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A REVIEW OF HUMAN CARCINOGENS

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International Agency for Research on Cancer
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LEATHER DUST

Leather dust was considered by previous IARC Working Groups in 1980 and 1987 (IARC, 1981, 1987). Since that time, new data have become available, these have been incorporated in the *Monograph*, and taken into consideration in the present evaluation.

1. Exposure Data

1.1 Identification of the agent

Leather is the product obtained by tanning skins and hides by any one of several methods. By convention, the term 'hide' generally refers to the skin-covering of larger animals (cows, steers, horses, buffaloes, etc.), and the term 'skins', to those of smaller animals (calves, sheep, goats, pigs, etc.). Although the physical properties of these different skins vary, their basic chemical, physical, and histological characteristics are similar (IARC, 1981).

1.2 Chemical and physical properties of the agent

The skin is mainly composed of proteins, although it also contains lipids, carbohydrates, inorganic salts, and water. From the point of view of leather manufacture, the proteins of the skin are the most important components. These proteins include collagen (constitutes the bulk of the fibrous portion), and reticulin (similar to collagen, but differing in its ability to combine readily with silver salts). Elastin, also a fibrous protein, is present in very small quantities, mainly in the grain area, and to a small extent in the blood vessels. Most of the non-collagenous proteins are removed during pre-tanning operations, which are effectively a means of preparing a matrix of relatively pure collagen fibres that will subsequently be stabilized by tanning (IARC, 1981).

Tanning is any process that renders animal hides or skins imputrescible without impairing their flexibility after drying. The most commonly used tanning agents have been vegetable tannins, and basic chromium (III) sulfate.

The vegetable tannins fall into two broad chemicals groups: hydrolysable tannins and condensed tannins. Condensed tannins are more complex chemical structures, and are more likely to be found in the bark or wood of a tree, whereas the hydrolysable tannins predominate in the leaves and fruits. Hydrolysable tannins are mainly glucosides (i.e. glucose esterified with polyhydroxyl phenyl carboxylic acids, such as gallic and ellagic acids) that readily ferment to release the free acid used in primitive tanning processes to control acidity. The chemistry of condensed tannins is complex, and they have been identified as oligomers containing 4–10 flavonoid units, each containing 4–6 hydroxyl groups. Molecular weights in non-aqueous solvents range from 1000–3000, although measurements in aqueous

Table 1.1 Leather uses in relation to type of hide or skin

Skin origin	Use
Cow and steer	Shoe and boot uppers, soles, insoles, linings; patent leather; clothing; work gloves; waist belts; luggage and cases; upholstery; transmission belting; sports goods; packings
Calf	Shoe uppers; slippers; handbags; wallets; hat sweatbands; bookbindings
Sheep and lamb	Grain and suede clothing; shoe linings; slippers; dress and work gloves; hat sweatbands; bookbindings; novelties
Goat and kid	Shoe uppers and linings; dress gloves; clothing; handbags
Pig	Shoe suede uppers; dress and work gloves; wallets; fancy leather goods
Deer	Dress gloves; moccasins; clothing
Horse	Shoe uppers; straps; sports goods
Reptile	Shoe uppers; handbags; fancy leather goods

Compiled by the Working Group

solution suggest aggregation or association to give an effective molecular weight of approximately 10000 (IARC, 1981).

In chrome tanning, the trivalent chromium ions form polynuclear complexes involving, typically, four chromium atoms. Ring structures containing coordinated sulfate and hydroxyl ligands are formed, giving an effective ionic weight of approximately 800. When skins are immersed in a solution of basic chromium (III) sulfate, carboxyl side chains on the collagen enter the coordination sphere of the chromium to form an insoluble complex. This reaction, which invariably involves cross-linking, is the basis of chrome tanning (IARC, 1981).

The composition of leather used in the leather-product industries varies. For example, leather used in shoe manufacture may come from the corium part of hide skin processed during tanning. The composition of crust leather varies depending on the tanning processes (Buljan *et al.*, 2000). The reported chromium (III) levels in dust from chrome-tanned leathers have varied from 0.1% to 4.5% by weight (IARC, 1981). Leather may also contain trace amounts of chromium (VI) formed by oxidation of trivalent chromium during the tanning process. For example, in a Danish study of 43 leather products, 35% ($n = 15$) contained chromium (VI) at levels above the detection limit of 3 mg/kg (Hansen *et al.*, 2002).

1.3 Use of the agent

The hides or skins from different animals possess unique physical properties that are inherent to the particular animal or breed of animal, due largely to differences in climate, type of feed, etc., to which the animal is exposed. They are thus used for different specific purposes (Table 1.1). For more detailed descriptions, refer to the previous *IARC Monograph* (IARC, 1981).

1.4 Occupational exposure

For detailed descriptions of historical exposures to leather dust and other agents in the workplace, refer to the previous *IARC Monograph* (IARC, 1981).

1.4.1 Extent of occupational exposure

Leather and leather-product industries have moved gradually from the industrialized countries to the developing world. For example, shoe manufacture in the United States of America decreased by more than 90% during 1965–2002, and the largest footwear exporter to the USA was the People's Republic of China (Markkanen & Levenstein, 2004). China produced 40% of all prepared shoes in the world at the end of the last century (Chen & Chan, 1999), and the

number of employees in shoe manufacture in China was estimated to be about 2 million (Wang *et al.*, 2006). It was reported that Asian countries supply over 80% of the footwear traded in the world market, and the largest production comes from China followed by India, Indonesia, Viet Nam, Thailand, and Pakistan (Vachayil, 2007). In several developing countries, large and medium-sized manufacturers and retailers are known to use subcontracting practices, informal employment, and so-called home-based shoe-making. There are no reliable estimates on the informal workforce, but it is assumed to be even higher than in the formal sector (Markkanen & Levenstein, 2004). According to statistics from the International Labor Organization, other major countries producing leather products were Mexico (n = 302000 employees), Brazil (n = 305000), Indonesia (n = 279000), the Russian Federation (n = 190000), and Italy (n = 168000) (ILO, 2004).

Although several million people are working in the leather and leather-product industries, only a fraction are exposed to leather dust and other air contaminants in the workplace. No worldwide estimates of the numbers of workers exposed were available to the Working Group.

1.4.2 Levels of occupational exposure

Leather dust concentrations in selected studies published since the previous *IARC Monograph* (IARC, 1981) are presented below.

(a) Footwear industry

In a Russian mortality study of 5185 shoe-manufacturing workers employed during 1940–76, Zaridze *et al.* (2001) reported leather dust concentrations in the range of 6.5–12 mg/m^3 in the following production departments: cutting, fitting, lasting and making, and finishing. In this factory, leather dust was present as a co-exposure with solvents and chloroprene.

