p>0.5$)
				Building industry	21 (23)	2.0 ($p<0.5$)
				Metal work and mechanics	16 (42)	0.7 ($p>0.5$)
				Agriculture	4 (15)	0.5 ($p>0.5$)
				Road transport	6 (15)	0.8 ($p>0.5$)
				Shipping and seamen	5 (10)	1.0 ($p>0.5$)
				Textile industry	12 (11)	2.4 ($p<0.5$)
				Woodwork	4 (1)	–
				Road works	5 (6)	1.8 ($p>0.5$)
				Service	20 (67)	0.5 ($p<0.5$)
				Others	5 (10)	1.0 ($p>0.5$)

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Merletti et al. [53], Italy, 1982–1984	86 men with oral cavity and pharynx cancer diagnosed among residents of Turin	Random sample stratified by gender and age from the files of residents of the city of Turin (1980–1984)	Job titles and economic activities were coded according to the International Standard Classification of Occupations of the International Labour Office and the International Standard Industrial Classification of the United Nations, respectively. For each occupational category and each industry, the subjects were classified as ever versus never employed. Duration was calculated for each period of employment. A latency analysis was also carried; then, occupational history after 1967 was ignored. A job-exposure matrix for 13 agents which are or may be related to respiratory cancer and three nonspecific exposures was applied to this database. Presented here are only the odds ratios (OR) with 95 % confidence intervals included	*Occupation* Service workers Working proprietors Cooks, waiters, and bartenders Service workers Production and related workers and transport equipment Chemical processers and related workers Tailors, dressmakers, and sewers Machinery fitters and assemblers and precision instrument makers (except electrical) Plumbers and pipe fitters *Activity branch* Railway equipment production Building industry Restaurant, bars, and hotels Social services Recreational and cultural private services	 15 (36) 3 (1) 3 (3) 3 (4) 69 (235) 4 (2) 3 (8) 18 (43) 6 (5) 3 (2) 29 (67) 6 (4) 10 (26) 3 (1)	 2.7 (1.0–4.6) 14.7 (1.0–206.5) 10.3 (1.3–81.2) 5.9 (1.0–35.4) 2.3 (1.1–5.0) 8.3 (1.3–55.0) 6.8 (1.4–38.7) 2.0 (1.0–4.0) 5.0 (1.8–21.5) 7.7 (1.0–63.2) 2.5 (1.3–4.5) 14.5 (2.8–75.7) 2.8 (1.1–6.7) 34.6 (2.3–524.0)	Odds ratios adjusted for age, education, area of birth, tobacco smoking, and alcohol drinking	Analysis considering probable or definitive exposure to asbestos, polycyclic aromatic hydrocarbons, chromium, nickel, arsenic, man-made mineral fibers, wood dust, leather dust, isopropyl alcohol, dimethyl sulfate, naphthalene, sulfuric acid, formaldehyde, dusts, gases, and solvents were conducted, but all RR had 95 % confidence intervals excluded

Vaughan and Davis [79], United States, 1983–1987	183 cases of oropharynx squamous cell carcinoma diagnosed in a single center	Controls were selected by random digit dialing matched to the cases by age and sex	Lifetime occupational histories were obtained, including a description of the duties involved in each job, as well as the associated industry. Jobs considered to entail significant exposure to wood dust included carpenters, forestry and logging workers, precision woodworkers (including patternmakers, cabinetmakers, and other furniture makers and finishers), and woodworking machine operators	Ever employed in wood-related occupations	14	0.6 (0.3–1.1)	RR adjusted for age, sex, cigarette smoking, and race	Reference category: never exposed
				Employed in wood-related occupations >15 years before diagnosis	12	0.5 (0.2–1.2)		
				Employment for 10 or more years taking place at least 15 years before the reference date	No information	1.5 (0.4–5.5)		

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Huebner et al. [83], United States, 1984–1985	1,114 incident cases of the oral cavity and oropharynx (762 men, 352 women) of ages 18–79 years	1,268 controls (837 men, 431 women) matched by gender, race, age, and study area	Employment history information was coded using four-digit job and industry codes (respectively, Standard Occupational Classification and Standard Industrial Classification). A list of 14 suspected high-risk jobs was elaborated; also a list of employment categories was examined according to specific anatomical sites. Ever/never employment or job was considered	*Suspected high-risk jobs*			RR adjusted for age, race, smoking, alcohol, and study location	Self-reported exposures to formaldehyde and to asbestos were also analyzed. But low OR were observed among men (formaldehyde 0.73, asbestos 0.82) and women (formaldehyde 0.36, asbestos 0.71)
				Men				
				Carpet installer	23 (4)	7.68 (2.37–24.9)		
				Semiconductor manufacturing	12 (10)	2.27 (0.83–6.19)		
				Resistor/transistor manufacturing	14 (10)	1.43 (0.56–3.65)		
				Brake repair work	41 (42)	1.15 (0.68–1.92)		
				Embalming fluid use/ manufacturing	16 (15)	1.09 (0.48–1.52)		
				Urea/phenol/resin manufacturing	6 (8)	1.02 (0.30–3.55)		
				Paint/varnish use/ manufacturing	125 (116)	0.99 (0.71–1.38)		
				Telegraph/telephone power work	24 (28)	0.79 (0.41–1.52)		
				TV/radio tube manufacturing	8 (11)	0.71 (0.25–2.03)		
				Other TV/radio parts manufacturing	7 (12)	0.60 (0.20–1.81)		
				Insulation manufacturing/ work	31 (44)	0.54 (0.31–0.97)		
				Women				
				Other TV/radio parts manufacturing	6 (7)	1.06 (0.29–3.90)		
				Resistor/transistor manufacturing	5 (6)	0.94 (0.23–3.82)		
				Paint/varnish use manufacturing	13 (17)	0.89 (0.37–2.14)		

Employment categories		
Tongue		
Males		
Boiler/furnace operator	6 (14)	2.32 (0.80–6.79)
Furniture/fixture industry worker	3 (26)	0.57 (0.16–2.04)
Iron/steel worker	6 (17)	1.23 (0.41–3.70)
Machinist	10 (31)	1.22 (0.51–2.93)
Painter	5 (18)	0.97 (0.33–2.84)
Petroleum industry worker	8 (11)	3.20 (1.15–8.90)
Primary metal industry worker	8 (35)	0.75 (0.30–1.89)
Transportation worker	23 (82)	0.92 (0.52–1.64)
Woodworking machine worker	1 (9)	0.34 (0.04–3.28)
Women		
Transportation equipment manufacturing worker	3 (27)	0.66 (0.19–2.34)
Mouth		
Males		
Boiler/furnace operator	8 (14)	1.67 (0.58–4.84)
Furniture/fixture industry worker	8 (26)	0.94 (0.37–2.40)
Iron/steel worker	6 (17)	1.08 (0.36–3.20)
Machinist	11 (31)	1.15 (0.51–2.59)
Painter	5 (18)	0.71 (0.22–2.34)

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
				Petroleum industry worker	1 (11)	0.41 (0.05–3.46)		
				Primary metal industry worker	13 (35)	1.03 (0.47–2.23)		
				Transportation worker	41 (82)	1.65 (1.04–2.61)		
				Woodworking machine worker	2 (9)	0.51 (0.09–2.96)		
				Women				
				Transportation equipment manufacturing worker	8 (27)	0.76 (0.29–1.98)		
				Pharynx				
				Males				
				Boiler/furnace operator	8 (14)	1.92 (0.63–5.83)		
				Furniture/fixture industry worker	14 (26)	2.17 (1.01–4.66)		
				Iron/steel worker	12 (17)	2.03 (0.83–5.13)		
				Machinist	15 (31)	1.93 (0.93–4.00)		
				Painter	12 (18)	2.03 (0.87–4.71)		
				Petroleum industry worker	7 (11)	2.31 (0.75–7.15)		
				Primary metal industry worker	22 (35)	2.22 (1.16–4.25)		
				Transportation worker	22 (82)	0.65 (0.36–1.18)		
				Woodworking machine worker	6 (9)	2.27 (0.69–7.44)		
				Women				
				Transportation equipment manufacturing worker	13 (27)	2.75 (1.13–6.66)		
Tisch et al. [126], Germany, 1988–1991	100 incident cases of oral cavity cancer	400 randomized controls	Ever/never employment as machine workers	Exposed or nonexposed as machine workers	22/34	3.4 (1.7–7.0)	Adjusted for tobacco and alcohol consumption	

Gustavsson et al. [54], Sweden, 1988–1990	Incident cases of cancers of the oral cavity ($n = 128$), pharynx ($n = 138$), esophagus ($n = 122$), and larynx ($n = 157$) of all Swedish men aged 40–79 years living in two regions of Sweden	641 controls were selected stratified by age and region as a random sample of the population base	Occupational history included all jobs held for more than 1 year over lifetime, recording the times of starting and stopping, job title, job tasks, and company for each job. An occupational hygienist examined the intensity and probability of the exposure to 17 specific occupational exposure factors	*Oral cavity*			Adjusted for geographical region, age, alcohol consumption, and tobacco smoking
				PAHs			
				Low	25	0.99 (0.57–1.73)	
				High	41	1.39 (0.86–2.25)	
				Asbestos			
				Low	17	0.64 (0.35–1.20)	
				High	16	0.67 (0.36–1.25)	
				Dust			
				Low	21	1.76 (0.98–3.16)	
				High	16	1.35 (0.70–2.60)	
				Wood dust	16	0.70 (0.38–1.29)	
				Quartz	20	0.85 (0.48–1.50)	
				Metal dust	19	0.76 (0.43–1.36)	
				Oil mist	15	0.69 (0.37–1.29)	
				Welding fumes	18	0.88 (0.48–1.60)	
				Formaldehyde	14	1.28 (0.64–2.54)	
				MMMF	6	0.51 (0.20–1.32)	
				Paper dust	6	0.63 (0.24–1.64)	
				Textile dust	4	0.80 (0.26–2.48)	
				Chromium	7	1.60 (0.63–4.06)	
				Phenoxy acids	7	1.61 (0.61–4.24)	
				Nickel	6	1.53 (0.57–4.16)	
				Acid mist	3	1.39 (0.34–5.58)	
				Leather dust	3	2.15 (0.54–8.67)	

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
				Pharynx				
				PAHs				
				Low	28	1.06 (0.61–1.82)		
				High	44	1.52 (0.94–2.45)		
				Asbestos				
				Low	24	1.01 (0.57–1.80)		
				High	22	1.08 (0.62–1.91)		
				Dust				
				Low	15	1.06 (0.55–2.05)		
				High	17	1.42 (0.74–2.72)		
				Wood dust	14	0.52 (0.27–0.99)		
				Quartz	27	1.29 (0.77–2.18)		
				Metal dust	31	1.40 (0.84–2.33)		
				Oil mist	19	0.78 (0.43–1.41)		
				Welding fumes	28	1.57 (0.91–2.71)		
				1–8 years		1.12 (0.53–2.35)		
				>8 years		2.26 (1.09–3.69)		
				Formaldehyde	13	1.01 (0.49–2.07)		
				MMMF	7	0.56 (0.23–1.38)		
				Paper dust	7	0.68 (0.27–1.69)		
				Textile dust	3	0.53 (0.14–1.93)		
				Chromium	3	0.66 (0.18–2.41)		
				Phenoxy acids	0	–		
				Nickel	2	0.45 (0.10–2.11)		
				Acid mist	4	1.21 (0.35–4.23)		
				Leather dust	5	2.83 (0.79–10.20)		

Schildt et al. [84], Sweden, 1980–1988	410 cases (276 men, 134 women) of squamous cell carcinoma of the oral cavity diagnosed and reported to Cancer Registry in four most northern counties in Sweden	410 controls matched by age, sex, and of the same county as cases	A questionnaire covered lifetime occupational history up to date of diagnosis and asked about exposure for some agents. All occupations were classified according to the Nordic Working Classification system	*OR*		
				Occupations (10 or more subjects)		
				Secretary and typist	4 (10)	0.4 (0.1–1.3)
				Miner and rock blaster	5 (11)	0.4 (0.1–1.4)
				Delivery boy	4 (9)	0.4 (0.1–1.5)
				Welder	7 (3)	2.3 (0.6–9.1)
				Wood and wood product workers	12 (3)	5.5 (1.2–25)
				Pulp industry worker	18 (6)	4.0 (1.3–12)
				Storemen	10 (5)	2.2 (0.6–7.4)
				Agents (10 or more subjects)		
				Organic solvents	69 (60)	1.2 (0.8–1.8)
				All pesticides	49 (43)	1.2 (0.7–1.8)
				Phenoxyacetic acids	20 (12)	1.7 (0.8–3.5)
				Herbicides	4 (6)	0.7 (0.1–2.4)
				DDT	8 (12)	0.6 (0.2–1.7)
				Mercurial seed dressing	6 (4)	1.5 (0.4–5.3)
				Impregnating agents	17 (16)	1.1 (0.5–2.3)
				Diesel oil	8 (8)	1.0 (0.3–2.7)
				Oil	7 (11)	0.6 (0.2–1.7)
				Chlorine	4 (6)	0.6 (0.1–2.6)
				Producer gas	6 (6)	1.0 (0.3–3.2)
				Sulfur compounds	7 (6)	1.2 (0.3–3.5)
				Plastics	7 (7)	1.0 (0.3–2.9)

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Marchand et al. [100], France, 1989–1991	206 incident cases of hypopharynx cancer in men recruited from 15 hospitals in six French cities	305 men hospital-based controls with other (non-respiratory) cancers	Subjects' past occupational exposure to asbestos and to four types of MMVF (mineral wool, refractory ceramic fibers, glass filaments, and microfibers) was evaluated through a job-exposure matrix	Asbestos			RR adjusted for age, smoking, and alcohol consumption. In the analysis of joint effect of exposure to asbestos and smoking, RR adjusted for age and alcohol consumption	
				Never exposed	40 (110)	1.0		
				Ever exposed	161 (185)	1.80 (1.08–2.99)		
				Cumulative level				
				Low	52 (67)	1.92 (1.03–3.57)		
				Intermediate	52 (67)	1.40 (0.74–2.63)		
				High	57 (51)	2.14 (1.14–4.01)		
				Asbestos				
				None/low and smoking <30 pack-years		1.0		
				None/low and smoking >30 pack-years		3.95 (2.16–7.24)		
				Intermediate/high and smoking <30 pack-years		1.19 (0.61–2.32)		
				Intermediate/high and smoking >30 pack-years		6.22 (3.41–11.36)		
				Mineral wools				
				Ever exposed	99 (99)	1.55 (0.99–2.41)		
				Ceramic fibers				
				Ever exposed	7 (9)	0.78 (0.26–2.38)		
				Glass filaments				
				Ever exposed	8 (11)	0.91 (0.30–2.76)		
				Microfibers				
				Ever exposed	7 (9)	0.78 (0.26–2.38)		
Garrote et al. [50], Cuba, 1996–1999	200 incident cases of oral cavity and oropharynx cancer (143 men, 57 women)	200 hospital controls (136 men, 64 women) matched by age and gender with cases	Four major occupational groups	White collar	51 (85)	1.0	Adjusted for gender, age, area of residence, education, smoking, and drinking habits	
				Blue collar	68 (57)	1.73 (0.97–3.09)		
				Farmers	37 (19)	2.22 (0.97–5.10)		
				Housewives	35 (30)	1.94 (0.87–4.33)		

Coble et al. [127], Puerto Rico, 1992–1995	327 incident cases (286 men, 41 women) of oral cavity and pharynx cancer among Puerto Rican residents aged 21–79 years	499 population-based controls (413 men, 86 controls) matched on age, gender, and area of residence with cases	Occupation classified according to industry categories and occupation categories. A job-exposure matrix was used to examine the potential exposure to dusts, metals, and solvents	*Oral cavity* Agriculture industry Sugarcane industry Sugarcane farmers *Pharynx* Agriculture industry Sugarcane industry Sugarcane farmers *Oral cavity and pharynx* Dusts None Low Medium High Metals None Low Medium High Solvents None Low Medium High	 36 (64) 16 (13) 14 (10) 24 (64) 5 (13) 3 (10) 119 (197) 25 (51) 60 (70) 82 (94) 234 (350) 20 (23) 24 (32) 8 (7) 205 (321) 28 (33) 41 (54) 12 (4)	 1.4 (0.8–2.6) 3.4 (1.2–9.4) 4.4 (1.4–13.6) 1.6 (0.8–3.2) 1.0 (0.3–3.8) 0.8 (0.2–4.0) 1.0 0.5 (0.3–1.0) 1.3 (0.7–2.1) 1.1 (0.7–1.7) 1.0 1.1 (0.5–2.6) 1.2 (0.6–2.5) 2.7 (0.7–10.6) 1.0 1.0 (0.5–2.1) 1.6 (0.9–2.9) 3.2 (0.8–12.6)	Adjusted for age, smoking, and alcohol consumption. P-value for trend: dusts 0.5, metals 0.2, and solvents 0.03	
Menvielle et al. [51], France, 1989–1991	504 incident cases of hypopharynx ($n=201$) and larynx cancer ($n=303$) in men from 15 French hospitals in six cities	242 hospital-based controls, men with non-respiratory cancers	Occupation classified in ever manual or never manual	*Hypopharynx* Never manual Ever manual Adjusted Age + alcohol and tobacco + occupational exposure	 27 174 	 1.0 3.50 (2.14–5.73) 2.65 (1.51–4.66) 1.84 (0.97–3.48)	RR adjusted by alcohol intake, smoking, and occupational exposures: asbestos, coal dust (ever/never), and formaldehyde (maximal probability of exposure)	
Andreotti et al. [80], Brazil, 1999–2001	325 incident cases of oral cavity and pharynx (274 men, 51 women) from seven hospitals in the city of Sao Paulo	362 hospital-based controls without cancer, matched by age and gender	Occupation classified according to industry categories and occupation categories and considering periods of exposure in each category (>10 years, >10 years, and >20 years of latency)	*Working in vehicle maintenance shop* Ever exposed >10 years >10 years and >20 latency years *Vehicle repair worker* Ever exposed >10 years >10 years and >20 latency years	 26 (12) 21 (3) 19 (3) 14 (7) 13 (1) 11 (1)	 2.45 (1.14–5.27) 7.90 (2.03–30.72) 7.38 (1.88–28.98) 2.10 (0.78–5.68) 26.21 (2.34–294.06) 24.46 (2.10–284.60)	Adjusted for age, smoking, and alcohol consumption	Analysis conducted only with men workers. We reported only the occupation or industry with RR statistically significant

(continued)

Table 4.1 (continued)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Vlajinac et al. [55], Serbia and Montenegro, 1998–2000	100 incident cases (89 men, 11 women) of oropharynx cancer (including base of the tongue, neoplasm of the palate, neoplasm of the tonsils) recruited in a single center	100 controls recruited among patients treated in the same period as cases of some nonmalignant diseases of head and neck matched with cases according to age, sex, and place of residence	Occupational exposure was assessed by asking the participants whether they have ever been exposed to the items listed	*OR*			OR adjusted for education, BMI, smoking, alcohol consumption, and family history of oropharynx cancer	
				High temperature	49 (52)	0.51 (0.12–2.09)		
				Low temperature	56 (56)	0.82 (0.42–1.58)		
				High humidity	52 (45)	1.04 (0.53–2.05)		
				Dry air	57 (73)	0.30 (0.14–0.64)		
				Coal dust	16 (14)	0.88 (0.36–2.14)		
				Cement dust	16 (12)	1.58 (0.58–4.33)		
				Aniline dyes	11 (7)	1.41 (0.44–4.44)		
				Wood dust	22 (12)	2.33 (0.96–5.66)		
				Metal dust	23 (30)	0.57 (0.27–1.18)		
				Chemical dust or smoke	24 (30)	0.71 (0.34–1.48)		
				Nickel and chromium	6 (5)	1.33 (0.30–5.90)		
				Mortar	16 (11)	1.68 (0.57–4.97)		
				Formaldehyde	8 (2)	4.48 (0.63–31.63)		
Jayaprakash et al. [81], United States, 1982–1988	1,522 men of upper aerodigestive and respiratory cancers (241 oral and pharynx)	1,522 controls matched on age and smoking, selected from hospital visitors with a cancer suspicion and those who were screened as outpatients in the same hospital of cases, but not diagnosed with any malignant or benign tumors	Wood dust exposure was assessed through several questions about prior exposure at work. If exposed, they were queried about the frequency and duration exposure and also the year of first exposure	*Oral and pharynx cancers*			RR adjusted for age, pack-years of smoking, body mass index, smoking status, education, and alcoholic drinks per week and year of enrolment	
				Wood dust exposure				
				Never	188 (1.153)	1.0		
				Occasionally	32 (262)	0.72 (0.48–1.08)		
				Regularly	21 (107)	1.14 (0.68–1.92)		
				Squamous cell carcinoma of oral cavity and pharynx				
				Wood dust exposure				
				Never	169 (1.153)	1.0		
				Occasionally	28 (262)	0.68 (0.44–1.06)		
				Regularly	21 (107)	1.27 (0.76–2.14)		

Table 4.2 Cohort studies on occupation and cancer of the oral cavity and pharynx

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Moulin et al. [98], France	1,374 men workers of a single man-made mineral fibers present at the factory (1975–1984) and who had been working for at least one full year. No clear definition of period of beginning of exposure, but the first production lines started in 1940. Cancer incidence follow-up (1975–1984)	Environmental surveys were performed in 1981 in order to measure the pollution by fibers	Oral cavity and pharynx		*SIR*			Both SIR estimates were not statistically significant
				Oral cavity				
				9		3.01		
				Pharynx				
				5		1.40		
Blair et al. [56], United States	26,561 workers first employed in 10 formaldehyde-producing or formaldehyde-using plants before 1996. Mortality follow-up (1980)	A job-exposure matrix was prepared for industrial hygienists considering each job-work area-calendar year combination. Measures of exposure to formaldehyde used in the analysis included level or intensity, duration, average, cumulative or peak exposure, presence of particulates, and measures that excluded recent exposures from the exposure index		Several tumors	*SMR* Oral cavity and pharynx			Black women were excluded from analysis because of small numbers ($n=26$). SMR based on US national rates. NS = nonstatistically significant
					White men			
				18	Exposed	96 (57–152)		
				3	Nonexposed	54 (11–157)		
					White women			
				0	Exposed	–		
				0	Nonexposed	–		
					Black men			
				3	Exposed	–		
				3	Nonexposed	–		
					Intensity of exposure (white men)			
				2	0	89 (NS)		
				1	>0–<0.1	30 (NS)		
				4	0.1–0.4	59 (NS)		
				14	0.5–1.9	130 (NS)		
				0	>2.0	–		
					Lip			
				0	Cumulative formaldehyde exposure			

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
				1	0 ppm-year	–		
				0	<0.5 ppm-year	477 (NS)		
				1	0.51–5.5 ppm-year	–		
					>5.5 ppm-year	764 (NS)		
					Tongue			
				0	Cumulative formaldehyde exposure			
				0	0 ppm-year	–		
				2	<0.5 ppm-year	–		
				0	0.51–5.5 ppm-year	96 (NS)		
					>5.5 ppm-year	–		
					Gum, floor, and other mouth sites			
					Cumulative formaldehyde exposure			
				0	0 ppm-year	–		
				1	<0.5 ppm-year	66 (NS)		
				0	0.51–5.5 ppm-year	–		
				1	>5.5 ppm-year	88 (NS)		
					Oropharynx			
					Cumulative formaldehyde exposure			
				0	0 ppm-year	–		
				4	<0.5 ppm-year	443 ($p < 0.05$)		
				1	0.51–5.5 ppm-year	95 (NS)		
				0	>5.5 ppm-year	–		
					Hypopharynx			
					Cumulative formaldehyde exposure			
				1	0 ppm-year	594 (NS)		
				1	<0.5 ppm-year	172 (NS)		
				0	0.51–5.5 ppm-year	–		
				0	>5.5 ppm-year	–		
					Other pharynx			
					Cumulative formaldehyde exposure			
				0	0 ppm-year	–		
				1	<0.5 ppm-year	73 (NS)		
				0	0.51–5.5 ppm-year	–		
				0	>5.5 ppm-year	–		

Stayner et al. [62], United States	11,030 workers from three garment manufactures who had been working for at least 3 months (1955–1977). Mortality follow-up until end of 1982	Workers of the cohort were compared with the US population. Exposure assessment considered duration of employment, latency, and first-year exposure	All tumors		*SMR*		Workers who were employed only in clerical or administrative positions were excluded from the analysis. We reported here only risk estimates for oral cavity and pharynx tumors. NS = nonstatistically significant
					Oral cavity		
				4	White men	343 (118–786)	
				0	White women	–	
				4	Nonwhite men	485 ($p<0.01$)	
					Nonwhite women	–	
				0	Plant 1	–	
				2	Plant 2	306 (NS)	
				2	Plant 3	886 ($p<0.01$)	
				0	Latency period (3 months–9 years)	–	
					Duration of exposure		
				0	3 months–3 years	–	
				0	4–9 years	–	
				0	10 + years	–	
				0	Overall latency period (10–19 years)	–	
					Duration of exposure		
				0	3 months–3 years	–	
				0	4–9 years	–	
				2	10 + years	822 ($p<0.01$)	
				2	Overall latency period (20 + years)	357 (NS)	
					Duration of exposure		
				0	3 months–3 years	–	
				1	4–9 years	315 (NS)	
				1	10 + years	654 (NS)	
				2	Overall year of first exposure	705 ($p<0.01$)	
				0	1955–1962		
				0	1963–1970		
				4	1971–1978	440 ($p<0.01$)	
					Pharynx		
				2	White men	–	
				1	White women	359 (NS)	
				1	Nonwhite men	239 (NS)	
				0	Nonwhite women	86 (NS)	
				0	Plant 1	–	
				1	Plant 2	100 (NS)	
				0	Plant 3	–	
				0	Latency period (3 months–9 years)	–	
					Duration of exposure		
				0	3 months–3 years	–	
				0	4–9 years	–	
				0	10 + years	–	
				0	Overall latency period (10–19 years)	–	
					Duration of exposure		
				1	3 months–3 years	368 (NS)	
				1	4–9 years	490 (NS)	
				0	10 + years	–	
				0	Overall latency period (20 + years)	233 (NS)	
					Duration of exposure		
				0	3 months–3 years	–	
				0	4–9 years	–	
				0	10 + years	–	
					Overall year of first exposure	–	
				1	1955–1962	76 (NS)	
				1	1963–1970	273 (NS)	
				0	1971–1978	–	

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Lynge and Thygesen [128], Denmark	Cohort included people aged 20–64 years at the census on 9 November 1970. Ten-year follow-up for cancer incidence (1970–1980)	Industry and occupation were recorded only for people economically active at the time of census, through the International Standard Industrial Classification and a special Danish code, respectively	Pharynx cancer		*RR*			Here we reported only RR with 95 % confidence interval excluded 1
					Occupation/industry			
				12	Waiter	12.08 (6.26–21.17)		
				8	Bricklayer	2.69 (1.16–5.31)		
				6	Painter	3.30 (1.21–7.18)		
				5	Dock laborer	5.23 (1.69–12.16)		
				4	Self-employed/groceries	3.89 (1.06–9.94)		
				3	Chief engineer at sea	5.00 (1.03–14.62)		
				3	Cashier	8.94 (1.82–25.79)		
				2	Other banking staff	9.90 (1.21–36.10)		
					Selected occupational groups			
				1	Skilled workers and painter in metal industry	1.95 (0.05–10.92)		
				6	Skilled workers and painter in paint workshop	3.30 (1.21–7.18)		
				0	Skilled workers and painter/other industries	–		
				3	Self-employed and painter in paint workshop	1.73 (0.34–5.07)		
				10	All painters	2.27 (1.09–4.18)		
Gardner et al. [57], United Kingdom	14,017 men employed in six of formaldehyde-producing or formaldehyde-using plants (7,660 first employed before 1965, 6,357 first employed after 1964); mortality follow-up until the end of 1989	Exposure to formaldehyde was on the basis of recorded titles of jobs undertaken by each of the men before 1982. Exposures have been qualitatively classified after detailed discussions on past working conditions	All tumors		*SMR*			Here we reported only the risks for oral cavity and pharynx cancer
					Employed before 1965			
				3	Oral cavity	137 (28–401)		
				7	Pharynx	147 (59–303		
					Employed after 1964			
				1	Oral cavity	190 (5–10.59)		
				0	Pharynx	–		
Johnson [94], United States	Cohort with 10,841 members of meatcutter union in Baltimore (6,906 men, 3,935 women) employed for at least 1 year; mortality follow-up (1949–1989)	Subjects who ever worked in the meat department of supermarkets or grocery stores	Oral cavity and pharynx		*SMR*			
					Meat department			
					Men	1.8 (1.0–3.0)		
					Women	1.5 (0.3–4.4)		
					Other departments			
					Men	1.7 (0.8–3.2)		
					Women	0.5 (0.0–2.6)		

Pukkala et al. [86], Finland	Cohort of persons born in Finland during 1906–1945. Follow-up (1971–1985) detected 3,178 cases (2,369 in men, 809 in women) of cancer of the lip, tongue, oral cavity, and pharynx	Occupations were coded at Statistics Finland using a modified Nordic Classification of Occupations	Oral cavity (lip, tongue) and pharynx		*SIR*		SIR adjusted for social class	We reported here only SIR with 95 % confidence interval excluded 1
					Tongue (men only)			
				3	Journalists	6.84 (1.41–20.0)		
					Oral cavity (men/women)			
				16	Services	1.82 (1.04–2.96)		
				48	Economically inactive	1.62 (1.20–2.15)		
					Oral cavity (men)			
				5	Civilian guards	4.13 (1.34–9.63)		
				10	Electrical workers	2.29 (1.10–4.21)		
					Oral cavity (females)			
				2	Railway traffic supervisors	13.64 (1.65–49.3)		
				3	Vocational teachers	8.28 (1.71–24.2)		
				6	Waitresses	3.01 (1.11–6.56)		
					Pharynx (men/women)			
				97	Economically inactive	7.81 (1.61–22.8)		
					Pharynx (men)			
				3	Electronics and telefitters	5.18 (1.07–15.1)		
				3	Administrative managers	5.18 (1.07–15.1)		
				8	Artistic/literary workers	3.20 (1.38–6.31)		
					Pharynx (women)			
				8	Cutting/sewing workers	2.34 (1.01–4.61)		
				15	Farmers	1.80 (1.01–2.98)		
Andjelkovich et al. [58], United States	3,929 men with potential exposure to formaldehyde for at least 6 months between 1960 and 1987 at an automotive iron foundry; mortality follow-up until end of 1989. An internal referent population of 2,032 men who had worked in jobs with no exposure to formaldehyde during the same period was selected for comparison	Work history of each subject, including all jobs, department number, and job title, was examined by an industrial hygienist as associated with high, medium, and low or no formaldehyde and silica exposure	All malignant tumors		*SMR*			We reported only risks for oral cavity and pharynx cancer. Reference group for RR estimates consists of white nonsmokers with nonexposure to formaldehyde and cumulative silica exposure in first quartile
					Oral cavity and pharynx			
				6	Exposed	131(48–286)		
				5	Smokers	191 (NS)		
				0	Nonsmokers	–		
				5	Unexposed	169 (54–395)		
				1	Smoker	71 (NS)		
				2	Nonsmokers	392 (NS)		
					RR			
					Formaldehyde			
					Exposed	0.59 (0.14–2.93)		
					Quartile 3 + Quartile 4	1.16 (0.20–6.51)		
					Nonwhite	4.41 (1.004–22.7)		
					Ever smoking	1.00 (0.23–6.84)		
					Silica			
					Quartile 2	0.43 (0.02–4.54)		
					Quartile 3	0.48 (0.06–4.00)		
					Quartile 4	0.37 (0.06–2.91)		
Coggon and Wield [97], England and Wales	Cohort of men, 4,018 butchers and 2,062 cooks, identified from 1961 Census; mortality follow-up until the end of 1992 (79.9 % of the cohort)		Oral cavity and pharynx		*SMR*			
					Butchers			
				1	Oral cavity	0.55 (0.01–3.08)		
				2	Pharynx	0.53 (0.06–1.91)		
					Cooks			
				4	Oral cavity	5.57 (1.52–14.26)		
				4	Pharynx	2.66 (0.73–6.81)		

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Boffetta et al. [99], Denmark, Finland, Norway, Sweden	6,296 workers employed >1 year in 9 factories (3,685 rock-slag wool; 2,611 glass wool) (1933–1961); follow-up (1995) (94.2 % of the cohort)		Oral cavity and pharynx		*SIR*			
				38	Total cohort	1.65 (1.17–2.26)		
				27	Rock-slag wool	1.84 (1.22–2.68)		
				11	Glass wool	1.31 (0.65–2.34)		
		Medium and high exposure to wood dust; employment duration: <10 years, 10–19 years, > and 20 years; formaldehyde exposure (no/possible)	Oral cavity or pharynx		*SIR*			
					Men			
				12	Oral cavity	1.22 (0.63–2.13)		
				9	Pharynx	1.82 (0.83–3.46)		
					Medium exposure			
				5	Oral cavity	3.66 (1.19–8.55)		
				3	Pharynx	4.02 (0.83–11.75)		
					High exposure			
				6	Oral cavity	0.76 (0.28–1.65)		
				6	Pharynx	1.51 (0.58–3.29)		
					<10 years			
				9	Oral cavity	1.50 (0.68–2.84)		
				7	Pharynx	2.18 (0.88–4.49)		
					10–19 years			
				3	Oral cavity	1.36 (0.28–3.98)		
				2	Pharynx	2.12 (0.26–7.66)		
					>20 years			
				0	Oral cavity	0.00		
				0	Pharynx	0.00		
					Women			
				4	Oral cavity	1.84 (0.50–4.71)		
				0	Pharynx	0.00		
					Medium exposure			
				2	Oral cavity	2.47 (0.30–8.91)		
				0	Pharynx	0.00		
					High exposure			
				2	Oral cavity	1.61 (0.19–5.81)		
				0	Pharynx	0.00		
					<10 years			
				1	Oral cavity	0.75 (0.02–4.20)		
				–	Pharynx	–		
					10–19 years			
				0	Oral cavity	0.00		
				–	Pharynx	–		
					>20 years			
				3	Oral cavity	8.10 (1.67–23.68)		
				–	Pharynx	–		
					Formaldehyde exposure (men and women)			
					No			
					Oral cavity	1.58 (0.43–4.05)		
					Pharynx	3.57 (0.97–9.14)		
					Possible			
					Oral cavity	1.25 (0.62–2.23)		
					Pharynx	1.17 (0.38–2.73)		

Boffetta et al. [95], Sweden	25,049 men butchers or meat workers from 1960 to 1970; follow-up for incidence (1971–1989)	Three categories: butchers in the meat industry, butchers employed in other industries, and non-butchers in meat industry	Oral cavity and pharynx		*SIR*		Relative risk adjusted for age, calendar period, geographical region, and urban setting	RR reference category: other workers, excluding other animal-related jobs
				73	Butcher or meat workers	1.1 (0.8–1.3)		
				14	Butcher in meat industry	1.5 (0.8–2.5)		
					RR			
				14	Butchers in meat industry	1.6 (1.0–2.7)		
				2	Butcher in other industries	1.3 (0.3–5.1)		
				5	Non-butchers in meat industry	0.7 (0.3–1.6)		
Boffetta et al. [93], Sweden	Exposed men (7,400,000 person-years) and women (240,000) to diesel engine emissions according to 1960 Census occupation and industry of employment of Swedish population; mortality follow-up (1971–1989)	Job-exposure matrix elaborated according to jobs and industry titles of cohort members (men and women with available occupational data from Census of 1960 and 1970) considering probability and intensity of exposure to diesel engine emissions	Oral cavity and pharynx		*SIR*		Relative risk adjusted for age, calendar period, geographical region, and urban/rural residence	RR reference category: unexposed to diesel engine emissions
				1,733	Men	1.05 (1.00–1.10)		
				31	Women	1.64 (1.11–2.33)		
					RR			
					Men			
					Probability			
				633	Low	1.2 (1.11–1.26)		
				559	Medium	1.11 (0.99–1.18)		
				439	High	1.1 (0.99–1.21)		
					Intensity			
				1,150	Low	1.2 (1.11–1.26)		
				280	Medium	1.2 (0.95–1.21)		
				201	High	0.98 (0.85–1.13)		
					Women			
					Probability			
				18	Low	1.4 (0.91–2.30)		
				4	Medium	1.2 (0.46–3.31)		
				6	High	1.7 (0.75–3.74)		
					Intensity			
				22	Low	1.4 (0.77–2.84)		
				6	Medium-high	1.7 (0.77–3.84)		