Shoe repairers are exposed to the dusts generated during scouring. In a Finnish study of shoe repairers from 11 shops, the time-weighted average concentrations of dust were in the range of 0.07–1.0 mg/m^3 in the vicinity of the roughing, scoring, and finishing machines. The dust concentration depended on the age and type of the machine, and the performance of its local exhaust. Electron-microscopic studies showed that the dust samples collected during the machining of shoes contained leather, polymers, and finishing materials. Several degradation products of polymers were present. Dust was formed mainly during the machining of shoes. Dust samples contained also low concentrations of insoluble chromium (0.10–0.32 μg/m^3), and hexavalent chromium (0.01–0.08 μg/m^3) (Uuklainen *et al.*, 2002).

In a Polish study, dust concentrations were higher in shoe-repair shops than in shoe manufacture. In the repair shops, the recorded concentration of inhaled dust fraction was in the range of 0.5 mg/m^3 (glueing of shoes and soles, zipper exchange, and heel abrasion) to 0.9 mg/m^3 (sewing of uppers and scouring of heels), with high short-term (> 1 minute) fluctuations in the range of 0.1–14.6 mg/m^3. In the shoe factories, the mean concentration of inhalable particles (sample duration > 8 hours) was in the range of 0.12–0.91 mg/m^3, but there were high short-term (> 1 minute) fluctuations in the range of 0.62–6.4 mg/m^3 (Stroszejn-Mrowca & Szadkowska-Stańczyk, 2003).

(b) Leather-tanning and -processing industry

Dust is produced during several processes in tanning operations: chemical dust can be produced during the loading of hide-tanning drums; and leather dust impregnated with chemicals is produced during some mechanical operations, including buffing (IARC, 1981). Total dust levels (personal and static) measured in three countries were presented in Table 2 of the previous *IARC Monograph* (IARC, 1981).

Personal levels ranged from a low of 0.1 mg/m^3 in buffing to a high of 21 mg/m^3 in semi-automatic staking (IARC, 1981).

1.4.3 Particle size distribution

Leather dusts can contain both fibres and grains; the fibres can vary from 30–1200 μm in length and from 10–30 μm in diameter. Grains are usually < 10 μm in diameter. In several surveys in Italy, more than 50% of the total dust in tanneries were reported with having a particle diameter of < 5 μm (IARC, 1981).

Particle sizes have been measured in the dust generated at various workstations in the shoe trade in Poland. The median particle diameter was about 10 μm, and the proportion of extrathoracic particles which would lodge in the nasal fossae was 35–52%, depending on the occupation (Stroszejn-Mrowca & Szadkowska-Stańczyk, 2003).

1.4.4 Exposure to other agents

(a) Footwear industry

Appendices 5 and 6 of the previous *IARC Monograph* list the various chemicals which may occur in the footwear industry. Most are different solvents used in adhesives, lacquers or cleaning agents. They include petroleum hydrocarbons, chlorinated hydrocarbons, ketones, esters, and alcohols (IARC, 1981). Benzene was previously widely used as a solvent in the shoe industry, and exposure levels during that period may have been high. For example, in Italy, the estimated concentrations of benzene in one shoe factory during 1939–65 were in the range of 0–92 ppm (300 mg/m^3). The highest exposures occurred in 1954–60, and benzene was banned by legislation in Italy in 1965 (Seniori Costantini *et al.*, 2003).

Wang *et al.* (2006) reviewed 182 articles on benzene exposure in the shoemaking industry in China during 1978–2004. In 1979–2001, 65% of the measurements exceeded the national occupational exposure limit (OEL) of 40 mg/m^3 (13 ppm), and 20% of these exceeded 500 mg/m^3 (154 ppm). Benzene levels above 1000 mg/m^3 (308 ppm) were not uncommon, and some were in excess of 4500 mg/m^3 (1385 ppm). It was also reported that, in some cases, pure benzene was used during the 1980s. The national OEL was lowered to 6 mg/m^3 (2 ppm) in 2002, but only 24% of the reported measurements in 2002–04 were below the OEL. The average benzene levels in 2002–04 were 25.1 mg/m^3 (8 ppm) in fitting uppers with soles, and 73.6 mg/m^3 (23 ppm) in the making of soles. The tasks where exposure occurred most often were fitting uppers with soles, soles-making, uppers-embedding, and uppers-making. Benzene-based adhesives are now banned in China and the national standard for benzene in adhesives is regulated to be less than 0.5% (Wang *et al.*, 2006).

At a large shoe factory in Tianjin, China, as part of a cross-sectional study, Vermeulen *et al.* (2006) collected dermal, inhalation, and urine samples (n = 113) from 70 subjects performing representative tasks and operations at the plant. Mean airborne concentrations of benzene and toluene were 1.52 (standard deviation (SD) 2.82) and 7.49 (SD 11.60) ppm, respectively.

Historically, many toluene-based adhesives manufactured in China contained about 10–30% of benzene as impurity (Chen & Chan, 1999). Exposure to other solvents varies widely, but the levels in some factories may be high. For example, in Viet Nam the national OEL of toluene 100 mg/m^3 (26 ppm) was exceeded by six times or more in different sections of a shoe-manufacturing plant in 1996. The concentration of acetone was 6–18 times the Vietnamese OEL 200 mg/m^3 (84 ppm) (Chen & Chan, 1999).

Leather dust may also contain agents originating from the processing of leather in tanneries. Levels of chromium (VI) compounds in leather dust are usually very low (see Section 1.4.2a). Leather dust may also contain dyes. Dyes which have been used in the boot and shoe

industry include seven dyes classified by IARC in Group 2B (*possibly carcinogenic to humans*): CI Acid Red 114 (CAS, 6459-94-5), auramine (CAS, 492-80-8), benzyl violet 4B (CAS, 1694-09-3), Trypan blue (CAS, 72-57-1), Ponceau MX (CAS, 3761-53-3), Ponceau 3R (CAS, 3564-09-8), and Rosaline (CAS, 632-99-5) in Magenta (IARC, 1981).

Other agents that may or may not have occurred in the footwear industry include salts of chlorophenols (preservative of leather), acrylic resins, isocyanates (reactive primers, two-part adhesives), polyurethanes and other polymers (artificial leather), chloroprene (component of polychloroprene latex), and wood dust (making of wooden shoes and models) (IARC, 1981).

(b) Leather-tanning and -processing industry

Appendices 5 and 6 of Volume 25 list chemicals that may occur in leather tanning (IARC, 1981).

Exposure to chromium (III) salts or vegetable tannins may occur during the weighing and introduction of chromium salts into rotating drums. Also, small amounts of chromium (VI) may be present. Sodium chlorophenates may be used to prevent the deterioration of leather during tanning, and to protect it from mould. Other possible exposures in the tanyard are sulfuric acid and hydrogen sulfide. If dimethylamine is used in the tanning process, *N*-nitrosodimethylamine may be produced (IARC, 1981).

The use of benzidine-based dyes has been reported in the retanning, colouring, and fat-liquoring departments of the leather-tanning and –processing industry. A wide array of chemical solvents (e.g. tetrachloroethylene, toluene, xylene, methyl ethyl ketone and isopropanol), pigments, and waxes may be used in the finishing departments. Exposure to formaldehyde may also occur (IARC, 1981).

(c) Other leather-product industries

Exposures in industries producing leather bags, wallets, suitcases, leather-wearing apparel, harnesses, leather furniture and other miscellaneous leather goods are similar to those that occur in the footwear industry (see Section 1.4.2a).

2. Cancer in Humans

The boot and shoe industry was first reviewed in the previous *IARC Monograph* IARC (1981). The then Working Group reviewed the results of case series on cancer of the nasal cavity and paranasal sinuses (referred below as sinonasal cancer), several of which compared the history of exposure among adenocarcinoma cases to other cancer controls. The then *Monograph* Working Group also reviewed the results of case series and case reports of leukaemia, as well as other studies focused on bladder, lymphatic and haematopoietic, oral/pharyngeal, lung, and stomach cancer. The Working Group concluded that "Employment in the boot and shoe industry is causally associated with the development of nasal adenocarcinomas" and that "It is most likely that exposure to leather dust plays a role in the association." The Working Group also concluded that an increased risk for other histological types of nasal cancer "may exist." They also observed that "The occurrence of leukaemia and aplastic anaemia among shoe workers exposed to benzene is well documented." They noted that excesses of bladder cancer were associated with the leather industry, but it was not clear if these could be attributed to shoe workers. They also reported that hypothesis-generating studies had observed excesses associated with cancer of the lung, oral cavity, pharynx, and stomach.

The boot and shoe industry was re-reviewed as part of the previous *IARC Monograph* Supplement 7 (IARC, 1987). In the period

following the publication of Volume 25 several new studies had been published. The Working Group for supplement 7 had access to a new retrospective cohort study, three new proportionate mortality studies, as well as new case–control studies of sinonasal cancer and other cancer sites. The conclusions of the Working Group for Supplement 7 were concordant with those of Volume 25. They also concluded that nasal adenocarcinoma was associated with the boot and shoe industry, and that the highest risk was among those with high exposures to leather dust. They also noted that there was evidence for other types of nasal cancer, and that there was further evidence of an increased risk of leukaemia associated with exposure to benzene in the industry. Mixed evidence that may indicate an excess risk of bladder cancer among shoe workers was also noted. Some associations with lung, oral, pharynx, and stomach cancer as well as kidney cancer and mesothelioma were also observed.

In this *Monograph*, studies published in the time following Supplement 7, as well as others that were not previously considered, are reviewed. Of special note are the retrospective cohort studies. The previously reviewed retrospective cohort study of workers in the boot and shoe industry in three English towns (Pippard & Acheson, 1985) has been updated and the end of follow-up extended to 1991, and the cohort study of Florence shoe workers exposed to benzene (Paci *et al.*, 1989) has also been updated and the follow-up extended to 1991 for a pooled analysis (Fu *et al.*, 1996). A US study of shoe workers focused on exposure to solvents, mostly toluene (Walker *et al.*, 1993), has also been updated (Lehman & Hein, 2006). A Russian study of shoe manufacturing workers focused on exposure to chloroprene has also been published (Bulbulyan *et al.*, 1998). The results of registry-based studies are presented in Table 2.1. Descriptive studies with information based only on death certificates are not included. The methods and results of relevant cohort and related studies are summarized in Table 2.2. Only the most recent results are presented in cases where the cohorts were updated. Also included in Table 2.2 are the methods and results of the previously reported proportionate mortality studies.

The results of relevant case–control studies of sinonasal cancer, including those previously reviewed, are summarized in Table 2.3. Studies of other respiratory cancers are summarized in Table 2.4. Case–control studies of bladder cancer are summarized in Table 2.5. Case–control studies of other cancer sites are summarized in Table 2.6. For case–control studies, only those that assessed the association with boot/shoe workers, the broader category of leather products, or with leather dust are included. Those that explicitly included tannery workers, which have a very different set of exposures, were excluded.

2.1 Sinonasal cancer

An unusual high prevalence of sinonasal cancer among boot and shoe or other leather workers observed in case series from the Northamptonshire region of England first cast suspicion on a possible association between the malignancy and the occupation (Acheson *et al.*, 1970a, b; Acheson, 1976). In the period following the previous *IARC Monograph* Supplement 7, case series continued to report cases of sinonasal cancer among workers that had been employed as shoe workers or exposed to leather dust. For example, Barbieri *et al.* (2005) reported that seven of 100 epithelial sinonasal cancer cases in the Province of Brescia, Italy, were exposed to leather dust with an average latency of 44 years. A large French adenocarcinoma case series reported that 11 of 418 cases had been exposed to leather dust, whereas 353 had been exposed to wood dust (Choussy *et al.*, 2008). [The Working Group noted that even though leather workers are the second most frequently reported group in these sinonasal cancer case series, it is difficult to interpret these results without knowing