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Marsh et al. [59], United States	7,328 workers (6,859 men, 469 women) employed at a plastic-producing plant (1941–1984); mortality follow-up until 1998	Exposure estimation was based on an examination of the available sampling data and job descriptions and verbal descriptions of jobs and tasks	Oral cavity and pharynx		*SMR*			
					Cancer			
				31	Oral cavity + pharynx	1.80 (1.22–2.55)		
				1	Lip	3.23 (0.08–18.0)		
				3	Tongue	0.76 (0.16–2.22)		
				3	Gum and other mouth sites	1.20 (0.25–3.51)		
				2	Floor of the mouth	2.07 (0.25–7.48)		
				22	Pharynx (including nasopharynx)	2.63 (1.65–3.98)		
				5	Oropharynx	2.17 (0.71–5.07)		
				3	Hypopharynx	2.25 (0.46–6.58)		
				7	Pharynx, unspecified	2.11 (0.85–4.35)		
					All pharyngeal cancers (including nasopharyngeal)			
				12	Short term (<1 year)	2.35(1.22–4.11)		
				10	Long term (1 + years)	2.10 (1.01–3.86)		
					Year of hire			
				1	1941–1946	0.46 (0.01–2.56)		
				18	1947–1956	3.24 (1.92–5.12)		
				3	1957+	1.41 (0.29–4.12)		
					DOE (year) (all workers)			
				12	<1	2.34 (1.21–4.09)		
				5	1–9	1.89 (0.61–4.42		
				5	10+	2.36 (0.76–5.50)		
					TSFE (year)			
				4	<20	1.41 (0.38–3.61)		
				7	20–29	2.32 (0.93–4.78)		
				11	30+	2.75 (1.37–4.92)		
					Formaldehyde exposure			

				2	Unexposed	1.24 (0.15–4.49)
				20	Exposed	2.42 (1.48–3.74)
					Duration of exposure	
				11	>0–<1	2.35 (1.17–4.21)
				5	1–9	1.81 (0.49–4.63)
				6	10+	3.65 (1.18–8.52)
					Cumulative exposure	
				6	>0–<0.004	3.31 (1.22–7.21)
				7	0.004–0.129	2.06 (0.83–4.24)
				7	0.22+	2.30 (0.92–4.73)
					AIE to formaldehyde (ppm)	
				6	>0–<0.03	2.02 (0.74–4.40)
				7	0.03–0.159	3.82 (1.54–7.88)
				7	0.16+	2.03 (0.82–4.19)
					Formaldehyde >0.2 ppm	
				8	Unexposed	1.72 (0.74–3.39)
				14	Exposed	2.68 (1.46–4.49)
					Duration (year)	
				6	>0–<1	2.19 (0.80–4.77)
				3	1–9	1.68 (0.34–4.90)
				5	10+	7.35 (2.39–17.16)
					Formaldehyde >0.7 ppm	
				16	Unexposed	2.12 (1.21–3.45)
				6	Exposed	2.55 (0.94–5.56)
					Duration (year)	
				4	>0–<1	2.58 (0.70–6.61)
				2	1+	2.50 (0.30–9.03)
Brown et al. [87], Sweden	Cohort of individuals identified in Census of 1960 and 1970 in Sweden. Participants were employed in painting trades and paint manufacturing cohorts: men painters (42,433), men lacquerers (12,331), men artists (6,662), men employed in paint and varnish plants (5,741), women lacquerers (974), women glazers (882), women artists (2,136), and alive and free of cancer in 1971. Follow-up (1971–1989) for cancer incidence	The jobs of individuals at either Census (1960, 1970) were classified according to Swedish Occupational Classification	Oral cavity		*SIR*	
					Men	
				122	Painters	1.0 (0.8–1.1)
				30	Any lacquerers	1.0 (0.7–1.5)
				22	Metal lacquerers	0.9 (0.6–1.4)
				10	Wood lacquerers	2.1 (1.0–3.9)
				29	Artists	1.5 (1.0–2.1)
				13	Paint/varnish workers	0.8 (0.4–1.3)
					Women	
				4	Lacquerers	3.8 (1.0–9.7)
				4	Glazers	4.6 (1.2–11.8)
				2	Artists	0.9 (0.1–3.2)

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Coggon et al. [60], United Kingdom	14,014 men employed in six of formaldehyde-producing or formaldehyde-using plants; each individual was followed starting at the latest of 1 January 1941; mortality follow-up until the end of 2000	Exposure to formaldehyde was on the basis of recorded titles of jobs undertaken by each of worker occupational history. A separate job-exposure matrix was constructed for each factory. Exposure to formaldehyde was classified as follows: background (<0.1 ppm), low (0.1–0.5 ppm), moderate (0.6–2.0 ppm), high (>2.0 ppm), and unknown	All tumors	Total cohort (1941–2000)	*SMR*			This study is an update of the cohort of Gardner et al. [57]. See above in this table. Here we reported only the risks for oral cavity and pharynx cancer
				4	Tongue	0.84 (0.23–2.14)		
				6	Oral cavity	1.28 (0.47–2.78)		
				15	Pharynx	1.55 (0.87–2.56)		
					Men with high exposure (1941–2000)			
				3	Tongue	1.91 (0.39–5.58)		
				2	Oral cavity	1.32 (0.16–4.75)		
				6	Pharynx	1.91 (0.70–4.17)		
Pinkerton et al. [63], United States	11,039 workers (2,015 men, 9,024 women) exposed to formaldehyde in three garment manufactures who had been working for at least 3 months (1955–1977). Mortality follow-up until the end of 1998	Workers of the cohort were compared with the US population. Exposure assessment considered duration of employment, latency, and first-year exposure	All tumors		*SMR*			This study is an update of the cohort of Stayner et al. [129. See above in this table. Here we reported only the risks for oral cavity and pharynx cancer
					Original study period (1955–1982)			
				6	Oral cavity + pharynx	1.58 (0.58–3.45)		
				4	Oral cavity	3.53 (0.96–9.02)		
				2	Pharynx	1.15 (0.14–4.15)		
					Updated period (1983–1998)			
				2	Oral cavity + pharynx	0.31 (0.04–1.14)		
				0	Oral cavity	–		
				1	Pharynx	0.34 (0.01–1.87)		
					Total study period (1955–1998)			
				8	Oral cavity + pharynx	0.79 (0.34–1.55)		
				4	Oral cavity	1.33 (0.36–3.41)		
				3	Pharynx	0.64 (0.13–1.86)		

Hauptmann et al. [61], United States	Cohort of 25,619 workers (22,493 men, 3,126 women) employed in 10 US formaldehyde-producing or formaldehyde-using plants prior 1966; mortality from solid cancer follow-up until the end of 1994	Exposure to formaldehyde (nonexposed and exposed) was estimated from job titles, tasks, visits to the plants, discussion with workers and managers, by industrial hygienists, and defining average intensity, peak of exposure, cumulative exposure, and duration of exposure	Oral cavity		*SMR*		RR adjusted for calendar year, age, gender, race (black/white), and pay category (salary/wage)	This study is an update of the cohort of Blair et al. [56]. See above in this table. (*) 95 % confidence interval does not include 1. (NS) 95 % confidence interval include 1
				13	Nonexposed	0.99 (0.58–1.71)		
					Exposed	1.01 (0.77–1.34)		
					RR			
					Intensity (ppm)			
					0	2.42 (*)		
					>0–<0.5	1.0		
					0.5–<1.0	2.41 (*)		
					>1.0	1.89 (NS)		
					Peak (ppm)			
					0	2.08 (NS)		
					>0–<2.0	1.0		
					2.0–<4.0	1.07 (NS)		
					>4.0	1.83 (NS)		
					Cumulative (ppm-year)			
					0	1.98 (NS)		
					>0–<1.5	1.0		
					1.5–<5.5	1.59 (NS)		
					>5.5	1.74 (NS)		
					Duration (years)			
					0	1.87 (NS)		
					>0–<5	1.0		
					5–<15	1.74 (NS)		
					>15	0.95 (NS)		
Ji and Hemminki [89], Sweden	Swedish population economically active (men, 1960 Census, 1,644,958; women, 1970 Census, 1,154,091); follow-up of incidence of upper aerodigestive tract cancer until the end of 2000	Occupation was coded according to national adaptations of the Nordic Occupational Standard Classification of Occupation. We defined 53 occupational groups	Tongue, oral cavity, and pharynx		*SIR*			We reported here only occupations with SIR statistically significant
					Men (1960 Census)			
					Tongue cancer			
				7	Dentists	2.88 (1.14–5.41)		
				90	Sale	1.36 (1.09–1.65)		
				36	Shop	1.44 (1.01–1.94)		
				5	Beverage	5.95 (1.88–12.31)		
				13	Cooks	4.83 (2.56–7.82)		
				8	Waiters	5.41 (2.31–9.80)		
				9	Hairdressers	2.41 (1.09–4.25)		
					Oral cancer			
				129	Sale	1.27 (1.06–1.50)		
				43	Painter	1.40 (1.01–1.85)		
				27	Printer	1.52 (1.00–2.15)		
				9	Cooks	2.27 (1.03–4.00)		

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
					Pharynx cancer			
				173	Technical	0.85 (0.73–0.98)		
				26	Artistic	1.87 (1.22–2.66)		
				160	Sale	1.19 (1.02–1.39)		
				80	Shop	1.52 (1.20–1.97)		
				16	Seamen	1.85 (1.06–2.87)		
				38	Printer	1.53 (1.08–2.06)		
				24	Launderers	1.83 (1.17–2.64)		
					Women (1970 census)			
					Pharynx cancer			
				8	Artistic	3.83 (1.63–6.94)		
				14	Mechanics	2.27 (1.24–3.62)		
				9	Hairdressers	2.49 (1.13–4.39)		
Purdue et al. [101], Sweden	Cohort of 307,799 Swedish men workers in Swedish construction industry; follow-up (1971–2001)	Exposure to diesel exhaust, asbestos, organic solvents, metal dust, asphalt, wood dust, stone dust, mineral wool, and cement dust were assessed through a semiquantitative job-exposure matrix	Oral cavity or pharynx		*RR*		Adjusted for age, smoking status, and snuff use	Included only occupational exposures with RR equal or higher than 1.5 in some level of exposure
					Oral cavity			
					Asbestos			
				161	Never	1.0		
				10	Ever	1.3 (0.7–2.6)		
				9	Moderate	1.7 (0.9–3.3)		
				1	High	0.5 (0.1–5.2)		
					Pharynx			
					Cement dust			
				92	Never	1.0		
				20	Ever	1.9 (1.2–3.1)		
				16	Moderate	1.9 (1.1–3.2)		
				4	High	1.9 (0.7–5.0)		
					Asphalt			
				1.0	Never	1.0		
				1.8	Ever	1.8 (0.7–4.9)		
Krstev et al. [85], United States	Cohort of all workers employed at the US Coast Guard shipyard workers (4,413 men; 289 women) (1950–1964); mortality follow-up until the end of 2001 (completed for 93.3 % of cohort)	Occupation groups. An exposure inventory identifying agents, such as specific metals, solvents, acids, asbestos, and others in order to classify workers as exposed or nonexposed in shipyard	Oral cavity, pharynx, and nasopharynx	18	*SMR*		Adjusted for age, sex, and race	We reported here only occupational groups with SMR >1.5 SMR was observed for a group of tumors including oral cavity, pharynx, and nasopharynx taken together. RR reference category: no occupational exposure
					Men	0.89 (0.53–1.40)		
				8	≤10 years job	0.64 (0.28–1.27)		
				10	>10 years job	1.28 (0.61–2.35)		
				18	Exposed in shipyard	0.94 (0.56–1.49)		
					Occupational groups			
				3	Carpenters	1.53 (0.31–4.48)		
				3	Machinists	2.06 (0.41–6.02)		
				6	Woodworkers	6.20 (2.27–13.50)		
				1	Professionals	2.04 (0.03–11.33)		
				0	Women	–		

Marsh et al. [107], United States	7,345 workers employed at a plastic-producing plant (1941–1984); mortality follow-up until 2003 (obtained for 98 % and cause of death for 95 % of the cohort)	Exposure assessment obtained by work histories	Tongue, gum and other oral sites unspecified, floor of the mouth, and pharynx		*SMR*			
					Tongue			
				5		1.08 (0.55–2.53)		
					Gum and other oral sites unspecified			
				4		1.36 (0.37–3.50)		
					Floor of mouth			
				2		1.91 (0.23–6.92)		
				Pharynx				
				23		2.38 (1.51–3.57)		
Tarvainen et al. [69], Finland	Cohort comprised all Finns (725,868 men and 825,528 women) born during 1906–1945; incidence follow-up (1971–1995)	Occupational branches, specific occupations, and national job-exposure matrix (FINJEM) for 43 chemical agents; cumulative exposure (annual average of exposed people X mean level of exposure in the occupation) for every 5-year birth cohort	Oral cavity and pharynx (excluding nasopharynx)		*SIR*		SIR adjusted for age, calendar period and social class. Reference total Finnish population	SIR reported here only for equal or higher than 1.2 and 95 %CI statistically significant.
					Men			
				4	Lawyers	5.70 (1.55–14.59)		
				2	Authors	9.32 (1.13–33.65)		
				10	Journalists	3.28 (1.57–6.03)		
				4	Performing artists	5.60 (1.53–14.35)		
				7	Musicians	3.03 (1.15–5.90)		
				6	Electronics, telefitters	2.92 (1.07–6.35)		
				21	Painters, building	1.63 (1.01–2.49)		
				48	Building hands	1.58 (1.16–2.09)		
				15	Dockers	2.28 (1.28–3.76)		
				7	Hotel porters	3.51 (1.41–7.23)		
					Women			
				9	Private secretaries	2.20 (1.00–4.17)		
				12	Dressmakers	2.42 (1.25–4.23)		
				2	Shoemakers and cobblers	17.42 (2.11–62.94)		
				23	Waiters	1.80 (1.14–2.70)		
				2	Pursers and stewardesses	9.56 (1.16–34.52)		
					Men and women			
					Cumulative exposure			
					Lowest			
				105	Asbestos	1.32 (1.08–1.60)		
				104	Iron	1.23 (1.00–1.49)		
				164	Lead	1.32 (1.12–1.53)		
				90	Cadmium	1.45 (1.17–1.78)		
				185	Carbon monoxide	1.26 (1.08–1.45)		
				102	Diesel engine exhaust	1.26 (1.03–1.53)		
				130	Gasoline engine exhaust	1.28 (1.07–1.52)		
				38	Fungicides	1.48 (1.05–2.04)		
					Middle			

(continued)

Table 4.2 (continued)

Reference, location	Cohort description	Exposure assessment	Tumor site	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
				37	Chlorinated hydrocarbon	1.42 (1.00–1.96)		
				87	Engine exhaust	1.34 (1.08–1.66)		
				51	Gasoline engine exhaust	1.37 (1.02–1.80)		
					Highest			
				22	Aliphatic and alicyclic hydrocarbons	1.97 (1.23–2.98)		
				23	Petroleum-based products	1.60 (1.02–2.41)		
				88	Asbestos	1.26 (1.01–1.55)		
				25	Engine exhaust	1.68 (1.09–2.48)		
				20	Diesel engine exhaust	1.62 (0.99–2.50)		
					RR		RR included age, calendar period, socioeconomic status and all three occupational exposure (high, middle, low)	RR reference category: no occupational exposure
					Men and women			
					High level of cumulative exposure			
				22	Aliphatic and alicyclic hydrocarbons	1.69 (1.06–2.71)		
				10	Pesticides	1.92 (1.00–3.68)		
				25	Engine exhaust	1.37 (0.90–2.09)		
Andersen et al. [130], Denmark	3.22 million Danish born 1925–1973 and aged >30 years in the incidence period 1994–2003				*IRR*		IRR adjusted for calendar period, age, level of education, and disposable income	
					Men			
					Affiliation to work market			
				956	Working	1.00		
				427	Unemployed early retirement	2.98 (2.63–3.37)		
				480	Retirement	4.52 (4.01–5.11)		
					Social class			
				69	Creative core	0.69 (0.52–0.90)		
				224	Creative professional	0.65 (0.56–0.76)		
				20	Bohemian	1.80 (1.15–2.82)		
				517	Service	0.92 (0.83–1.03)		
				1,022	Manual	1.00		
				47	Agricultural	0.31 (0.23–0.42)		
				182	Unknown	0.95 (0.81–1.12)		
					Women			
					Affiliation to work market			
				273	Working	1.00		
				172	Unemployment	2.46 (2.02–2.99)		
				217	Early retirement	3.90 (3.22–4.72)		
					Social class			
				11	Creative core	0.70 (0.37–1.33)		
				48	Creative professional	0.60 (0.42–0.87)		
				1	Bohemian	0.47 (0.07–3.37)		
				412	Service	0.81 (0.63–1.04)		
				74	Manual	1.00		
				2	Agricultural	0.12 (0.03–0.47)		
				227	Unknown	1.20 (0.92–1.57)		

SIR standardized incidence ratio, *SMR* standardized mortality ratio, *IRR* incidence rate ratio, *RR* relative risk

oral cancer in those employed after 1964. Andjelkovich et al. [58] found SMR 131 (95 % CI 48–286) for workers exposed to formaldehyde in an automotive iron foundry. Marsh et al. [59] in a cohort of workers in a plastic-producing plant found for oral and pharynx cancers SMR of 1.80 (95 % CI 1.22–2.55). Other results from this study, including exposure duration and cumulative exposure to formaldehyde, are difficult to interpret as analysis for pharynx cancer included nasopharyngeal carcinoma. A cohort study in the United Kingdom [60] found SMRs below 2.0 for men with high exposures (estimated as greater than 2.0 ppm). Hauptmann et al. [61] expanded the follow-up from previously cited Blair et al.'s [56] cohort study. Even though risks for oral cavity cancer above 2.0 were found for some average-intensity exposure levels, no dose-response effect was detected. Stayner et al. [62] conducted a mortality cohort study in garment manufacturers, as workers in this industry are potentially exposed to formaldehyde. They concluded that there was a possible relationship between formaldehyde and oral cavity cancer (SMR 343, 95 % CI 118–786). An extension of this cohort until 1998 [63] confirmed increased risks, particularly for oral cavity cancer SMR (3.53, 95 % CI 0.96–9.02), for the original cohort exposure period, but revealed decreased SMRs for the updated period. Several other cohorts were conducted specifically with formaldehyde-exposed professionals, such as pathologists, anatomists, medical laboratory technicians, embalmers, and funeral directors [64–68], but revealed decreased risks of oral and pharynx cancers. A Finnish cohort population [69] did not find any increased risk at the lowest, middle, or highest exposure levels to formaldehyde for oral cavity and pharynx cancer. Innos et al. [70] in a cohort of furniture workers in Estonia detected slight risks for those with possible exposure to formaldehyde. Bosetti et al. [71] conducted the most recent meta-analysis of cohort studies on formaldehyde and cancer risk; related to oral cavity and pharynx, they found RR of 1.09 (95 % CI 0.88–1.34) for industrial workers and RR of 0.96 (95 % CI 0.75–1.23) for professionals. The results of all available studies are inconsistent, and no clear association could be established between exposure to formaldehyde and oral and pharynx cancers [72, 73].