Table 2.1 Descriptive and census-based studies

Reference, location, name of study	Population description	Exposure assessment	Organ site (ICD code)	Exposure and histology	No. of cases/ deaths	RR* (95%CI) *(unless indicated otherwise)	Adjustment for potential confounders	Comments
Acheson *et al.* (1970a, b) Incidence study of nasal cancer in Northamptonshire United Kingdom	Comparison of the estimated rate among boot and shoe trade workers (1953–67) to expected numbers based on rates in the Southern Register Areas of England	Occupational history from medical records and mailed survey or interview	Sinonasal cancer, histologically confirmed carcinomas	Boot & shoe workers			Age	
				All types	17	8 [NR]		
				Adenocarcinomas	7	35 [NR]		
				Squamous carcinomas	7	4 [NR]		
Acheson *et al.* (1981) Incidence study of nasal cancer in England and Wales United Kingdom	1602 cases diagnosed 1963–67 from The Office of Population Censuses and Surveys	Cases were categorized by occupation	Nasal cancer (160, 160.2–160.9)	All leather workers	26	4.4[a]	SIR, adjusted for snuff and tobacco	[a]indicates significance at the 0.01 level
				Shoe makers & repairers	–	7.1[a]		
				Cutters, lasters & sewers	–	4.3[a]		
Acheson *et al.* (1982) Incidence study of nasal cancer in Northamptonshire United Kingdom	Comparison of the estimated rate among boot and shoe trade workers (1953–67) to expected numbers based on rates in Northamptonshire	Occupational history from medical records & mailed survey or interview	Sinonasal cancer	Male boot & shoe workers			SIR, adjusted for age	
				All types	27	4.8 (3.5–7.9)		
				Adenocarcinomas	11	7.8 (3.7–14.3)		
				Squamous carcinomas	9	3.1 (1.4–5.9)		
				Preparation/ finishing	21	4.5 (2.8–6.8)		
Olsen (1988) Pension fund cancer incidence linkage Denmark	382 Cases from the Danish Cancer Registry diagnosed 1970–84. Registry records linked with the Danish supplementary Pension fund	Longest held occupation from Pension Fund	Sinonasal cancer (160.0, 160.2–160.9)	Manufacture of leather products and footwear (except wooden shoes)			SPIR	SPIR for women not provided
				Men	3	12.3 (3.1–33.4)		
				Women	1	0.3 expected		

Table 2.1 (continued)

Reference, location, name of study	Population description	Exposure assessment	Organ site (ICD code)	Exposure and histology	No. of cases/ deaths	RR* (95%CI) *(unless indicated otherwise)	Adjustment for potential confounders	Comments
Andersen *et al.* (1999) Census cancer incidence linkage Nordic countries	Linkage of 1970 Census with incident cancer cases diagnosed in Denmark (1971–87), Finland (1971–90), Norway (1971–91) and Sweden (1971–89)	Leather and shoe workers	All cancers (140–204)	Men employed in the category of shoe and leather workers in the 1970 census	1436	1.1 (1.0–1.1)	SIR, adjusted for age and calendar period	
			Stomach (151)		92	1.0 (0.8–1.3)		
			Colon (153)		107	1.1 (0.9–1.4)		
			Rectum (154)		80	1.1 (0.9–1.4)		
			Nose (160)		11	2.9 (1.5–5.3)		
			Larynx (161)		25	1.1 (0.7–1.6)		
			Lung (162)		264	1.1 (0.9–1.2)		
			Kidney (180.0)		41	0.9 (0.6–1.2)		
			Bladder (181)		114	1.1 (0.9–1.3)		
			Acute leukaemia (204.3)		12	0.9 (0.5–1.6)		
			Other leukaemia (204.0–2, 4)		22	1.0 (0.6–1.5)		
Vasama-Neuvonen et. al. (1999) Census cancer incidence linkage Finland	892591 occupationally active Finnish women at 1970 Census linked with the Finnish Cancer Registry for incidence of ovarian cancer cases during 1971–95	Occupations with proportion exposed ≥ 20% exposure to leather dust using FINJEM	Ovary (183)	No exposure to leather dust		1.0 (ref)	SIR stratified for birth cohort, follow-up period and social status; adjusted for mean number of children, mean age at first birth and turnover rate	Partial overlap with Andersen *et al.* (1999)
				Low (> 0.009 mg/m^3)		1.3 (1.0–1.8)		
				Medium/high		no data		
				Occupation:				
				Cutter for footwear	6	2.5 (0.9–5.4)		
				Pattern maker; cutter	27	1.7 (1.1–2.5)		
				Tanner, fellmonger, pelt dresser	3	0.8 (0.2–2.3)		
				Leather sewer	4	0.6 (0.2–1.5)		

Table 2.1 (continued)

Reference, location, name of study	Population description	Exposure assessment	Organ site (ICD code)	Exposure and histology	No. of cases/ deaths	RR* (95%CI) *(unless indicated otherwise)	Adjustment for potential confounders	Comments
Tarvainen *et al.* (2008) Census cancer incidence linkage Finland	All Finns born during 1906–45 (725868 men, 825528 women). Census data linked with the Finnish Cancer Registry 1971–95	Exposure to leather dust using FINJEM	Mouth and pharynx (exluding the nasopharynx) (140–149)	Shoe makers/ cobblers	2	17.4 (2.1–62.9)	SIR, adjusted for age, calendar period and socioeconomic status. Lag time 10 yr	Partial overlap with Andersen *et al.* (1999)
				Leather dust:				
				Low (< 5 mg/ m^3–yr)	5	0.9 (0.3–2.0)		
				Medium (5–19 mg/m^3–yr)	3	1.8 (0.4–5.1)		
				High (20+ mg/ m^3–yr)	0	0.0 (0.0–15.6)		

CI, confidence interval; FINJEM, Finnish job exposure matrix; NR, not reported; RR, relative risk; SIR, standardized incidence ratio; SPIR, standardized proportionate incidence ratio; yr, year or years

Table 2.2 Cohort studies of boot and shoe workers

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Decouflé & Walrath (1983) USA	Analysis of 3754 deaths (2144 men, 1610 women) among shoe-manufacturing workers identified using union records. Non-whites and persons of unknown sex, race or age were excluded. Deaths were listed from 1966–77 inclusive as obituaries in union newsletters	None	All cancers (140–209)	Men	464	1.10[a]	PMRs calculated from observed and expected deaths adjusted for age and calendar period	[a] indicates statistical significance at the 0.05 level. No sinonasal cancers observed vs 2.2 expected
				Women	430	1.12[a]		
			Oral & pharynx (140–149)	Men (women: $n = 0$)	17	[1.35]		
			Stomach (151)	Men	25	[1.15]		
				Women	19	[1.43]		
			Rectum (154)	Men	22	[1.57[a]]		
				Women	19	[1.81[a]]		
			Liver/gallbladder (155–6)	Men	14	[1.82[a]]		
				Women	17	[2.02[a]]		
			Larynx (161)	Men (women: $n = 1$)	3	[0.48]		
			Lung (162–163)	Men	155	[1.20[a]]		
				Women	35	[0.92]		
			Bladder (188)	Men	11	[0.72]		
				Women	7	[1.37]		
			Kidney (189)	Men	6	[0.61]		
				Women	6	[0.98]		
			Leukaemia (204–207)	Men	20	[1.20]		
				Women	16	[1.24]		
Garabrant & Wegman (1984) Massachusetts USA	Analysis of death certificates of 1962 shoe workers (1195 men, 767 women) who died in Brockton, Haverhill or Peabody (Massachusetts) during 1954–74 identified by indication of an occupation in leather or shoe manufacturing on death certificates	None	All cancers (140–209)	Men	217	1.08	PMRs calculated from observed and expected deaths adjusted for age and calendar period	No sinonasal cancers observed
				Women	131	0.95		
			Oral & pharynx (140–149)	Men (women: $n = 0$)	5	0.93		
			Digestive tract (150–159)	Men	84	1.4 (1.1–1.7)		
				Women	44	0.99		
			Stomach (151)	Men	17	1.49		
				Women	5	0.82		
			Larynx (161)	Men (women: $n = 0$)	3	1.16		
			Lung (162)	Men	55	1.04		
				Women	13	1.07		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Garabrant & Wegman (1984) (contd.)			Bladder (188)	Men	5	0.56		
				Women	7	2.5 (1.2–5.1)		
			Leukaemia (204)	Men	8	0.95		
				Women	2	0.52		
Walrath *et al.* (1987) New York State USA	Analysis of 4734 death (3512 men, 1222 women) certificates from employees of one shoe-manufacturing company identified using newspaper obituaries. Deaths occurred during 1960–79	None	All cancers (140–209)	Men	689	1.09[a]		[a] indicates statistical significance at the 0.05 level No sinonasal cancers observed vs 1.9 expected
				Women	274	1.08		
			Oral & pharynx (140–149)	Men (women: $n = 1$)	22	1.22		
			Larynx (161)	Men (women: $n = 0$)	7	0.78		
			Lung and pleura (162 163)	Men	163	0.93		
				Women	18	0.84		
			Stomach (151)	Men	71	1.83[a]		
				Women	14	1.28		
			Colon (153)	Men	100	1.53[a]		
				Women	49	1.41[a]		
			Rectum (154)	Men	33	1.42[a]		
				Women	16	1.97[a]		
			Bone (170)	Men (women: $n = 0$)	6	2.23[a]		
			Bladder (188)	Men (women: $n = 1$)	24	0.91		
			Kidney (189)	Men	16	1.16		
				Women	5	1.17		
			Multiple myeloma (203)	Men	10	1.93[a]		
				Women	8	3.46[a]		
			Leukaemia (204–207)	Men	22	0.86		
				Women	7	0.79		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Fu *et al.* (1996) United Kingdom and Italy	Pooled analysis of 2 updated shoe-manufacturing cohorts. 4215 English (follow-up 1950–91, Pippard & Acheson, 1985) and 2008 Italian (follow-up 1950–90, Paci *et al.*, 1989) shoe workers	Workers classified as exposed to leather dust or solvents based on work history (Italian) or 1939 Census (English)	All causes (001–999)	English cohort	3314	0.8 (0.8–0.8)	SMR, adjusted for sex, age, & calendar period using national rates	High exposure to benzene in the Italian cohort before 1963. Exposure to leather dust in the English cohort in the range of 0.5–7.5 mg/m^3 in 1976
				Italian cohort	333	0.9 (0.8–1.0)		
			All cancers (140–208)	English cohort	646	0.8 (0.7–0.8)		
				Italian cohort	127	1.2 (1.0–1.4)		
			Stomach (151)	English cohort	77	0.7 (0.6–0.9)		
				Italian cohort	25	1.9 (1.2–2.8)		
			Colon (153)	English cohort	57	0.9 (0.7–1.2)		
				Italian cohort	10	1.7 (0.8–3.0)		
			Rectum (154)	English cohort	51	1.1 (0.8–1.4)		
				Italian cohort	5	1.4 (0.5–3.3)		
			Pancreas (157)	English cohort	25	0.7 (0.5–1.0)		
				Italian cohort	2	0.5 (0.1–2.0)		
			Nose (160)	English cohort	12	8.1 (4.2–14.1)		
				Probable leather dust	9	11.7 (5.3–22.2)		
				High leather dust	1	25.0 (0.6–139)		
				Probable solvent	2	3.9 (0.5–13.9)		
				High solvent	0	0		
				Italian cohort	1	13.0 (0.31–70.0)		
				Probably leather dust	0	0.0		
				High leather dust	0	0.0		
				Probable solvent	1	20 (0.5–99)		
				High solvent	1	20 (0.5–99)		
			Larynx (161)	English cohort	6	0.7 (0.2–1.4)		
				Italian cohort	2	0.7 (0.1–2.5)		
			Lung (162)	English cohort	186	0.6 (0.5–0.7)		
				Italian cohort	24	1.0 (0.7–1.5)		
			Bone (170)	English cohort	6	2.1 (0.8–4.5)		
				Italian cohort	0	0		
			Bladder (188)	English cohort	34	0.8 (0.6–1.2)		
				Italian cohort	3	0.9 (0.2–2.51)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Fu *et al.* (1996) (contd.)			Kidney (189)	English cohort	8	0.7 (0.3–1.4)		