Leather Dust and Leather Industry Work

A case-control study conducted in the United States [74] showed evidence of oral and pharynx cancers in leather industry workers (RR 3.58; $p<0.01$). However, three subsequent case-control studies reporting specifically on the leather industry or exposure to leather dust showed less emphatic results: in Brazil [75] the risk was low (RR 1.3), in Italy [53] risk deficits were observed (RR 0.4 for any exposure to leather dust and RR 0.9 for probable or definitive exposure), and in Sweden [54] risks higher than 2.0 were observed, but they were not statistically significant. A cohort study in Finland [69] reported increase risk of oral and pharynx cancers from exposure to leather dust as standardized incidence ratio (SIR) 1.75 (95 % CI 0.36–5.13) for those with medium-category exposure, as no cases were observed at high exposure level. There is no specific cohort study with workers in leather industry. Even though leather dust has been classified by the International Agency for Research on Cancer (IARC) as definitively carcinogenic for humans, into Group 1 [76, 77], from results of available case-control and cohort studies which have investigated exposure to leather dust and oral and pharynx cancers, no conclusive association can be assumed.

Wood Dust and Wood Industry Work

Many case-control studies that have reported an association between wood dust exposure or jobs in wood-related work and oral and pharynx cancers have revealed decreased risks or risks around unity [53, 54, 75, 78–81]. Other studies have found risks ranging from 1.5 to 2.0 for pharyngeal cancer [55, 82, 83]. A case-control study [84] observed a high risk for oral cavity cancer in wood and wood product workers (RR 5.5, 95 % CI 1.2–25.0); and other case-control study [53] found increased risk (RR 5.5, 95 % CI 0.7–44.6) for those exposed for 16 years or more in wood furniture production. A cohort study of United States Coast Guard shipyard workmen [85] detected a high risk (RR 6.20, 95 % CI 2.27–13.50) of oral and pharynx cancers in woodworkers, but analysis included nasopharynx cancer. In Finland, two cohort studies did not reveal any risks of oral and pharynx cancers in woodworkers. In the first [86], decreased risks for oral cancer in construction carpenters and pharynx cancer in woodworkers were found. In the second [69], authors found a protection (SIR 0.79, 95 % CI 0.62–0.99) for oral and pharynx cancers in woodworkers but SIR 1.3 (95 % CI 0.7–2.1) for men and women in the highest category of exposure to hardwood dust. Innos et al. [70] conducted a cohort study in two large furniture factories; they found increased risk of pharynx cancer in men (RR 1.82, 95 % CI 0.83–3.46) and oral cavity cancer in women (RR 1.84, 95 % CI 0.50–4.71). Brown et al. [87] observed increased risk of oral cancer in male wood lacquerers (SIR 2.1, 95 % CI 1.0–3.9), but probably in the context of this cohort study, agents other than those habitually used in wood industry were involved, such as the basic components of paint, varnish, and lacquer, including pigments, resins, and solvents. In general, the risks of oral and pharynx cancers for wood dust or wood industry exposure were imprecise, and no dose-response effect could be observed considering level or time of exposure.

Gustavsson et al. [54] speculated that lowered risk to wood dust exposure could be due to residual confounding from low smoking levels in these workers because of the obvious fire hazard in this activity; however, after subdividing smoking habits into eight increasing cumulative tobacco

classes, low RR associated with exposure to wood dust persisted. IARC has classified wood dust in Group 1 [77]; however, specifically for oral and pharynx cancers, results from studies conducted until now do not allow conclusive answers on a causal relationship between wood dust exposure and oral and pharynx cancers.

Cotton Dust and Textile Work

A case-control study of women in the United States [88] found increased risk (RR 3.9, 95 % CI 1.2–12.0) of oral cancer in those with presumed exposure to dust in textile industry for 1–4 years, but no risk was observed for those exposed for 10 years or more. Increased risks were also found in France [78] for pharynx cancer (RR 2.4, 95 % CI 1.0–5.7) and in Italy [53] for oral cancer (RR 2.5, 95 % CI 0.5–9.9). However, many other case-control studies have revealed risk deficits or close to unity values for oral and pharynx cancers in textile dust exposure or textile work [54, 75, 80, 82, 83]. Tarvainen et al. [69] in a cohort study also found risk deficits in men and women exposed to any level of textile dust. This inconsistency in results does not allow the supposition of a causal relationship between cotton dust exposure or textile work and oral and pharynx cancers.

Welding Fumes and Welding as an Occupation

There are many different welding methods which involve exposure to chemicals, such as irritant gases, chromium, polycyclic aromatic hydrocarbons, and metal dust. A case-control study in Sweden [54] found risk excess of pharynx cancer (RR 2.26, 95 % CI 1.09–3.69) in workers exposed to welding fumes for more than 8 years. In another case-control study in Sweden [84], increased risk of oral cancer was detected in welders (RR 2.3, 95 % CI 0.6–9.1). There is little consistency between these findings and results from other case-control [53, 80, 82, 83] and cohort studies [85, 89]. Exposure to welding fumes clearly needs further investigation in order to arrive at a definite conclusion of carcinogenicity for the oral cavity and pharynx anatomical regions.

Diesel Engine Exhaust and Vehicle Repair Mechanics

Recently, IARC considered the evidences of causal association between diesel engine exhaust and cancer as sufficient, particularly for lung cancer [90]. This decision was taken considering a large US National Cancer Institute/National Institute for Occupational Safety and Health study conducted among underground miners [91, 92].

Boffetta et al. [93] conducted a cohort study to evaluate exposure to diesel engine emissions in a Swedish population and found a general SIR of 1.64 (95 % CI 1.11–2.33) for oral and pharynx cancers in women, but no risk was detected for men. Using a job-exposure matrix, exposure was categorized according to probability and intensity as low, medium, and high. Some tenuous positive relative risks were observed, but without a dose-response effect. A cohort study in Finland [69] detected increased risks of mouth and pharynx cancer in men and women with medium levels of exposure to engine exhaust (SIR 1.34, 95 % CI 1.08–1.66) and at the highest level of exposure to engine exhaust (SIR 1.68, 95 % CI 1.09–2.48). Vaughan [82] in a case-control study found a risk higher than 2.0 for vehicle mechanics in repair services, but they examined oral cavity, pharynx, and nasopharynx tumors all together. In a case-control study in Brazil, Andreotti et al. [80] found increased risks, greater than 2.0, for oral and pharynx cancers in every occupation of vehicle mechanic, and for every vehicle repair service job, these risks were augmented considering the restrictions of 10 or more years of exposure and induction period (equal to or greater than 20 years before diagnosis). Vehicle mechanics are potentially exposed to diesel and gasoline engine exhaust, but they are also exposed to other hazardous agents, such as solvents, mineral oils, strong acid fumes, and metal dust. They are therefore exposed to a complex mixture of potential carcinogens. Vehicle mechanics in repair and diesel and gasoline exhaust services are potentially at increased risk of contracting oral and pharynx cancers, but more studies are needed to confirm this relationship.

Other Occupations

Several other occupations, industries, and agents have been linked to oral cavity and pharynx cancer. Certainly, all these circumstances require further studies before a definitive view can be taken on their possible role in the causal chain for the disease.

Exposures in meat industry, such as viruses, nitrosamines, and polycyclic aromatic hydrocarbons, may contribute for elevated cancer risks. Two cohorts have identified increased risks for oral and pharynx cancers in butchers. Johnson et al. [94] in a mortality cohort in the United States found increased risk of oral cavity and pharynx cancer in male meat cutters working in supermarket or grocery store meat departments (SMR 1.8, 95 % CI 1.0–3.0); there was also increased risk for those working as meat cutters in other departments (SMR 1.7, 95 % CI 0.8–3.2). Boffetta et al. [95] in a cohort of butchers and meat workers in Sweden found increased risk for butchers in meat industry (RR 1.6, 95 % 1.0–2.7). Also, a case-control study in Uruguay [96] found increased risk of oral and pharynx cancers in butchers (RR 2.0, 95 % CI 0.4–9.5). In contrast, Coggon and Wield [97] in a cohort study in England and Wales found deficit risks for oral and pharynx cancers in butchers.

Moulin et al. [98] in a cohort study of workers at a man-made mineral fiber (MMMF) factory in France found SIRs of 3.0 for oral and 1.4 for pharynx cancer, both not statistically significant. A Scandinavian cohort of employees in

nine factories producing rock-slag wool and glass wool [99] found increased risk of oral cavity and pharynx cancer in those exposed to rock-slag wool (SIR 1.84, 95 % CI 1.22–2.68) but a lower risk for glass wool exposure (SIR 1.31, 95 % CI 0.65–2.34). Two case-control studies reported results for exposure to MMMF; the first [54] found risk deficits for oral or pharynx cancer, and the second [100] reported increased risk for hypopharynx cancer in those ever exposed to mineral wools (RR 1.55, 95 % CI 0.99–2.41).

Marchand et al. [100] found increased risks for those with any exposure to asbestos once (RR 1.80, 95 % CI 1.08–2.99) or cumulative low (RR 1.92, 95 % CI 1.03–3.57) or high exposure (RR 2.14, 95 % CI 1.14–4.01). However, previous case-control studies did not find increased risks of oral and pharynx cancers associated to asbestos [53, 54, 83]. A cohort of Finns born between 1906 and 1945 [69] found increased risks with cumulative asbestos exposure at the lowest (SIR 1.32, 95 % CI 1.08–1.60) and highest levels (SIR 1.26, 1.01–1.55). In a cohort study with construction industry workers [101], an RR of 1.7 was detected (95 % CI 0.9–3.3) for those with moderate exposure to asbestos, but the risk dropped for those with high exposure (RR 0.5, 95 % CI 0.1–5.2).

Several other agents such as chromium, nickel, lead, iron, cadmium, phenoxy acids, solvents, cement dust, asphalt, pesticides, and aliphatic and alicyclic hydrocarbons; occupations such as blacksmiths, bricklayers, drivers, electricians, railway workers, industrial mechanics, painters, metal workers, chemical workers, plumbers and pipe fitters, plastic transformation workers, printers, carpet installers, boiler, furnace and petroleum industry workers, dockers, shoemakers and cobblers, sugarcane farmers, glazers, cutting/sewing workers, hairdressers, dentists, and journalists; and industries such as rubber, paper, pulp, plastics, mining, and building have all been cited as presenting increased risks for oral and pharynx cancers in different cohort and case-control studies. In general, these increased risks were tenuous and imprecise and based in small number of observed cases.

Cooks, waiters, and bartenders, as well as workers at restaurants, bars, and hotels, have shown consistently increased risks of oral and pharynx cancers through some case-control and cohort studies [53, 69, 86]. However, the main hypothesis for these increased risks is the higher prevalence of heavy tobacco smoking and alcohol consumption among these workers.

Nasopharynx Cancer

Tables 4.3 and 4.4 show results of 14 case-control and 7 cohort studies, which examined the association between occupation or exposure to some agents and nasopharynx cancer. Formaldehyde and wood dust showed strong evidence of carcinogenicity to nasopharynx; however, the effect for some other agents and occupations was inconclusive because of results inconsistency among studies.

Formaldehyde

The first epidemiological evidence suggesting an association between exposure to formaldehyde and nasopharynx cancer came in 1986. A mortality cohort study of workers in ten plants producing or using formaldehyde [56] found increased SMRs for different formaldehyde exposure levels. Also a case-control study [52] found increased relative risks for longer exposures. These epidemiological studies were conducted after research with animal models had indicated nasal squamous cell carcinomas occurring in rodents submitted to formaldehyde vapor inhalation [102, 103]. A case-control study in the Philippines [104] has found increased risk for those with long induction period (25 or more years since first exposure). In a cohort study with 14,014 British chemical workers exposed to formaldehyde and followed up for almost 60 years [60], the only death from nasopharynx cancer was of a man whose exposure was classified as low. However, there was evidence of increased death rates from nasopharynx cancer in a cohort of formaldehyde-industry workers by Hauptmann et al. [61], an update of the Blair et al. cohort [56]. This cohort revealed an exposure-response effect for peak and cumulative exposure to formaldehyde, but not for average-intensity exposure or duration.

The study by Hauptmann et al. [61] was a major component in the epidemiological evidence evaluated by the IARC when making their decision on classifying formaldehyde as a definite carcinogen for humans in 2004 [105–107]. Some criticisms on the Haptmann et al.'s [61] cohort study have been addressed, such as the detected association was mainly from one cluster of deaths in a single plant, where five of nine nasopharynx deaths occurred [107]. However, as pointed out by Cogliano et al. [106], in order to classify an agent as carcinogenic, if evidence in humans is insufficient, one should consider that mechanistic evidence and sufficient evidence in experimental animals led to the agent being classified in IARC Group 1. This decision has been upheld in a recent new IARC evaluation [72, 73], and formaldehyde was listed as a known human carcinogen in the 12th Report on Carcinogens of the US National Institute of Environmental Health Sciences [108].

Wood Dust and Wood Industry Work

As well as dust, workers in wood industry may also be exposed to formaldehyde, chlorophenol, and other chemical substances, giving them increased risk of nasopharyngeal cancer. Even so, this increased risk seems to be attributable to wood dust exposure independent to other exposures in the workplace, as the other chemicals do not present relative risks of the magnitude associated to wood dust exposure [77, 109].

Table 4.3 Case-control studies on occupation and nasopharynx cancer

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Henderson et al. [121], United States	156 cases of nasopharynx squamous cell carcinoma (105 men, 51 women) diagnosed (1960–1974)	267 controls (179 men, 88 women) recruited in hospitals from the same two cities of cases	Detailed occupational history was obtained through questionnaire, and for each occupation each subject was asked if he was usually exposed to fumes, dust, smoke, chemicals, or heat	*RR* Fumes			RR adjusted for age at diagnosis, race, sex, socioeconomic class, and city of residence	Reference category: never exposed. NS = nonsignificant
				Ever		2.0 ($p = 0.006$)		
				<10 years		1.9 (NS)		
				>10 years		1.7 ($p < 0.05$)		
				Dust				
				Ever		1.5 ($p = 0.07$)		
				<10 years		1.3 (NS)		
				>10 years		1.2 (NS)		
				Smoke				
				Ever		3.0 ($p = 0.008$)		
				<10 years		1.5 (NS)		
				>10 years		7.5 ($p < 0.005$)		
				Chemicals				
				Ever		2.4 ($p = 0.006$)		
				<10 years		2.3 ($p < 0.05$)		
				>10 years		2.7 ($p < 0.05$)		
				Heat				
				Ever		1.6 (0.053)		
				<10 years		1.4 ($p < 0.05$)		
				>10 years		1.6 ($p < 0.05$)		
Armstrong [110], Malaysia	100 cases of nasopharynx squamous cell carcinoma (65 men, 35 women), Malaysian Chinese, diagnosed (1973–1980)	100 neighborhood controls matched by age and sex	Occupational history obtained through interviews using a questionnaire	*RR* Ever			RR adjusted for salted fish intake	Reference category: never exposed. NS = nonsignificant
				Smoke	13 (3)	6.0 ($p = 0.006$)		
				Wood, paper, and grass smoke	8 (2)	7.0 ($p = 0.04$)		
				Other smokes	5 (1)	5.0 ($p = 0.11$)		
				Dust	52 (25)	4.0 ($p < 0.001$)		
				Wood dust and sawdust	17 (10)	2.2 ($p = 0.08$)		
				Construction-related dust	15 (9)	1.9 ($p = 0.13$)		
				Quarry dust	10 (1)	∞ ($p = 0.002$)		
				Road dust	11 (2)	5.5 ($p = 0.01$)		
				Other dusts	17 (8)	2.3 ($p = 0.05$)		
				Smoke and/or dust	58 (26)	5.0 ($p < 0.001$)		
				Men				
				Never	26 (46)	1.0		
				1–9 years	19 (11)	3.3 (NS)		
				10 + years	22 (8)	8.4 (NS)		

				Women				
				Never	18 (28)	1.0		
				1–9 years	8 (4)	3.5 (NS)		
				10 + years	9 (3)	∞ (NS)		
				Under age 45				
				Never	19 (43)	1.0		
				1–9 years	20 (11)	4.3 (NS)		
				10 + years	17 (2)	∞ (NS)		
				Age 45+				
				Never	23 (31)	1.0		
				1–9 years	7 (4)	2.7 (NS)		
				10 + years	14 (9)	3.3 (NS)		
				Total				
				Never	42 (74)	1.0		
				1–9 years	27 (15)	3.4 (NS)		
				10 + years	31 (11)	11.4 ($p < 0.001$)		
Yu et al. [49], Hong Kong	250 cases of nasopharynx carcinoma (160 men, 90 women) of Chinese in Hong Kong, diagnosed after 1981	250 controls friend of cases, matched by sex and age	Occupational history obtained through interviews using a questionnaire	*RR*			RR adjusted for salted fish intake	Reference category: never exposed. NS = nonsignificant
				Domestic exposure				
				Wood cooking fuel	183 (161)	1.4 (NS)		
				3 years ago				
				Incense	186 (170)	1.4 (NS)		
				Antimosquito coils	61 (58)	2.4 (NS)		
				At age 10 years				
				Incense	208 (193)	0.9 (NS)		
				Antimosquito coils	78 (76)	1.8 (NS)		
				At birth (by mother)				
				Incense	108 (107)	0.6 (NS)		
				Antimosquito coils	29 (37)	0.8 (NS)		
				Carried subject while cooking				
				Occasionally	52 (63)	0.8 (NS)		
				Often	40 (41)	0.7 (NS)		
				Occupational exposure				
				Smoke	10 (3)	0.6 (NS)		
				Dust	59 (41)	1.2 (NS)		
				Chemical fumes	75 (49)	0.7 (NS)		

(continued)

Table 4.3 (continued)

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Vaughan et al. [52], United States	285 cases (186 men, 99 women) of oro- and hypopharynx cancer ($n=205$), nasopharynx cancer ($n=27$), and sinus and nasal cavity cancer ($n=53$) selected from a population-based cancer registry (1980–1983)	552 controls (327 men, 225 women) were identified via random digit dialing	Occupational formaldehyde exposure was assessed via a job-exposure matrix	*Nasopharynx* Exposure level Background Low Medium High Number of years exposed 0 1–9 10+ Exposure score (all years) 0–4 5–19 20+ Exposure score induction (excluding 15 years before diagnosis) 0–4 5–19 20+	 41 (381) 9 (121) 3 (42) 0 (8) 41 (381) 9 (127) 3 (44) 48 (464) 3 (59) 2 (29) 48 (490) 4 (40) 1 (22)	 1.0 0.8 (0.5–1.4) 0.8 (0.4–1.7) 0.6 (0.1–2.7) 1.0 0.6 (0.3–1.0) 1.3 (0.7–2.5) 1.0 0.6 (0.3–1.2) 1.5 (0.7–3.0) 1.0 0.9 (0.4–1.8) 1.3 (0.6–3.1)	Odds ratio adjusted for age, sex, cigarette smoking, and alcohol consumption	
Roush et al. [117], United States	173 men with nasopharynx cancer registered by the Connecticut Tumor Registry and dying (of any cause) in the period 1935–1975	605 controls sampled from Connecticut death certificates in the same time period as cases of deaths	An industrial hygienist classified each subject according to potential formaldehyde exposure on the basis of job title industry, specific employment, and year of employment. Analysis was conducted as yes/no exposed to each of the four potential levels of exposure to formaldehyde	*OR* *I* Probably exposed to some level for most of working life *II* Probably exposed to some level for most of working life and probably exposed to some level at 20 + years prior to death *III* Probably exposed to some level for most of working life and probably exposed to high level in some year *IV* Probably exposed to some level for most of working life and probably exposed to high level at 20 + years prior to death	 21 (79) 17 (51) 9 (27) 7 (14)	 1.0 (0.6–1.7) 1.3 (0.7–2.4) 1.4 (0.6–3.1) 2.3 (0.9–6.0)	OR adjusted for age at death, year at death, and availability of occupational information	
Kawachi et al. [112], New Zealand	19,904 cases of cancer in men of 20 years of age or older at the time of registration in the New Zealand Cancer Registry (1980–1984)	For each cancer site examined, registrants from other tumor sites formed the control group	Exposed and nonexposed in wood-related occupations and specific type of woodwork	*All woodwork* Type of woodwork Forestry and logging Sawmiller, pulp, and paper mill Cabinet makers Carpenters	2.46 (0.86–6.60) 2 (102) 0 (108) 0 (91) 5 (741)	5 (741) 6.02 (1.01–28.41) – – 2.51 (0.62–8.53)	Adjusted for age	

Yu et al. [118], China	306 cases of nasopharynx carcinoma (209 men, 97 women) in residents in Guangzhou City under the age of 50 years diagnosed in a main hospital, primary facility for treatment of this disease (1983–1985)	For each case, a control was matched for sex and date of birth (within 5 years) from neighborhood of case residence at the time of diagnosis	Subjects were asked to indicate, for each job that was held for longer than 6 months, whether exposure to dust, smoke, or chemical fumes had occurred and the name of the specific substances involved. Additionally, an industrial hygienist checked the exposure based on the job title and the industry of employment and also reviewed all specific substances named by each study participant	*RR*			RR adjusted for intake frequencies of salted fish, moldy bean curd, preserved plum, and tomatoes at age 10 years	Reference category: never exposed. NS = nonsignificant. For products of combustion and cotton dust, there are no information if assessment were done from subject response or by occupational hygienist
				Dust				
				Subject response				
				Ever	145 (134)	1.2 (NS)		
				1–9 years	74 (71)	1.2 (NS)		
				10–19 years	46 (33)	1.6 (NS)		
				20+ years	25 (30)	0.9 (NS)		
				Industrial hygienist				
				Ever	138 (146)	1.0 (NS)		
				1–9 years	67 (78)	1.0 (NS)		
				10–19 years	41 (45)	1.0 (NS)		
				20+ years	30 (23)	1.1 (NS)		
				Smoke				
				Subject response				
				Ever	62 (37)	2.4 ($p<0.05$)		
				1–9 years	31 (28)	1.6 (NS)		
				10+ years	31 (9)	7.6 ($p<0.05$)		
				Industrial hygienist				
				Ever	72 (50)	1.8 ($p<0.05$)		
				1–9 years	39 (35)	1.4 (NS)		
				10+ years	33 (15)	2.7 ($p<0.05$)		
				Chemical fumes				
				Subject response				
				Ever	111 (81)	1.7 ($p<0.05$)		
				1–9 years	54 (44)	1.5 (NS)		
				10–19 years	39 (28)	1.8 ($p<0.05$)		
				20+ years	18 (9)	2.7 (NS)		
				Industrial hygienist				
				Ever	138 (139)	1.1 (NS)		
				1–9 years	67 (85)	0.9 (NS)		
				10–19 years	53 (40)	1.5 (NS)		
				20+ years	18 (14)	1.3 (NS)		
				Combustion products				
				Ever	63 (33)	2.7 ($p<0.05$)		
				1–9 years	32 (24)	1.9 ($p<0.05$)		
				10+ years	31 (9)	10.1 ($p<0.05$)		
				Cotton dust				
				Ever	6 (19)	0.3 ($p<0.05$)		
				1–9 years	5 (12)	0.4 (NS)		
				10+ years	1 (7)	0.2 (NS)		

(continued)

Table 4.3 (continued)

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
Vaughan and Davis [79], United States	21 cases of nasopharynx squamous cell carcinoma diagnosed in a single center (1983–1987)	Controls were selected by random digit dialing matched to the cases by age and sex	Lifetime occupational histories were obtained, including a description of the duties involved in each job, as well as the associated industry. Jobs considered to entail significant exposure to wood dust included carpenters, forestry and logging workers, precision woodworkers (including patternmakers, cabinetmakers, and other furniture makers and finishers), and woodworking machine operators	*OR*			OR adjusted for age, sex, cigarette smoking, and race	Reference category: never exposed
				Ever employed in wood-related occupations	3	1.2 (0.2–4.6)		
				Employed in wood-related occupations >15 years before diagnosis	3	1.5 (0.2–6.1)		
				Employment for 10 or more years taking place at least 15 years before the reference date	No information	7.3 (1.4–34.2)		
Sriamporn et al. [113], Thailand	120 cases (80 men, 40 women) diagnosed (1987–1990) in a single hospital in Thailand	120 controls were recruited in the same hospital admitted for other diseases excluding neoplasms and respiratory diseases, matched by sex and age	Several potential factors for the etiology of nasopharynx cancer were studied including occupation. Then, occupations reported were grouped into a few broad categories, but employment in sawmills and jobs such as wood cutting or rice husking were investigated specifically, since these entail high exposures to dust	Not agriculture, not wood cutting	20 (47)	1.0	Adjusted for alcohol intake, type of cigarette, salted fish consumption, education, and area of residence	
				Wood cutting, not agriculture	5 (3)	4.1 (0.8–22.1)		
				Agriculture, not wood cutting	76 (64)	2.8 (1.3–6.2)		
				Agriculture and wood cutting	19 (6)	8.0 (2.3–28.2)		

West et al. [104], Philippines	104 incident cases of nasopharynx carcinoma (76 men, 28 women) recruited in a single hospital	104 controls matched with cases for sex, age, and hospital ward type (private vs public) and 101 community controls matched to cases for sex, age, and neighborhood	Occupations reported were reviewed by an industrial hygienist using various sources of exposure information. Each occupation was classified as likely or unlikely to involve exposure to any of the following factors: formaldehyde, solvents, wood dust, dust, and pesticides. This information was combined with the complete occupational history: overall duration of exposure, duration of exposure excluding exposure in the 10 years immediately preceding diagnosis (for cases) or interview (for controls), number of years since first exposure, and age at first exposure	*RR* Formaldehyde <25 years since 1st exposure 25+ years since 1st exposure Dust/exhaust <35 years since 1st exposure 35+ years since 1st exposure Antimosquito coils <Daily Daily	 12 (12) 14 (10) 49 (59) 30 (40) 24 (36) 21 (6)	 1.2 (0.4–3.6) 4.0 (1.3–12.3) 2.5 (1.1–5.9) 4.4 (1.1–17.5) 1.4 (0.6–2.8) 5.9 (1.7–20.1)	RR adjusted for education, processed meat intake, fresh fish intake, smoking, and herbal medicines	
Armstrong et al. [111], Malaysia	282 cases (195 men aged 19–72 years, 87 females aged 24–74 years) diagnosed (1987–1992)	282 controls matched by sex and age and with no history of cancer of the head and neck and respiratory system, selected from the general Chinese population of the study area using a standard procedure of multistage area sampling	Exposure to 20 inhalants and heat from two sources were recorded by trade or profession with calendar years, frequency (days per week), and duration (hours per day) of exposure. Inhalant selection was limited to those dusts, smoke, and gases associated with deposition or absorption in the nasopharynx, with special attention to formaldehyde	*Dusts* Construction Fertilizer Metal Talc Tin Textile Wood Others *Fumes* Cooking Engine exhaust Wood Others	 22 % (14.2 %) 1.4 % (1.4 %) 16 % (9.6 %) 3.6 % (2.5 %) 3.2 % (1.8 %) 7.8 % (5 %) 24.8 % (12.1 %) 39.7 % (31.2 %) 6.7 % (4.6 %) 20.9 % (19.9 %) 9.6 % (5.3 %) 10.3 % (5.3 %)	 1.06 (0.93–1.20) 0.82 (0.51–1.32) 1.14 (0.96–1.35) 0.86 (0.61–1.21) 1.16 (0.83–1.61) 1.16 (0.94–1.42) 1.24 (1.07–1.44) 1.07 (0.96–1.19) 0.97 (0.78–1.21) 1.00 (0.88–1.14) 1.08 (0.84–1.38) 1.12 (0.91–1.39)	Adjusted for diet and cigarette smoke	The study includes cases of incidents ($n=163$), diagnosed in 1990–1992 and cases of prevalence ($n=119$) diagnosed before 1990 (initiation of data collection)

(continued)

Table 4.3 (continued)

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
				Chemicals				
				Biocides	6.7 % (6.7 %)	0.93 (0.74–1.17)		
				Dyes	2.1 % (1.8 %)	1.07 (0.73–1.58)		
				Formaldehyde	9.9 % (8.2 %)	0.88 (0.70–1.12)		
				Glues	11.0 % (6.7 %)	1.09 (0.88–1.34)		
				Other chemicals	7.1 % (3.2 %)	1.20 (0.92–1.56)		
				Motor fuel and oil	29.4 % (19.9 %)	1.05 (0.91–1.22)		
				Paints and varnishes	16.0 % (9.6 %)	1.08 (0.91–1.29)		
				Resins	2.8 % (4.6 %)	0.74 (0.54–1.01)		
				Heat				
				Solar	18.1 % (11 %)	1.02 (0.89–1.18)		
				Industrial	17 % (6.7 %)	1.21 (1.01–1.45)		
Vaughan et al. [114], United States	196 incident cases of nasopharynx cancer (133 men, 63 women), aged 18–74 years, identified at five population-based cancer registries from 1987 to 1991	244 controls were selected over the same period from the general population through random digit dialing and frequency matched to the cases by age, sex, and cancer registry	Exposure to formaldehyde and wood dust was carried with the occupational history (job-by-job basis for each subject) including industry description, job title, duties, and dates started and stopped	*OR*			OR for formaldehyde adjusted for age, sex, race, cancer registry, smoking, proxy status, and education. OR for wood dust adjusted beyond all these variables, adjusted for cumulative exposure to formaldehyde	Reference category: never exposed
				Formaldehyde				
				Ever				
				Possible, probable, or definite	61 (79)	1.6 (1.0–2.8)		
				Probable or definite	27 (30)	2.1 (1.1–4.2)		
				Definite	10 (2)	13.3 (2.5–70.0)		
				Possible, probable, or definite				
				Duration				
				1–5 years	16 (41)	0.9 (0.4–2.1)		
				6–17 years	20 (19)	1.9 (0.9–4.4)		
				18+ years	25 (19)	2.7 (1.2–6.0)		
				Cumulative exposure (ppm-year)				
				0.05–0.40	15 (40)	0.9 (0.4–2.0)		
				>0.40–1.10	22 (20)	1.8 (0.8–4.1)		
				>1.10	24 (19)	3.0 (1.3–6.6)		
				Wood dust				
				Ever				
				Maximum exposure (mg/m3)	17 (24)	1.2 (0.5–2.7)		
				>0.00–0.55	10 (15)	1.3 (0.5–3.6)		
				>0.55–1.50	6 (4)	2.0 (0.5–8.1)		
				>1.50	1 (5)	0.2 (0.0–2.1)		
				Duration				
				1–4 years	8 (12)	1.4 (0.5–4.4)		
				5–13 years	4 (6)	1.3 (0.3–5.4)		
				14+ years	5 (6)	0.8 (0.2–3.7)		
				Cumulative exposure (mg/m^3-years)				
				>0.0–2.75	5 (13)	0.7 (0.2–2.5)		
				>2.75–15.70	10 (5)	3.0 (0.9–9.8)		
				>15.70	2 (6)	0.4 (0.1–2.3)		

Hildesheim et al. [22], Taiwan	375 incident cases (260 men, 115 women) of nasopharynx cancer recruited in two hospitals in Taipei (1991–1994)	325 controls (233 men, 92 women) recruited from the lists of the National Household Registration System and matched on age, sex, and district/township of residence	Occupational history was obtained through a questionnaire and was reviewed by an industrial hygienist. Each job was classified according to industry and occupation classification. The probability and intensity of exposure to formaldehyde, wood, and organic solvents were evaluated. Years of exposure, intensity and probability of exposure, cumulative exposure, age at first exposure, and years since first exposure were considered. Duration of exposure was recalculated after exclusion of exposures occurring in the 10 years preceding diagnosis (cases) and interview (controls)	*RR* All subjects Wood exposure			RR adjusted for age, sex, education, and ethnicity	Reference category not exposed. Authors conducted an analysis only with subjects (cases and controls) who are Epstein-Barr virus positive. For wood exposure and solvent exposures, the results did not suffer important changes; however, for formaldehyde exposure, some relevant modifications were observed: ever exposed RR = 2.7 (95 % CI 1.2–6.2); years since first exposure (>20 year) RR = 2.8 (95 % CI 1.1–7.6); and age at first exposure (<25 years) RR = 2.6 (95 % CI 1.1–6.5)
				Ever exposed	52 (26)	1.7 (1.0–3.0)		
				Duration (overall)				
				<10 years	21 (15)	1.2 (0.60–2.5)		
				>10 years	31 (11)	2.4 (1.1–5.0)		
				Duration (excluding 10 years before diagnosis/interview)				
				<10 years	26 (14)	1.7 (0.85–3.5)		
				>10 years	21 (8)	2.2 (0.93–5.3)		
				Cumulative exposure (intensity X duration)				
				<25	20 (15)	1.2 (0.58–2.5)		
				>25	32 (11)	2.4 (1.2–5.1)		
				Years since first exposure				
				<20 years	21 (8)	2.4 (1.0–5.8)		
				>20 years	31 (18)	1.4 (0.75–2.7)		
				Age at first exposure				
				<25 years	37 (15)	2.3 (1.2–4.4)		
				>25 years	15 (11)	1.1(0.47–2.5)		
				Formaldehyde exposure				
				Ever exposed	74 (41)	1.4 (0.93–2.2)		
				Duration (overall)				
				<10 years	31 (21)	1.3 (0.69–2.3)		
				>10 years	43 (20)	1.6 (0.91–2.9)		

(continued)

Table 4.3 (continued)