				Probable leather dust	5	0.9 (0.3–2.0)		
				High leather dust	1	3.1 (0.1–17.4)		
				Probable solvent	1	0.3 (0.01–1.4)		
				High solvent	0	0		
				Italian cohort	3	2.2 (0.5–6.3)		
				Probable leather dust	0	0 (0–18.5)		
				High leather dust	0	0 (0–92.2)		
				Probable solvent	3	3.5 (0.7–10.3)		
				High solvent	3	4.0 (0.8–11.7)		
			Multiple myeloma (203)	English cohort	7	1.0 (0.4–2.1)		
				Probable solvent	3	1.2 (0.2–3.4)		
				High solvent	1	5.3 (0.1–29.3)		
				Italian cohort	3	3.7 (0.8–10.8)		
				Probable solvent	1	2.2 (0.5–12.1)		
				High solvent	1	2.4 (0.6–13.6)		
			Leukaemia (204–208)	English cohort	14	0.9 (0.5–1.4)		
				Probable solvent	4	0.7 (0.2–1.8)		
				High solvent	0	0 (0–7.9)		
				Italian cohort	7	2.4 (1.0–5.0)		
				Probable solvent	4	2.5 (0.7–6.4)		
				High solvent	4	2.8 (0.8–7.2)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Bulbulyan *et al.* (1998) Russian Federation	Retrospective study of 5815 Russian shoe-manufacturing workers (4569 women, 616 men) employed for 2 mo during 1940–76, followed from 1979 through 1993. Workers employed in auxiliary departments and management employees were excluded	Exposure categories based on chloroprene industrial hygiene data from 1970s Chloroprene exposure: High, 20 mg/m^3 (with co-exposures of benzene) Medium, 0.4–1 mg/m^3 (with co-exposures of formaldehyde, leather dust) No exposure (with co-exposure of leather dust)	All causes (001–999)	Full cohort	900	1.03 (0.97–1.1)	SMR, adjusted for age and sex using 1992 Moscow rates. RR in dose–response analysis adjusted for sex, age, gender and calendar period	Bladder cancer among men SMR, 2.1 (95%CI: 0.4–6.1) All 5 leukaemia cases in the high chloroprene exposure group employed before 1960 RR, 4.1 (95% CI: 1.1–17), co-exposure to benzene possible
				Any chloroprene	640	1.1 (1.0–1.3)		
				Medium chloroprene	446	1.1 (0.9–1.3)		
				High chloroprene	194	1.2 (1.0–1.5)		
			All cancers (140–208)	Full cohort	265	1.2 (1.1–1.4)		
				Any chloroprene	184	1.0 (0.8–1.3)		
				Medium chloroprene	128	1.0 (0.8–1.4)		
				High chloroprene	56	1.2 (0.9–1.7)		
			Stomach (151)	Full cohort	48	1.2 (0.9–1.6)		
				Any chloroprene	36	1.3 (0.7–2.6)		
				Medium chloroprene	26	1.3 (0.7–2.7)		
				High chloroprene	10	1.3 (0.3–3.1)		
			Colon (153)	Full cohort	21	1.1 (0.7–1.7)		
				Any chloroprene	16	1.4 (0.5–3.8)		
				Medium chloroprene	8	0.9 (0.3–2.8)		
				High chloroprene	8	2.6 (0.8–7.9)		
			Rectum (154)	Full cohort	14	1.1 (0.6–1.9)		
				Any chloroprene	8	0.7 (0.2–2.0)		
				Medium chloroprene	6	0.7 (0.2–2.3)		
				High chloroprene	2	0.5 (0.1–2.7)		
			Liver (155)	Full cohort	10	2.4 (1.1–4.3)		
				Any chloroprene	9	4.2 (0.5–33)		
				Medium chloroprene	6	3.8 (0.5–34)		
				High chloroprene	3	4.9 (0.5–47)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Bulbulyan *et al.* (1998) (contd.)			Lung (162)	Full cohort	31	1.4 (0.9–2.0)		
				Any chloroprene	23	0.9 (0.4–2.2)		
				Medium chloroprene	18	0.9 (0.4–2.1)		
				High chloroprene	5	1.1 (0.4–3.5)		
			Kidney (189)	Full cohort	10	1.8 (0.9–3.4)		
				Any chloroprene	9	3.8 (0.5–31)		
				Medium chloroprene	7	4.1 (0.5–34)		
				High chloroprene	2	3.3 (0.3–37)		
			Leukaemia (204–208)	Full cohort	13	1.9 (1.0–3.3)		
				Any chloroprene	9	1.1 (0.3–3.7)		
				Medium chloroprene	4	0.7 (0.2–2.7)		
				High chloroprene	5	2.2 (0.6–8.4)		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Lehman & Hein (2006) USA	Update of Walker *et al.* (1993). An SMR analysis of 7828 shoe-manufacturing workers (2545 men, 5283 women) employed for 1 mo or more during 1940–79 at two Ohio manufacturing plants	Exposure data was based on toluene industrial hygiene data from 1970s. Toluene exposure by duration of employment for specific cancers (< 6 mo, 6 mo–1 yr, 2 yr– < 10 yr, > 10 yr)	All causes (0–999)	Men	1367	1.1 (1.0–1.1)	SMR, adjusted for age and calendar period	Results for sinonasal cancer not reported. Reported 'no evidence of any significant level of exposure to leather dust' Reported 'Benzene was not detected in these surveys and company management asserted that benzene had never been present in the solvents used at either of the plants.'
				Women	1768	1.0 (1.0–1.1)		
				Employment:				
				1 mo– < 6 mo	831	1.0 (1.0–1.1)		
				6 mo–2 yr	747	1.0 (1.0–1.1)		
				2 yr– < 10 yr	838	1.1 (1.0–1.2)		
				≥ 10 yr	719	1.0 (1.0–1.1)		
			All cancers (140–208)	Men	314	1.1 (1.0–1.2)		
				Women	482	1.0 (0.9–1.1)		
				Employment:				
				1 mo– < 6 mo	233	1.1 (1.0–1.3)		
				6 mo–2 yr	202	1.1 (0.9–1.2)		
				2 yr– < 10 yr	202	1.0 (0.9–1.2)		
				≥ 10 yr	159	0.9 (0.8–1.1)		
			Buccal cavity & pharynx (140–149)	Men	8	1.1 (0.5–2.2)		
				Women	1	0.2 (0.0–1.0)		
			Stomach (151)	Men	4	0.3 (0.1–0.8)		
				Women	6	0.5 (0.2–1.1)		
			Lung (162)	Men	138	1.4 (1.2–1.7)		
				Women	110	1.3 (1.0–1.5)		
				Employment:				
				1 mo– < 6 mo	75	1.5 (1.2–1.9)		
				6 mo–2 yr	74	1.6 (1.3–2.0)		
				2 yr– < 10 yr	52	1.1 (0.8–1.5)		
				≥ 10 yr	47	1.2 (0.9–1.5)		
			Bladder (188, 189.3–189.9)	Men	9	1.1 (0.5–2.1)		
				Women	6	1.0 (0.4–2.2		