Reference, study location, and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No cases (controls)	Relative risk (95 % CI)	Adjustment for potential confounders	Comments
				Duration (excluding 10 years before diagnosis/interview)				
				<10 years	34 (18)	1.6 (0.89–3.0)		
				>10 years	34 (20)	1.2 (0.67–2.2)		
				Cumulative exposure (intensity X duration)				
				<25	29 (19)	1.3 (0.70–2.4)		
				>25	45 (22)	1.5 (0.88–2.7)		
				Years since first exposure				
				<20 years	19 (7)	2.3 (0.95–5.8)		
				>20 years	55 (34)	1.2 (0.76–2.0)		
				Age at first exposure				
				<25 years	62 (38)	1.3 (0.80–2.0)		
				>25 years	12 (3)	3.4 (0.94–12)		
				Solvent exposure				
				Ever exposed	178 (130)	1.2 (0.84–1.7)		
				Duration (overall)				
				<10 years	89 (54)	1.5 (0.99–2.3)		
				>10 years	89 (76)	0.93 (0.61–1.4)		
				Duration (excluding 10 years before diagnosis/interview)				
				<10 years	88 (65)	1.1 (0.74–1.6)		
				>10 years	61 (48)	0.94 (0.58–1.5)		
				Cumulative exposure (intensity X duration)				
				<40	93 (68)	1.3 (0.86–1.9)		
				>40	85 (62)	1.1 (0.70–1.6)		
				Years since first exposure				
				<20 years	74 (57)	1.2 (0.76–1.8)		
				>20 years	104 (73)	1.2 (0.79–1.8)		
				Age at first exposure				
				<25 years	133 (98)	1.1 (0.78–1.6)		
				>25 years	45 (32)	1.3 (0.78–2.2)		
Marsh et al. [107], United States	22 cases who died from pharyngeal cancer, 7 of nasopharynx cancer, from a cohort study at a plastic-producing plant between 1945 and 1998	Four controls selected randomly from the remaining living and deceased members of the cohort were matched on exact age, race, sex, and year of birth to each case	Exposure to formaldehyde (nonexposed and exposed) was estimated from job titles, tasks, visits to the plants, visits to the plant, discussion with workers and managers, by industrial hygienists, and defining average intensity, peak of exposure, cumulative exposure, and duration of exposure	*Exposure to formaldehyde*			Adjusted for smoking and the combined silversmithing and other metal work job groups	See results of a cohort study with these deaths by nasopharynx cancer in Table 4.4
				Unexposed	0 (8)	1.0		
				Exposed	7 (47	2.87 (0.21–α)		
				Duration of exposure				
				<1 year	4 (35)	1.0		
				1–9 years	1 (11)	1.81 (0.03–36.4)		
				10+ years	2 (9)	2.72 (0.16–145.6)		
				Cumulative exposure				
				<0.004	1 (16)	1.00		
				0.004–0.219	3 (21)	1.65 (0.03–173.1)		
				0.22+	3 (18)	5.91 (0.16–950.3)		
				Average intensity of exposure				
				<0.03	1 (24)	1.00		
				0.03–0.159	4 (6)	11.41 (0.80–668.5)		
				0.16+	2 (25)	2.18 (0.09–133.8)		

Table 4.4 Cohort studies on occupation and nasopharynx cancer

Reference, location	Cohort description	Exposure assessment	No of cases/ deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Blair et al. [56], United States	26,561 workers first employed in 10 formaldehyde-producing or formaldehyde-using plants before 1996. Mortality follow-up (1980)	A job-exposure matrix was prepared for industrial hygienists considering each job-work area-calendar year combination. Measures of exposure to formaldehyde used in the analysis included level or intensity, duration, average, cumulative or peak exposure, presence of particulates, and measures that excluded recent exposures from the exposure index		*SMR*			Black women were excluded from analysis because of small numbers ($n=26$). All SMRs were not statistically significant
				Cumulative formaldehyde exposure			
			1	0 ppm-year	530		
			2	<0.5 ppm-year	271		
			2	0.51–5.5 ppm-year	256		
			2	>5.5 ppm-year	433		
Malker et al. [125], Sweden	Cohort of men in occupational groups defined by employment in 1960; incidence follow-up (1961–1979)	Occupation and industries defined according to job title		*SIR*		Adjusted for age and region	Only statistically significant increases of SIR are reported for specific occupations and industries
				Occupation			
			3	Glassmaker	6.2 ($p<0.05$)		
			3	Bookbinders	6.1 ($p<0.05$)		
			5	Shoemaker	3.8 ($p<0.05$)		
				Industries			
			5	Shoe repair	4.0 ($p<0.05$)		
			4	Fiberboard plant	3.9 ($p<0.05$)		

(continued)

Table 4.4 (continued)

Reference, location	Cohort description	Exposure assessment	No of cases/deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Demers et al. [116], United Kingdom and United States	28,704 persons (26,506 men, 2,198 women) from five mortality cohort studies in wood-related industries (4 American and 1 British). These cohorts had different periods of entrance and also different follow-up periods. A total of 9 deaths by nasopharynx cancer were observed	The cohorts included in the pooled analysis differed in the amount and detail of data collected exposure. To analyze the risk of cancer associated with wood dust exposure, a special classification scheme was developed incorporating the exposure information available for each study		*SMR*			
			9	Woodworkers combined	2.4 (1.1–4.5)		
			7	Furniture workers	2.9 (1.2–5.9)		
			2	Plywood workers	4.6 (0.6–16.4)		
				Wood dust exposure for all woodworkers			
			4	Possible	2.9 (0.8–7.5)		
			0	Probable	–		
			5	Definite	5.3 (1.7–12.4)		
				Calendar period of first employment for all woodworkers			
			3	Prior to 1940	7.7 (1.6–22.5)		
			5	1940–1949	5.3 (1.7–12.3)		
			0	1950–1959	–		
			1	1960 or later	1.7 (0.0–9.3)		
				Years since first employment for all woodworkers			
			0	<10 years	–		
			2	10–19 years	1.6 (0.2–5.9)		
			0	20–29 years	–		
			7	>30 years	8.9 (3.6–18.3)		
				Wood dust exposure for furniture workers			
			2	Possible	2.2 (0.3–7.8)		
			0	Probable	–		
			5	Definite	7.3 (2.4–16.9)Z		
				Calendar period of first employment for furniture workers			

3	Prior to 1940	8.6 (1.8–25.1)
4	1940–1949	7.7 (2.1–19.7)
0	1950–1959	–
0	1960 or later	–
	Years since first employment for furniture workers	
0	<10 years	–
0	10–19 years	–
0	20–29 years	–
7	>30 years	10.8 (4.3–22.2)
	Wood dust exposure for plywood workers	
2	Possible	11.8 (1.4–42.5)
0	Probable	–
0	Definite	–
	Calendar period of first employment for plywood workers	
0	Prior to 1940	–
1	1940–1949	5.0 (0.1–27.9)
0	1950–1959	–
1	1960 or later	25.0 (0.6–99.9)
	Years since first employment for plywood workers	
0	<10 years	–
2	10–19 years	13.3 (1.6–48.2)
0	20–29 years	–
0	>30 years	–

(continued)

Table 4.4 (continued)

Reference, location	Cohort description	Exposure assessment	No of cases/deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Marsh et al. [59], United States	7,328 workers (6,859 men, 469 women) employed at a plastic-producing plant (1941–1984); mortality follow-up until 1998	Exposure estimation was based on an examination of the available sampling data and job descriptions and verbal descriptions of jobs and tasks		*SMR*			
			7	Nasopharynx	4.94 (1.99–10.19)		
			4	Short term (<1 year)	5.35 (1.46–13.71)		
			3	Long term (1 + years)	4.59 (0.95–13.42)		
				Year of hire			
			0	1941–1946	–		
			6	1947–1956	8.13 (2.98–17.69)		
			1	1957+	2.63 (0.07–14.64)		
				DOE (year) (all workers)			
			4	<1	5.33 (1.45–14.64)		
			1	1–9	2.62 (0.06–14.57)		
			2	10+	7.49 (0.91–27.06)		
				TSFE (year)			
			2	<20	5.01 (0.61–18.08)		
			3	20–29	8.72 (1.80–25.48)		
			2	30+	3.04 (0.37–11.00)		
				Formaldehyde exposure			
			0	Unexposed	–		
			7	Exposed	6.03 (2.42–12.42)		
				Duration of exposure			
			4	>0–<1	5.84 (1.59–14.94)		
			1	1–9	3.17 (0.08–17.68)		

2	10+	12.46 (1.51–45.02)
	Cumulative exposure	
1	>0–<0.004	3.97 90.10–22.10)
3	0.004–0.129	5.89 (1.22–17.22)
3	0.22+	7.51 (1.55–21.93)
	AIE to formaldehyde (ppm)	
1	>0–<0.03	2.41 (0.06–13.44)
4	0.03–0.159	15.27 (4.16–39.10)
2	0.16+	4.13 (0.50–14.91)
	Formaldehyde >0.2 ppm	
2	Unexposed	3.01 (0.36–10.87)
5	Exposed	6.79 (2.21–15.85)
	Duration (year)	
2	>0–<1	4.81 (0.58–17.37)
1	1–9	4.04 (0.10–22.51)
2	10+	27.61 (3.34–99.73)
4	Formaldehyde >0.7 ppm	3.64 (0.99–9.31)
3	Unexposed	9.98 (2.06–29.17)
	Exposed	
	Duration (year)	
2	>0–<1	9.51 (1.15–34.37)
1	1+	11.07 (0.28–61.67)

(continued)

Table 4.4 (continued)

Reference, location	Cohort description	Exposure assessment	No of cases/deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
Hauptmann et al. [61], United States	Cohort of 25,619 workers (22,493 men, 3,126 women) employed in 10 US formaldehyde-producing or formaldehyde-using plants prior 1966; mortality from solid cancer follow-up until the end of 1994	Exposure to formaldehyde (nonexposed and exposed) was estimated from job titles, tasks, visits to the plants, visits to the plant, discussion with workers and managers, by industrial hygienists, and defining average intensity, peak of exposure, cumulative exposure, and duration of exposure		*SMR*		RR adjusted for calendar year, age, gender, race (black/white), and pay category (salary/wage)	None of RR were statistically nonsignificant
			2	Nonexposed	1.56 (0.39–6.23)		
			8	Exposed	2.10 (1.05–4.21)		
				RR			
				Intensity (ppm)			
			2	0	1.0		
			0	>0–<0.5	NA		
			1	0.5–<1.0	0.38		
			6	>1.0	1.67		
				Peak (ppm)			
			2	0	1.0		
			0	>0–<2.0	NA		
			0	2.0–<4.0	NA		
			7	>4.0	1.83		
				Cumulative (ppm-year)			
			2	0	2.40		
			3	>0–<1.5	1.0		
			1	1.5 - ≤ 5.5	1.19		
			3	>5.5	4.14		
				Duration (years)			
			2	0	1.77		
			4	>0–<5	1.0		
			1	5–<15	0.83		
			2	>15	4.18		

Li et al. [119], China	Cohort of 267,400 women in 526 factories in the Shanghai Textile Industry Bureau; all currently working and retired employees, who were born in 1925–1958 were eligible to participate; incidence follow-up (1989–1998)	Job categories; a job-exposure matrix was used for estimate exposure to several potential risk factors in textile industry		*HR*	
				Job categories	
				Cotton handing, processing, and spinning	
			4	<10 years	1.9 (0.7–5.3)
			11	>10 years	1.3 (0.6–2.4)
				Mixed fiber handling, processing, and spinning process	
			2	<10 years	0.8 (0.2–3.6)
			6	>10 years	1.0 (0.4–2.3)
				Dyeing	
			1	<10 years	1.8 (0.2–14.1)
			3	>10 years	3.6 (1.0–12.1)
				Finishing	
			1	<10 years	2.6 (0.3–21.3)
			1	>10 years	1.6 (0.2–12.5)
				Weaving	
			4	<10 years	0.7 (0.3–2.1)
			12	>10 years	0.6 (0.3–1.2)
				Printing	
			2	<10 years	9.2 (1.7–48.9)
			1	>10 years	2.0 (0.3–16.3)
				Cutting/sewing	
			2	<10 years	0.9 (0.2–3.9)
			6	>10 years	1.3 (0.6–3.2)
				Warehouse, packing, and quality control	
			3	<10 years	0.7 (0.2–2.1)
			5	>10 years	0.6 (0.3–1.6)
				Occupational exposures	
				Cotton dust	
			19	<1 year	1.0
			48	>1 year	1.8 (1.1–3.2)
				Wood dust	
			61	<1 year	1.0
			6	>1 year	0.6 (0.3–1.5)
				Skill dust	
			64	<1 year	1.0
			3	>1 year	0.9 (0.3–3.0)
				Synthetic fiber dust	
			42	<1 year	1.0
			25	>1 year	0.9 (0.5–1.5)
				Non-textile dust	
			61	<1 year	1.0
			6	>1 year	0.5 (0.2–1.2)

(continued)

Table 4.4 (continued)

Reference, location	Cohort description	Exposure assessment	No of cases/deaths	Exposure categories	SIR, SMR, IRR, or RR (95 % CI)	Adjustment for potential confounders	Comments
				Solvents			
			53	<1 year	1.0		
			14	>1 year	1.3 (0.7–2.5)		
				Bleaching agents			
			64	<1 year	1.0		
			3	>1 year	2.4 (0.7–8.2)		
				Acids, bases, and caustics			
			56	<1 year	1.0		
			11	>1 year	1.8 (0.9–3.6)		
				Dyes			
			62	<1 year	1.0		
			5	>1 year	2.1 (0.8–5.5)		
				Inks			
			63	<1 year	1.0		
			4	>1 year	5.0 (1.6–15.4)		
				Pesticides			
			65	<1 year	1.0		
			2	>1 year	1.9 (0.4–8.1)		
				Endotoxin			
			42	<1 year	1.0		
			25	>1 year	1.6 (0.9–2.6)		
Marsh et al. [107], United States	7,345 workers employed at a plastic-producing plant (1941–1984); mortality follow-up until 2003; vital status was obtained for 98 % and cause of death for 95 %	Exposure assessment obtained by work histories	7	*SMR (United States)* 4.34 (1.74–8.94) SMR (local county) 4.43 (1.78–9.13)			See results of a nested case-control study with these deaths by nasopharynx cancer in Table 4.3

SIR standardized incidence ratio, *SMR* standardized mortality ratio, *IRR* incidence rate ratio, *RR* relative risk

In 1983, Armstrong et al. [110] reported increased risk of nasopharynx squamous cell carcinoma in Malaysian Chinese ever exposed to wood dust (RR of 2.2, $p=0.08$). Another case-control study in the same population [111] found RR of 2.36 (95 % CI 1.33–4.19) for those exposed once to wood dust and RR of 1.24 (95 % CI 1.07–1.44) for those exposed to a tenfold increased exposure. Almost all other case-control studies that investigated the association between wood-related occupations and nasopharyngeal cancer have found increased risks [22, 79, 112, 113]. However, Vaughan et al. [114] did not find any evidence that exposure to wood dust increased the risk of nasopharyngeal carcinoma, as the modest crude association disappeared after controlling for potential exposure to formaldehyde. Also Siew et al. [115] in a large cohort of Finnish men born from 1906 to 1945 did not find any indication that wood dust and formaldehyde would increase the risk of nasopharyngeal cancer.

In a pooled reanalysis of four American cohorts and one British cohort of wood-related industries [116], excess risks of nasopharynx cancer were found for all combined woodworkers (SMR 2.4, 95 % CI 1.1–4.5), furniture workers (SMR 2.9 95 % CI 1.2–5.9), and plywood workers (SMR 4.6, 95 % CI 0.6–16.4). Mortality risk from nasopharynx cancer was higher in those employed in wood industry prior to 1940 (RR 7.7, 95 % CI 1.6–22.5), but this was restricted to workers from the British cohort as entry into the American cohorts only began in 1946. Increased risks were identified in workers definitively exposed to wood dust from any woodwork (RR 5.3, 95 % CI 1.7–12.4), for furniture workers definitively exposed to wood dust (RR 7.3, 95 % CI 2.4–16.9), and for plywood workers possibly exposed to wood dust (RR 11.8, 95 % CI 1.4–42.5).

The IARC has considered there is sufficient evidence that human exposure to wood dust is carcinogenic to the nasopharynx [109]. This was reaffirmed in a recent revision [77].

Cotton Dust and Textile Work

Several groups of chemicals are found in the textile manufacturing industry; these include flame retardants, textile dyes, solvents, preservatives, and textile prints. Some could be carcinogenic. Also some studies have suggested that cotton dust is a possible carcinogen for the nasopharynx.

In the United States, Roush et al. [117] found a deficit risk for nasopharynx cancer in textile work. In China, Yu et al. [118] also observed decreased risks for those ever exposed to cotton dust at any exposure duration. However, in Malaysia, Armstrong et al. [111] detected RR of 1.77 (95 % CI 0.76–4.11) for those ever exposed to cotton dust and RR of 1.16 (95 % CI 0.94–1.42) for those with a tenfold exposure to cotton dust. Li et al. [119] conducted a case-cohort study in Shanghai and detected increased risks of nasopharyngeal cancer for those exposed to cotton dust: RR of 2.7 (95 % CI 1.2–5.7) for less than 10 years and RR of 1.6 (95 % CI 0.9–2.9) for 10 years or more. An RR of 3.6 (95 % CI 1.8–7.2) was found for those with the highest cumulative exposure to cotton dust category (>143.4 mg/m^3 × years). The same study has also found increased risks of nasopharynx cancer for those in the textile industry exposed to acids, bases and caustics, dyes, and inks.

The IARC classifies cotton dust and working in textile industry as possibly carcinogenic to humans (Group 2B) [120]. Results from case-control studies conducted during the last decade of the twentieth century were more incisive on the relationship between cotton dust exposure and nasopharyngeal cancer. Also workers in textile industry have a possible increased risk of nasopharyngeal cancer. Nevertheless, no definite conclusion could be taken at this point on this relationship.

Other Occupations

Evidence linking nasopharynx cancer to other occupational risk factors is less definitive, as the number of studies is limited and results are conflicting. Henderson et al. [121] in a case-control study found increased risks of nasopharynx cancer for fumes, smoke, and chemicals, but not for dusts. Yu et al. [118] found increased risks for smoke and chemical fumes, but not for dusts. Armstrong et al. [111] did not find risks for exposure to chemicals, fumes, or dusts.

Chlorophenols are classified by IARC as possibly carcinogenic to humans – Group 2B [122]. A series of case-control studies have found relationships between exposure to chlorophenols and nasopharynx cancer. Hardell et al. [123] found about a sevenfold risk of nasopharyngeal and nasal cancer analyzed together for exposure to chlorophenols in the wood industry. Mirabelli et al. [124] also found high risks for those classified as ever exposed to high levels of chlorophenols (RR 2.64, 95 % CI 1.10–5.78) and even higher risks for those exposed for less than 10 years (RR 3.52, 95 % CI 1.07–9.73) or 10 years or more (RR 9.07, 95 % CI 1.41–42.9). Zhu et al. [23] found increased risks of nasopharyngeal squamous cell carcinoma in people exposed to chlorophenol (RR 2.2, 95 % CI 1.1–4.3).

Two case-control studies have examined the effect of industrial heat on nasopharynx cancer. Henderson et al. [121] found increased risks, around 1.5, but these were not statistically significant. Armstrong et al. [111] also found increased risks of nasopharynx cancer for heat exposure of RR of 1.23 ($p=0.021$), after adjustment for wood dust, diet, and cigarette smoke. Increased risks of nasopharynx cancer were also found for exposure to combustion products in a case-control study in China [118] with RR of 2.7 ($p<0.05$) for those with occasional exposure and RR of 10.1 ($p<0.05$) for those exposed for 10 years or more. The limited number of studies does not permit definitive conclusions to be made on the effect of industrial heat on nasopharynx cancer.

A case-control study in Taiwan [22] explored the effect of organic solvents on nasopharynx cancer, but risks were low and imprecise, and no dose-response effect was detected.

Zhu et al. [23] found increased risk for all histological types of nasopharyngeal cancer in people working with or around cutting oil (RR 1.9, 95 % CI 1.1–3.1); and increased risk of squamous cell carcinoma was found for occupational exposure to chromium compounds or alloys (RR 2.6, 95 % CI 1.1–6.1). Malker et al. [125] in a cohort study in Sweden found increased SIRs for glassmakers, bookbinders, and cobblers and in shoe repair and fiberboard industries.

Further studies are needed for all these occupational factors in order to have a clearer definition of their carcinogenic role on the nasopharynx.

Conclusion

The efforts to decrease major occupational risk factors for oral, pharyngeal, and nasopharyngeal cancers depend on the knowledge of potential carcinogen agents present in a particular occupation in different industry settings and the effective surveillance and prevention of workers' exposure to these agents. Table 4.5 shows the carcinogenicity evidence strength of some agents, occupations, or industries on oral cavity, pharyngeal, and nasopharyngeal anatomical sites.

Asbestos, diesel engine exhaust, leather and wood dust, man-made mineral fibers, and welding fumes have a possible association with oral and pharyngeal cancers. Waiters, cooks, and bartenders have a high risk of oral and pharyngeal cancers; however, the prevalence of tobacco smoking and alcohol consumption is higher among these workers than those in other occupations, and this fact could be the straightest explanation for the risk observed. Butchers, vehicle repair mechanics, welders, and woodworkers have showed evidences of possible increased risk of oral and pharyngeal cancers. Regarding the type of industry, jobs in the leather industry, man-made mineral fiber manufacturing, meat industry, vehicle repair service, and wood industry have also presented a possible impact on oral and pharyngeal cancer incidence.

There are convincing documentation on the causal relationship of exposure to chlorophenols, formaldehyde, and wood dust with nasopharyngeal cancer, as well as among woodworkers and in garment manufacturing. The carcinogenicity evidences of cotton dust and heat in the workplace to the nasopharynx are limited.

Additional studies are necessary to confirm the association of many suspicious agents, occupations, and industries with oral cavity, pharyngeal, and nasopharyngeal cancers. Nevertheless, the knowledge accumulated so far enables prevention and safety at work. That can be triggered in the context of surveillance programs, particularly considering exposure to chlorophenols, formaldehyde, and wood dust. For example, a well-oriented control of exposure to dust in the wood industry would prevent not only many cases of nasopharyngeal and sinonasal cancers but also probably some cases of pharyngeal, laryngeal, and lung tumors.

Table 4.5 Strength of evidence (low, possible, high) of association of exposure to some agents, occupations or industries, and oral cavity, pharynx, and nasopharynx cancers

Agent	Evidence	Occupation	Evidence	Industry	Evidence
Oral and pharynx cancers					
Asbestos	Possible	Butcher	Possible	Garment manufacture	Low
Diesel engine exhaust	Possible	Textile worker	Low	Leather industry	Possible
Dust		Vehicle repair mechanic	Possible	Man-made mineral fiber factory	Possible
Cotton	Low	Waiters and cooks	High	Meat industry	Possible
Leather	Possible	Welder and cutter	Possible	Textile industry	Low
Wood	Possible	Woodworker	Possible	Vehicle repair service	Possible
Formaldehyde	Low			Wood industry	Possible
Man-made mineral fibers	Possible				
Welding fumes	Possible				
Nasopharynx cancer					
Chlorophenols	High	Textile worker	Possible	Garment manufacture	High
Formaldehyde	High	Woodworker	High	Textile industry	Possible
Dust				Wood industry	High
Cotton	Possible				
Wood	High				
Industrial heat	Possible				

References

1. Ferlay J, Shin H-R, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GOBLOCAN 2008. Int J Cancer. 2010;127:2893–917.
2. Curado MP, Hashibe M. Recent changes in the epidemiology of head and neck cancer. Curr Opin Oncol. 2009;21:194–200.
3. Curado MP, Edwards B, Shin HR, Ferlay J, Heaune M, Boyle P, Storm H. Cancer incidence in five continents, IARC Scientific Publication, No 160, vol. IX. Lyon: IARC Press; 2009.
4. Wünsch Filho V, Camargo EA. The burden of mouth cancer in Latin America and the Caribbean: epidemiological issues. Semin Oncol. 2001;28:158–68.
5. Wünsch FV. The epidemiology of oral and pharynx cancer in Brazil. Oral Oncol. 2002;38:737–46.
6. Boing AF, Peres MA, Antunes JL. Mortality from oral and pharyngeal cancer in Brazil: trends and regional patterns, 1979–2002. Rev Panam Salud Publica. 2006;20:1–8.
7. Robinson KL, Macfarlane GJ. Oropharyngeal cancer incidence and mortality in Scotland: are rates still increasing? Oral Oncol. 2003;39:31–6.
8. Conway DI, Stockton DL, Warnakulasuriya KA, Ogden G, Macpherson LM. Incidence of oral and oropharyngeal cancer in United Kingdom (1990–1999) – recent trends and regional variation. Oral Oncol. 2006;41:586–92.
9. Hammarstedt L, Dahlstrand H, Lindquist D, Onelov L, Ryott M, Luo J, Dalianis T, Ye W, Munk-Wikland E. The incidence of tonsillar cancer in Sweden is increasing. Acta Otolaryngol. 2007;127:988–92.
10. Braakhuis BJ, Visser O, Leemans CR. Oral and oropharyngeal cancer in The Netherlands between 1989 and 2006: increasing incidence, but not in young adults. Oral Oncol. 2009;45:e85–9.
11. Kingsley K, O'Malley S, Ditmyer M, Chino M. Analysis of oral cancer epidemiology in the US reveals state-specific trends: implications for oral cancer prevention. BMC Public Health. 2008;8:87.
12. Schantz SP, Yu GP. Head and neck cancer incidence trends in young Americans, 1973–1997, with a special analysis for tongue cancer. Arch Otolaryngol Head Neck Surg. 2002;128:268–74.
13. Shiboski CH, Schimidt BL, Jordan RC. Tongue and tonsil carcinoma: increasing trends in the U.S. population ages 20–44 years. Cancer. 2005;103:1843–9.
14. Annertz K, Anderson H, Biörklund A, Möller T, Kantola S, Mork J, Olsen JH, Wennerberg J. Incidence and survival of squamous cell carcinoma of the tongue in Scandinavia, with special reference to young adults. Int J Cancer. 2002;101:95–9.
15. Gillison ML. Current topics in the epidemiology of oral cavity and oropharyngeal cancers. Head Neck. 2007;29:779–92.
16. Lee AWM, Foo W, Mang O, Sze WM, Chappell R, Lau WH, Ko WM. Changing epidemiology of nasopharyngeal carcinoma in Hong Kong over a 20-year period (1980–99): an encouraging reduction in both incidence and mortality. Int J Cancer. 2003;103:680–5.
17. Yang L, Parkin DM, Li L, Chen Y. Time trends in cancer mortality in China: 1987–1999. Int J Cancer. 2003;106:771–83.
18. Wei K-R, Yu Y-L, Yang Y-Y, Ji M-F, Yu B-H, Liang Z-H, Reng X. Epidemiological trends of nasopharyngeal carcinoma in China. Asian Pac J Cancer Prev. 2010;11:29–32.
19. Sun LM, Epplein M, Li CI, Vaughan TL, Weiss NS. Trends in the incidence rates of nasopharyngeal carcinoma among Chinese Americans living in Los Angeles County and the San Francisco Metropolitan Area, 1992–2002. Am J Epidemiol. 2005;162:1174–8.
20. Chang ET, Adami HO. The enigmatic epidemiology of nasopharyngeal carcinoma. Cancer Epidemiol Biomarkers Prev. 2006;15:1765–77.
21. Hildesheim A, Levine PH. Etiology of nasopharyngeal carcinoma: a review. Epidemiol Rev. 1993;15:466–85.
22. Hildesheim A, Dosemeci M, Chan CC, Chen CJ, Cheng YJ, Hsu MM, Chen IH, Mittl BF, Sun B, Levine PH, Chen JY, Brinton LA, Yang CS. Occupational exposure to wood, formaldehyde, and solvents end risk of nasopharyngeal carcinoma. Cancer Epidemiol Biomarkers Prev. 2001;10:1145–53.
23. Zhu K, Levine RS, Brann EA, Hall I, Caplan LS, Gnep DR. Case-control study evaluating the homogeneity and heterogeneity of risk factors between sinonasal and nasopharyngeal cancers. Int J Cancer. 2002;99:119–23.
24. Hashibe M, Brennan P, Benhamou S, Castellsague X, Chen C, Curado MP, Dal Maso L, Daudt AW, Fabianova E, Fernandez L, Wünsch-Filho V, Franceschi S, Hayes RB, Herrero R, Koifman S, La Vecchia C, Lazarus P, Levi F, Mates D, Matos E, Menezes A, Muscat J, Eluf-Neto J, Olshan AF, Rudnai P, Schwartz SM, Smith E, Sturgis EM, Szeszenia-Dabrowska N, Talamini R, Wei Q, Winn DM, Zaridze D, Zatonski W, Zhang ZF, Berthiller J, Boffetta P. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. J Natl Cancer Inst. 2007;99:777–89.
25. Ide R, Mizoue T, Fujino Y, Hoshiyama Y, Sakata K, Tamakoshi A, Yoshimura T, JACC Study Group. Cigarette smoking, alcohol drinking, and oral and pharyngeal cancer mortality in Japan. Oral Dis. 2008;14:314–9.
26. Purdue MP, Hashibe M, Berthiller J, La Vecchia C, Dal Maso L, Herrero R, Franceschi S, Castellsague X, Wei Q, Sturgis EM, Morgenstern H, Zhang ZF, Levi F, Talamini R, Smith E, Muscat J, Lazarus P, Schwartz SM, Chen C, Neto JE, Wünsch-Filho V, Zaridze D, Koifman S, Curado MP, Benhamou S, Matos E, Szeszenia-Dabrowska N, Olshan AF, Lence J, Menezes A, Daudt AW, Mates IN, Pilarska A, Fabianova E, Rudnai P, Winn D, Ferro G, Brennan P, Boffetta P, Hayes RB. Type of alcoholic beverage and risk of head and neck cancer – a pooled analysis within the INHANCE Consortium. Am J Epidemiol. 2009;169:132–42.
27. Hashibe M, Brennan P, Chuang SC, Boccia S, Castellsague X, Chen C, Curado MP, Dal Maso L, Daudt AW, Fabianova E, Fernandez L, Wünsch-Filho V, Franceschi S, Hayes RB, Herrero R, Kelsey K, Koifman S, La Vecchia C, Lazarus P, Levi F, Lence JJ, Mates D, Matos E, Menezes A, McClean MD, Muscat J, Eluf-Neto J, Olshan AF, Purdue M, Rudnai P, Schwartz SM, Smith E, Sturgis EM, Szeszenia-Dabrowska N, Talamini R, Wei Q, Winn DM, Shangina O, Pilarska A, Zhang ZF, Ferro G, Berthiller J, Boffetta P. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. 2009;18:541–50.
28. Lee YC, Boffetta P, Sturgis EM, Wei Q, Zhang ZF, Muscat J, Lazarus P, Matos E, Hayes RB, Winn DM, Zaridze D, Wünsch-Filho V, Eluf-Neto J, Koifman S, Mates D, Curado MP, Menezes A, Fernandez L, Daudt AW, Szeszenia-Dabrowska N, Fabianova E, Rudnai P, Ferro G, Berthiller J, Brennan P, Hashibe M. Involuntary smoking and head and neck cancer risk: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. 2008;17:1974–81.
29. Conway DI, Petticrew M, Marlborough H, Berthiller J, Hashibe M, Macpherson LM. Socioeconomic inequalities and oral cancer risk: a systematic review and meta-analysis of case-control studies. Int J Cancer. 2008;122:2811–9.
30. Boing AF, Ferreira Antunes JL, de Carvalho MB, de Góis Filho JF, Kowalski LP, Michaluart Jr P, Head and Neck Genome Project/GENCAPO, Eluf-Neto J, Boffetta P, Wünsch-Filho V. How much do smoking and alcohol consumption explain socioeconomic