Table 2.2 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure or Sex	Cases/ deaths	RR (95%CI) SMR	Adjustment for potential confounders	Comments
Lehman & Hein (2006) (contd.)			Kidney (189.0–189.2)	Men	6	0.9 (0.3–1.9)		
				Women	8	1.1 (0.5–2.1)		
			Leukaemia (204–208)	Men	8	0.7 (0.3 –1.4)		
				Women	19	1.2 (0.7–1.9)		
				Employment:				
				1 mo– < 6 mo	8	1.1 (0.5–2.2)		
				6 mo–2 yr	4	0.6 (0.2–1.6)		
				2 yr– < 10 yr	9	1.3 (0.6–2.5)		
				≥ 10 yr	6	1.0 (0.4–2.2)		

CI, confidence interval; mo, month or months; PMR, proportional mortality ratio; RR, relative risk; SMR, standardized mortality ratio; vs, versus; yr, year or years

Table 2.3 Case–control studies on sinonasal cancer in shoe workers or workers exposed to leather dust

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases/ deaths	OR (95%CI)	Adjustment for potential confounders	Comments
Cecchi *et al.* (1980) Hospital-based Florence, Italy 1963–77	Nose and paranasal sinuses	66 cases (46 men, 20 women) diagnosed with adenocarcinoma in Florence, records from the Otorhinolaryngology clinic and the Radiology Insititute of the University of Florence	Controls were matched to cases by sex, age (± 5 yr), place of residence, smoking habits and year of hospital admission. Each case had 2 non-cancer controls admitted to the department of internal medicine in the hospital	Social worker interview to collect data on occupational history	Shoe makers		Adenocarcinomas 7/11 cases 0/22 controls ($P < 0.001$)	Matched on sex, age, place or residence (as surrogate for SES), smoking habits and year of admission	
Hardell *et al.* (1982) Sweden 1970–79	Nose (ICD 160)	44 cases, age 25–85 and residents of Southern Sweden reported to the Swedish Cancer Registry 1970–79	541 controls referents from another study with the same region, 1970–78	Work history from mailed questionnaire	Leather work		1 case (2.8%) vs 5 controls (0.9%)		Case was 1 of 3 adenocarcinomas
Brinton *et al.* (1984) Hospital-based N. Carolina & Virginia, USA 1970–80	Nasal cavity and sinuses (160.0, 160.2–160.5, 160.8–160.9)	193 incident cases from 4 hospitals	2 controls per case matched on age, sex, race, and region. 232 hospital & 140 death certificate controls (deceased cases had 1 living & 1 dead control)	Telephone interview with subject or next-of-kin	Leather or shoe industry		1.3 (0.1–9.4)	Adjusted for sex	
					Leather exposure		0.7 (0.2–2.0)		

Table 2.3 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases/ deaths	OR (95%CI)	Adjustment for potential confounders	Comments
Merler *et al.* (1986) Vigevano, Italy 1968–82	Nasal epithelial tumours Nasal adenocarcinomas	21 cases (16 men, 5 women) from otolaryngology departments of three hospitals, the hospital cancer registry of the National Cancer Institute of Milan and city mortality records	2 controls per case were selected from the general population and matched by vital status, age, sex and residence	Interview to obtain occupational history. Estimated level of exposure based on specific tasks, workplaces, duration, technology and hygienic evaluation			All epithelial tumours: Light/Uncertain Heavy Adenocarcinoma: Light/Uncertain Heavy	Matched on age, sex, and residence	Matched and unmatched analyses yielded similar results. Unmatched results presented
						7 11 5 8	7.5 (1.8–31.7) 121 (17.3–844.3) 20.4 (2.7–152.0) 88.0 (12.1–642.0)		
Bimbi *et al.* (1988) Hospital-based Milan, Italy 1982–85	Nasal cavity and paranasal sinus (160.0–160.9) (epithelial neoplasms)	53 (40 men, 13 women) cases admitted to the Head and Neck Oncology Department of the National Institute for Study and Treatment of Cancer in Milan	217 controls selected from patients admitted in the same yr with malignant tumour of the nasopharynx, thyroid or salivary glands	Occupational history was taken from hospital records	Leather workers (3 cases, 0 controls)		RR is reported as incalculable because 0 controls reported working in the leather industry		
Loi *et al.* (1989) Hospital-based Pisa, Italy 1972–83	Nasal cavity and paranasal sinus (160.0–160.9)	38 incident cases (all male) of nasal and paranasal sinus cancer admitted to Pisa University Hospital between October 1972 and October 1983	186 hospital controls (5:1 match) matched for sex, age (± 3 yr), province of usual residence, admission date (± 6 mo), excluding nasal tumours, respiratory tract malignancies and lymphomas	Mailed-out questionnaire on employment in leather-working industries & specific occupational risk factors	Leather exposure: All tumours		8.1 (2.0–33.5)	Matched on age, sex, and residence	

Table 2.3 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases/ deaths	OR (95%CI)	Adjustment for potential confounders	Comments
Shimizu *et al.* (1989) Hospital-based Japan 1983–85	Maxillary sinus (160.2), squamous cell carcinomas only	66 cases aged 42–77 yr (45 men, 21 women) October 1983 to October 1985 six university hospitals in six prefectures	132 controls were randomly selected from the same jurisdiction as the cases residence and matched for age (± 5 yr) and sex (2:1 match)	Self-administered questionnaires, occupational exposures and other risk factors	Leather workers		2.1 (0.1–38.3)	Matched on age and sex	
Bolm-Audorff *et al.* (1989, 1990) Hospital-based Hessia, Germany 1983–85	Nasal and paranasal sinus cancer (160)	62 cases identified through 85 otorhinolaryngogical and 8 pathology departments	Patients with non-occupational bone fractures matched on age, sex, and residence	In-person interviews	Leather dust exposure		2/62 cases and 0/62 controls	Matched on age, sex, and residence	
Comba *et al.* (1992a) Hospital-based Verona, Vicenza, Siena, Italy 1982–87	Nasal cavity and paranasal sinus (160) (epithelial neoplasms)	78 cases (55 men, 23 women) from the University of Verona Institute of Pathology and ENT Clinic, ENT departments at the hospitals of Vincenza, Bussolengo, and Legnago and Institute of Pathology at the University of Siena	254 controls (184 men, 70 women) admitted to the same hospitals (excluding chronic rhinosinusal disease and actute nasal bleeding) matched for admission date, hospital, sex, age (± 5 yr) & residence	Interviews and/or mailed questionnaires collected information on occupational history with specific questions for leather workers	Leather workers Shoe makers Associated with leatherwork: Adenocarcinoma Squamous cell carcinoma	5	6.8 (2.2–15) 8.3 (1.9–36) 14.1 (2.6–76) 1.6 (0.21–12)	Matched on age, sex, and residence. 90% confidence limits used	

Table 2.3 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases/ deaths	OR (95%CI)	Adjustment for potential confounders	Comments
Comba *et al.* (1992b) Hospital-based Brescia, Italy 1980–89	Nasal cavity and paranasal sinus (160) (epithelial neoplasms)	35 cases diagnosed and treated by the ENT department of the radiotherapy unit of the Brescia Hospital	102 controls from ENT department and radiotherapy unit files with neoplastic diseases of the head and neck and matched for age (± 5 yr) and sex	Telephone interview to collect detailed occupational history, specific items related to shoe-manufacturing industries	Leather workers (1 case)		9.0	Matched on age and sex	
Magnani *et al.* (1993) Hospital-based Biella, Italy 1976–88	Nasal cavity and paranasal sinus (160.0, 160.2–160.9) (epithelial or unspecified neoplasms)	33 cases identified by the Local Health Authorities of Biella and Cossato	131 controls (4:1 match) randomly chosen and matched on age and sex admitted same hospital, same year	Mailed questionnaire to patient and next-of-kin with work history	Shoe-manufacturing or other leather industries	3	3.5 (0.6–2.-0.3)	Matched on age and sex	
Luce *et al.* (1992, 1993) Population-based France 1986–88	Nasal cavity and paranasal sinus (160.0, 160.2–160.9)	207 (167 men, 40 women) cases of primary malignancies of the nasal cavity and paranasal sinuses diagnosed between January 1986 and February 1988 at 27 hospitals in France	409 controls were obtained from: 1) hospital cancer patients, frequency-matched for age and sex 2) controls selected from lists provided by cases matching for sex, age (± 10 yr), and residence	Physician interview to collect detailed occupational history	Shoe and leather workers: Ever employed < 15 yr > 15 yr 15 yr induction Leather dust: Medium-high level	3 3	Squamous cell carcinomas: 2.1 (0.5–8.3) 1.9 (0.2–18.3) 2.3 (0.4–12.3) 2.1 (0.5–8.3) 3.1 (0.8–12.4) Adenocarcinomas: 0 cases identified	Matched on age and sex	