inequalities in head and neck cancer risk? J Epidemiol Community Health. 2011;65:708–14.
31. Freedman ND, Park Y, Subar AF, Hollenbeck AR, Leitzmann MF, Schatzkin A, Abnet CC. Fruit and vegetable intake and head and neck cancer risk in a large United States prospective cohort study. Int J Cancer. 2008;122:2330–6.
32. Peters ES, Luckett BG, Applebaum KM, Marsit CJ, McClean MD, Kelsey KY. Dairy products, leanness and head and neck squamous cell carcinoma. Head Neck. 2008;30:1193–205.
33. Gaudet MM, Olshan AF, Chuang SC, Berthiller J, Zhang ZF, Lissowska J, Zaridze D, Winn DM, Wei Q, Talamini R, Szeszenia-Dabrowska N, Sturgis EM, Schwartz SM, Rudnai P, Eluf-Neto J, Muscat J, Morgenstern H, Menezes A, Matos E, Bucur A, Levi F, Lazarus P, La Vecchia C, Koifman S, Kelsey K, Herrero R, Hayes RB, Franceschi S, Wunsch-Filho V, Fernandez L, Fabianova E, Daudt AW, Dal Maso L, Curado MP, Chen C, Castellsague X, Benhamou S, Boffetta P, Brennan P, Hashibe M. Body mass index and risk of head and neck cancer in a pooled analysis of case-control studies in the International Head and Neck Cancer Epidemiology (INHANCE) Consortium. Int J Epidemiol. 2010;39:1091–102.
34. IARC. Betel-quid and areca-nut chewing and some areca-nut-derived nitrosamines, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 85. Lyon: IARC Press; 2004.
35. Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens – part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. Lancet Oncol. 2009;10:1033–4.
36. IARC. A review of human carcinogens: personal habits and indoor combustions, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 100E. Lyon: IARC Press; 2012.
37. Guha N, Boffetta P, Wünsch Filho V, Eluf Neto J, Shangina O, Zaridze D, Curado MP, Koifman S, Matos E, Menezes A, Szeszenia-Dabrowska N, Fernandez L, Mates D, Daudt AW, Lissowska J, Dikshit R, Brennan P. Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: results of two multicentric case-control studies. Am J Epidemiol. 2007;166:1159–73.
38. Marques LA, Eluf-Neto J, Figueiredo RA, Góis-Filho JF, Kowalski LP, Carvalho MB, Abrahão M, Wünsch-Filho V. Oral health, hygiene practices and oral cancer. Rev Saude Publica. 2008;42:471–9.
39. Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens – part B: biological agents. Lancet Oncol. 2009;10:321–2.
40. Chaturvedi AK, Engels EA, Anderson WF, Gillison ML. Incidence trends for human papillomavirus-related and – unrelated oral squamous cell carcinoma in the United States. J Clin Oncol. 2008;26:612–9.
41. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. Lancet Oncol. 2010;11:781–9.
42. Negri E, Boffetta P, Berthiller J, Castellsague X, Curado MP, Dal Maso L, Daudt AW, Fabianova E, Fernandez L, Wünsch-Filho V, Franceschi S, Hayes RB, Herrero R, Koifman S, Lazarus P, Lence JJ, Levi F, Mates D, Matos E, Menezes A, Muscat J, Eluf-Neto J, Olshan AF, Rudnai P, Shangina O, Sturgis EM, Szeszenia-Dabrowska N, Talamini R, Wei Q, Winn DM, Zaridze D, Lissowska J, Zhang ZF, Ferro G, Brennan P, La Vecchia C, Hashibe M. Family history of cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Int J Cancer. 2009;124:394–401.
43. IARC. A review of human carcinogens: biological agents, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 100B. Lyon: IARC Press; 2011.
44. Yuan JM, Wang XL, Xiang YB, Gao YT, Ross RK, Yu MC. Non-dietary risk factors for nasopharyngeal carcinoma in Shanghai, China. Int J Cancer. 2000;85:364–9.
45. Lin TM, Chen KP, Lin CC, Hsu MM, Tu SM, Chiang TC, Jung PF, Hirayama T. Retrospective study on nasopharyngeal carcinoma. J Natl Cancer Inst. 1973;51:1403–8.
46. Mabuchi K, Bross DS, Kessler II. Cigarette smoking and nasopharyngeal carcinoma. Cancer. 1985;55:2874–6.
47. Nam JM, McLaughlin JK, Blot WJ. Cigarette smoking, alcohol, and nasopharyngeal carcinoma: a case-control study among U.S. whites. J Natl Cancer Inst. 1992;84:610–22.
48. Hirayama T, Ito Y. A new view of the etiology of nasopharyngeal carcinoma. Prev Med. 1981;10:614–22.
49. Yu MC, Ho JHC, Lai SH, Henderson BE. Cantonese-style salted fish as a cause of nasopharyngeal carcinoma: report of a case-control study in Hong Kong. Cancer Res. 1986;46:956–61.
50. Garrote LF, Herrero R, Reyes RMO, Vaccarella S, Anta JL, Ferbeye L, Muñoz N, Franceschi S. Risk factors for cancer of the oral cavity and oro-pharynx in Cuba. Br J Cancer. 2001;85:46–54.
51. Menvielle G, Luce D, Goldberg P, Leclerc A. Smoking, alcohol drinking, occupational exposures and social inequalities in hypopharyngeal and laryngeal cancer. Int J Epidemiol. 2004;33:799–806.
52. Vaughan TL, Strader C, Davis S, Daling JR. Formaldehyde and cancers of the pharynx, sinus and nasal cavity: I Occupations exposures. Int J Cancer. 1986;38:677–83.
53. Merletti F, Boffetta P, Ferro G, Pisani P, Terracini B. Occupation and cancer of the oral cavity or oropharynx in Turin, Italy. Scand J Work Environ Health. 1991;17:248–54.
54. Gustavsson P, Jakobsson R, Johansson H, Lewin F, Norell S, Rutkvist LE. Occupational exposures and squamous cell carcinoma of the oral cavity, pharynx, larynx, and oesophagus: a case-control study in Sweden. Occup Environ Med. 1998;55:393–400.
55. Vlajinac HD, Marinkovic JM, Sipetic SB, Andrejic DM, Adanja BJ, Stosic-Divjak SL. Case-control study of oropharyngeal cancer. Cancer Detect Prev. 2006;30:152–7.
56. Blair A, Stewart P, O'Berg M, Gaffey W, Walrath J, Ward J, Bales R, Kaplan S, Cubit D. Mortality among industrial workers exposed to formaldehyde. J Natl Cancer Inst. 1986;76:1071–84.
57. Gardner MJ, Pannett B, Winter PD, Cruddas AM. A cohort study of workers exposed to formaldehyde in the British chemical industry: an update. Br J Ind Med. 1993;50:827–34.
58. Andjelkovich DA, Janszen DB, Brown MH, Richardson RB, Miller FJ. Mortality of iron foundry workers: IV. Analysis of a subcohort exposed to formaldehyde. J Occup Environ Med. 1995;37:826–37.
59. Marsh GM, Youk AO, Buchanich JM, Cassidy LD, Lucas LJ, Esmen NA, Gathuru IM. Pharyngeal cancer mortality among chemical plant workers exposed to formaldehyde. Toxicol Ind Health. 2002;18:257–68.
60. Coggon D, Harris EC, Poole J, Palmer KT. Extended follow-up of a cohort of British chemical workers exposed to formaldehyde. J Natl Cancer Inst. 2003;95:1608–15.
61. Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality from solid cancers among workers in formaldehyde industries. Am J Epidemiol. 2004;159:1117–30.
62. Stayner LT, Elliot L, Blade L, Keenlyside R, Halperin W. A retrospective cohort mortality study of workers exposed to formaldehyde in the garment industry. Am J Ind Med. 1988;13:667–81.
63. Pinkerton LE, Hein MJ, Stayner LT. Mortality among a cohort of garment workers exposed to formaldehyde: an update. Occup Environ Med. 2004;61:193–200.
64. Walrath J, Fraumeni Jr JF. Mortality patterns among embalmers. Int J Cancer. 1983;31:407–11.
65. Walrath J, Fraumeni Jr JF. Cancer and other causes of death among embalmers. Cancer Res. 1984;44:4638–41.
66. Stroup NE, Blair A, Erikson GE. Brain cancer and other causes of death in anatomists. J Natl Cancer Inst. 1986;77:1217–24.
67. Hayes RB, Blair A, Stewart PA, Herrick RF, Mahar H. Mortality of US embalmers and funeral directors. Am J Ind Med. 1990;18:641–52.

68. Logue JN, Barrick MK, Jessup Jr GL. Mortality of radiologists and pathologists in the Radiation Registry of Physicians. J Occup Med. 1998;28:91–9.
69. Tarvainen L, Kyyrönen P, Kauppinen T, Pukkala E. Cancer of the mouth and pharynx, occupation and exposure to chemical agents in Finland [in 1971–95]. Int J Cancer. 2008;123:653–9.
70. Innos K, Rahu M, Rahu K, Lang I, Leon DA. Wood dust exposure and cancer incidence: a retrospective cohort study of furniture workers in Estonia. Am J Ind Med. 2000;37:501–11.
71. Bosetti C, McLaughlin JK, Tarone RE, Pira E, La Vecchia C. Formaldehyde and cancer risk: a quantitative review of cohort studies through 2006. Ann Oncol. 2008;19:29–43.
72. Baan R, Grosse Y, Straif K, Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens – part F: chemical agents and related occupations. Lancet Oncol. 2009;10:1143–4.
73. IARC. IARC monographs on the evaluation of carcinogenic risks to humans, A review of human carcinogens: chemical agents and related occupations, vol. 100F. Lyon: IARC Press; 2012.
74. Decoufle P. Cancer risks associated with employment in the leather and leather products industry. Arch Environ Health. 1979;34:33–7.
75. Franco EL, Kowalski LP, Oliveira BV, Curado MP, Pereira RN, Silva ME, Fava AS, Torloni H. Risk factors for oral cancer in Brazil: a case-control study. Int J Cancer. 1989;43:992–1000.
76. Straif K, Benbrahim-Tallaa L, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens – part C: metals, arsenic, dusts, and fibres. Lancet Oncol. 2009;10:453–4.
77. IARC. IARC monographs on the evaluation of carcinogenic risks to humans, A review of human carcinogens: arsenic, metals, fibres, and dusts, vol. 100C. Lyon: IARC Press; 2012.
78. Haguenoer JM, Cordier S, Morel C, Lefebvre JL, Hemon D. Occupational risk factors for upper respiratory tract and upper digestive tract cancers. Br J Ind Med. 1990;47:380–3.
79. Vaughan TL, Davis S. Wood dust exposure and squamous cell cancers of the upper respiratory tract. Am J Epidemiol. 1991;133:560–4.
80. Andreotti M, Rodrigues AN, Cardoso LMN, Figueiredo RAO, Eluf-Neto J, Wünsch-Filho V. Ocupação e câncer da cavidade oral e orofaringe [occupational status and cancer of the oral cavity and oropharynx]. Cad Saude Publica. 2006;22:543–52 [Portuguese].
81. Jayaprakash V, Natarajan KK, Moysich KB, Rigual NR, Ramnath N, Natarajan N, Reid ME. Wood dust exposure and the risk of upper aero-digestive and respiratory cancers in males. Occup Environ Med. 2008;65:647–54.
82. Vaughan T. Occupation and squamous cell cancers of the pharynx and sinonasal cavity. Am J Ind Med. 1989;16:493–510.
83. Huebner WW, Schoenberg JB, Kelsey JL, Wilcox HB, McLaughlin JK, Greenberg RS, Preston-Martin S, Austin DF, Stemhagen A, Blot WJ, Winn DM, Fraumeni JF. Oral and pharyngeal cancer and occupation: a case-control study. Epidemiology. 1992;3:300–9.
84. Schildt EB, Eriksson M, Hardell L, Magnuson A. Occupational exposures as risk factors for oral cancer evaluated in a Swedish case-control study. Oncol Rep. 1999;6:317–20.
85. Krstev S, Stewart P, Rusiecki J, Blair A. Mortality among shipyard coast guard workers: a retrospective cohort study. Occup Environ Med. 2007;64:651–8.
86. Pukkala E, Söderholm AL, Lindqvist C. Cancers of the lip and oropharynx in different social and occupational groups in Finland. Eur J Cancer B Oral Oncol. 1994;30B:209–15.
87. Brown LM, Moradi T, Gridley G, Plato N, Dosemeci M, Fraumeni JF. Exposures in the painting trades and paint manufacturing industry and risk of cancer among men and women in Sweden. J Occup Environ Med. 2002;44:258–64.
88. Winn DM, Blot WJ, Shy CM, Fraumeni JF. Occupation and oral cancer among women in the South. Am J Ind Med. 1982;3:161–7.
89. Ji J, Hemminki K. Occupation and upper aerodigestive tract cancers: a follow-up study in Sweden. J Occup Environ Med. 2005;47:785–95.
90. Benbrahim-Tallaa L, Baan RA, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Guha N, Loomis D, Straif K. Carcinogenicity of diesel-engine and gasoline-engine exhaust and some nitroarenes. Lancet Oncol. 2012;13:663–4.
91. Attfield MD, Schleiff PL, Lubin JH, Blair A, Stewart PA, Vermeulen R, Coble JB, Silverman DT. The diesel exhaust in miners study: a cohort mortality study with emphasis on lung cancer. J Natl Cancer Inst. 2012;104:869–83.
92. Silverman DT, Samanic CM, Lubin JH, Blair AE, Stewart PA, Vermeulen R, Coble JB, Rothman N, Schleiff PL, Travis WD, Ziegler RG, Wacholder S, Attfield MD. The diesel exhaust in miners study: a nested case-control study of lung cancer and diesel exhaust. J Natl Cancer Inst. 2012;104:855–68.
93. Boffetta P, Dosemeci M, Gridley G, Bath H, Moradi T, Silverman D. Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. Cancer Causes Control. 2001;12:365–74.
94. Johnson ES. Cancer mortality among workers in the meat department of supermarkets. Occup Environ Med. 1994;51:541–7.
95. Boffetta P, Gridley G, Gustavsson P, Brennan P, Blair A, Ekström AM, Fraumeni JF. Employment as butcher and cancer risk in a record-linkage study from Sweden. Cancer Causes Control. 2000;11:627–33.
96. Oreggia F, de Stefani E, Correa P, Rivero S, Fernàndez G, Leiva J, Zavala D. Exposición ocupacional en el cancer oral, faringeo y laringeo [occupational exposure in cancer of the mouth, pharynx and larynx]. An Otorrinolaringol Ibero Am. 1989;16:365–76 [Spanish].
97. Coggon D, Wield G. Mortality of butchers and cooks identified from the 1961 census of England and Wales. Occup Environ Med. 1995;52:157–9.
98. Moulin JJ, Mur JM, Wild P, Perreaux JP, Pham QT. Oral cavity and laryngeal cancers among man-made mineral fiber production workers. Scand J Work Environ Health. 1986;12:27–31.
99. Boffetta P, Andersen A, Hansen J, Olsen JH, Plato N, Teppo L, Westerholm P, Saracci R. Cancer incidence among European man-made vitreous fiber production workers. Scand J Work Environ Health. 1999;25:222–6.
100. Marchand JL, Luce D, Leclerc A, Goldberg P, Orlowski E, Bugel I, Brugère J. Laryngeal and hypopharyngeal cancer and occupational exposure to asbestos and man-made vitreous fibers: results of a case-control study. Am J Ind Med. 2000;37:581–9.
101. Purdue MP, Järvholm B, Bergdahl IA, Hayes RB, Baris D. Occupational exposures and head and neck cancers among Swedish construction workers. Scand J Work Environ Health. 2006;32:270–5.
102. Swenberg JA, Kerns WD, Mitchell RE, Gralla EJ, Pavkov KL. Induction of squamous cell carcinomas of the rat nasal cavity by inhalation exposure to formaldehyde vapor. Cancer Res. 1980;40:3398–402.
103. Albert RE, Sellakumar AR, Laskin S, Kuschner M, Nelson A, Snyder CA. Nasal cancer in the rat induced by gaseous formaldehyde and hydrogen chloride. J Natl Cancer Inst. 1982;68:597–603.
104. West S, Hildesheim A, Dosemeci M. Non-viral risk factors nasopharyngeal carcinoma in the Philippines: results from a case-control study. Int J Cancer. 1993;55:722–7.
105. IARC. Formaldehyde, 2-butoxyethanol, and 1-tert-butoxy-2-propanol, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 88. Lyon: IARC Press; 2004.
106. Cogliano VJ, Grosse Y, Baan RA, Straif K, Secretan MB, El Ghissassi F, Working Group for Volume 88. Meeting report: summary of IARC monographs on formaldehyde, 2-butoxyethanol, and 1-tert-butoxy-2-propanol. Environ Health Perspect. 2005;113:1205–8.

107. Marsh GM, Youk AO, Buchanich JM, Erdal S, Esmen NA. Work in the metal industry and nasopharyngeal cancer mortality among formaldehyde-exposed workers. Regul Toxicol Pharmacol. 2007; 48:308–19.
108. National Toxicology Program. National Institute of Environmental Health Science. National Institute of Health. The report on carcinogens. 12th ed. Washington: National Institute of Environmental Health Science; 2011.
109. IARC. Wood dust and formaldehyde, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 62. Lyon: IARC Press; 1995.
110. Armstrong RW, Armstrong MJ, Yu MC, Henderson BE. Salted fish and inhalants as risk factors for nasopharyngeal carcinoma in Malaysian Chinese. Cancer Res. 1983;43:2967–70.
111. Armstrong RW, Imrey PB, Lye MS, Armstrong MJ, Yu MC, Sani S. Nasopharyngeal carcinoma in Malaysian Chinese: occupational exposures to particles, formaldehyde and heat. Int J Epidemiol. 2000;29:991–8.
112. Kawachi I, Pearce N, Fraser J. A New Zealand cancer registry-based study of cancer in wood workers. Cancer. 1989;64:2609–13.
113. Sriamporn S, Vatanasapt V, Pisani P, Yongchaiyudha S, Rungpitarangsri V. Environmental risk factors for nasopharyngeal carcinoma: a case-control study in Northeastern Thailand. Cancer Epidemiol Biomarkers Prev. 1992;1:345–8.
114. Vaughan TL, Stewart PA, Teschke K, Lynch CF, Swanson GM, Lyon JL, Berwick M. Occupational exposure to formaldehyde and wood dust and nasopharyngeal carcinoma. Occup Environ Med. 2000;57:376–84.
115. Siew SS, Kauppinen T, Kyyrönen P, Hiekkilä P, Pukkala E. Occupational exposure to wood dust and formaldehyde and risk of nasal, nasopharyngeal, and lung cancer among Finnish men. Cancer Manag Res. 2012;4:223–32.
116. Demers PA, Boffetta P, Kogevinas M, Blair A, Miller BA, Robinson CF, Roscoe RJ, Winter PD, Colin D, Matos E, Vainio H. Pooled reanalysis of cancer mortality among five cohorts of workers in wood-related industries. Scand J Work Environ Health. 1995;21:179–90.
117. Roush GC, Walrath J, Stayner LT, Kaplan SA, Flannery JT, Blair A. Nasopharyngeal cancer, sinonasal cancer, and occupations related to formaldehyde: a case-control study. J Natl Cancer Inst. 1987;79:1221–4.
118. Yu MC, Garabrant DH, Huang TB, Henderson BE. Occupational and other non-dietary risk factors for nasopharyngeal carcinoma in Guangzhou, China. Int J Cancer. 1990;45:1033–9.
119. Li W, Ray RM, Gao DL, Fitzgibbons ED, Seixas NS, Camp JE, Wernli KJ, Astrakianakis G, Feng Z, Thomas DB, Checkoway H. Occupational risk factors for nasopharyngeal cancer among female textile workers in Shanghai, China. Occup Environ Med. 2005;63:39–44.
120. IARC. Some flame retardants and textile chemicals, and exposures in the textile manufacturing industry, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 48. Lyon: IARC Press; 1990.
121. Henderson BE, Louie E, Jing JS, Buell P, Gardner M. Risk factors associated with nasopharyngeal carcinoma. N Engl J Med. 1976;295:1101–6.
122. IARC. Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide, IARC monographs on the evaluation of carcinogenic risk to humans, vol. 71. Lyon: IARC Press; 1999.
123. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med. 1982;3: 247–57.
124. Mirabelli MC, Hoppin JA, Tolbert PE, Herrick RF, Gnepp DR, Brann EA. Occupational exposure to chlorophenol and the risk of nasal and nasopharyngeal cancers among U.S. men aged 30 to 60. Am J Ind Med. 2000;37:532–41.
125. Malker HSR, McLaughlin JK, Weiner JA, Silverman DT, Blot WJ, Ericsson JLE, Fraumeni JF. Occupational risk factors for nasopharyngeal cancer in Sweden. Br J Ind Med. 1990;47: 213–4.
126. Tisch M, Enderle G, Zöller J, Maier H. Cancer of the oral cavity in machine workers. Laryngorhinootologie. 1996;75(12): 759–63.
127. Coble JB, Brown LM, Hayes RB, Huang WY, Winn DM, Gridley G, Bravo-Otero E, Fraumeni JF Jr. Sugarcane farming, occupational solvent exposures, and the risk of oral cancer in Puerto Rico. J Occup Environ Med. 2003;45(8):869–74.
128. Lynge E, Thygesen L. Use of surveillance systems for occupational cancer: data from the Danish National system. Int J Epidemiol. 1988;17(3):493–500.
129. Stayner L, Dankovic D, Smith R, Steenland K. Predicted lung cancer risk among miners exposed to diesel exhaust particles. Am J Ind Med. 1998;34(3):207–19.
130. Andersen ZJ, Lassen CF, Clemmensen IH. Social inequality and incidence of and survival from cancers of the mouth, pharynx and larynx in a population-based study in Denmark, 1994–2003. European Journal of Cancer. 2008;44(14):1950–61.