Table 2.3 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases/ deaths	OR (95%CI)	Adjustment for potential confounders	Comments
Battista *et al.* (1995) Population-based Italy	Nasal cavity and paranasal sinus (160)	96 cases of malignant neoplasms of the nose and paranasal sinuses diagnosed during 1982–87 in the catchment areas of the hospitals of Verona, Vicenza and Siena	378 hospital controls matched for sex, age (± 5 yr), residence and time of admission; all diagnoses were accepted except chronic rhinosinusal disease, acute nasal bleeding	Interviews or mailed questionnaires to collect work history with specific questions in particular industries	Association with occupation: Leather workers Shoe makers	 2	 6.8 (1.9–25) 8.3 (1.9–36)	Matched on age, sex, and residence. 90% confidence limits used	
Teschke *et al.* (1997) Population-based Canada	Nasal cavity and paranasal sinus (160)	All incident cases with histologically confirmed primary malignant tumours age ≥ 19 yr, 1990–92	Controls were selected randomly from 5-yr age and sex strata of the provincial voters list; frequency-matched for age and sex	Occupational histories were obtained by interview	Shoe and leather workers		0/48 cases and 6/159 controls	Adjusted for age, sex, and smoking	
't Mannetje et al. (1999a) Pooled analysis Italy, France, Netherlands, Germany, Sweden	Nasal cavity and paranasal sinus (160) Adenocarcinomas and squamous cell carcinomas	555 cases (451 men, 104 women)	1705 controls (1464 men, 241 women) from the same studies. The control:case ratio ranged from 1 to 12.3, with an overall ratio of 3.1	Interviews were conducted to collect lifetime occupational histories. Exposures assessed with a job–exposure matrix	Exposure to leather dust: Women Men Adenocarcinomas Squamous cell carcinomas	 7 26 15 10	 2.7 (0.8–9.4) 1.9 (1.1–3.4) 3.0 (1.3–6.7) 1.5 (0.7–3.0)	Adjusted for age, study, sex (when applicable), smoking (when applicable)	The attributable risk for sinonasal cancer in relation to occupation was 33%. Data from Hardell *et al.* (1982), Hayes et al. (1986), Merler *et al.* (1986), Bolm-Audorff et al. (1989), Comba *et al.* (1992a, b), Luce *et al.* (1992), and Magnani *et al.* (1993)

CI, confidence interval; OR, odds ratio; RR, relative risk; SES, socioeconomic status; yr, year or years

Table 2.4 Case–control studies on respiratory cancer in shoe workers or workers exposed to leather dust

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders
Gustavsson *et al.* (1998) Community-based Sweden 1988–91	Oral cavity (143–145), pharynx (146–149), larynx (161), oesophagus (150)	545 incident cases (all male) of squamous cell carcinomas taken from the entire population of Swedish men aged 40–79 living in Stockholm or the southern region of Sweden	641 controls (all male) frequency-matched to cases for age and region	Interviewed by nurses on smoking history, use of oral snuff, alcohol habits and occupational history	Leather dust: All sites Oral cavity Pharynx Larynx Oesophagus	 16 3 5 5 3	 2.1 (0.9–4.9) 2.2 (0.5–8.7) 2.8 (0.8–10.2) 2.1 (0.7–6.6) 2.6 (0.6–10.7)	Matched on age and region. Adjusted for alcohol and smoking
Laforest *et al.* (2000) Population-based France 1989–91	Larynx (161) and hypopharynx (148) (squamous cell only)	497 incident (all male) histologically confirmed cases from 15 French hospitals	296 cancer controls from the same medical environment as cases were matched for age and recruited during 1987–91 in the same or nearby hospitals	Occupational physician interview to collect data on lifetime occupational history. Exposures assessed with a job–exposure matrix	Exposure to leather dust: Never exposed Ever exposed Never exposed Ever exposed	 288 8 198 3	Larynx 1.0 0.9 (0.6–1.3) Hypopharynx 1.0 0.8 (0.2–4.1)	Adjusted for age, smoking and alcohol consumption
Jöckel *et al.* (2000) Pooled analysis Germany 1988–93, 1990–96	Lung (162)	4184 (3498 men, 868 women) identified during 1988–93 in Bremen, Frankfurt, and during 1990–96 in North Rhine-Westphalia, Rhineland-Palatinate, East Bavaria, the Saarland, Thuringia, and Saxony	4253 (3541 men, 712 women) population controls matched for sex, age, and region of residence	Interviewed to collect information on job history and occupational exposure	Shoe workers: Men– Ever employed Exposed > 0–3 yr > 3–30 yr > 30 yr Women– Ever employed Exposed > 0–3 yr > 3–30 yr > 30 yr	 63 18 33 12 13 7 6 0	 1.6 (1.0–2.5) 0.7 (0.3–1.4) 2.5 (1.2–5.1) 2.8 (0.9–9.2) 2.7 (0.8–8.8) 3.6 (0.4–32.1) 3.0 (0.6–14.5) no data	Adjusted for smoking and asbestos exposure

Table 2.4 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders
Matos *et al.* (2000) Hospital-based Argentina 1994–96	Lung (162)	199 male patients residents in the city or in the province of Buenos Aires and admitted for treatment in any of four hospitals	393 controls; two male control subjects hospitalized for conditions unrelated to tobacco use during the same period and residents in the same area, matched by hospital and age (± 5 yr)	Occupational history obtained by interview; occupational exposure assessed by job–exposure matrix	Occupation: leather shoes & repair Industry: leather shoes & repair	8 12	1.5 (0.5–4.2) 2.2 (0.8–5.8)	Adjusted for age group, hospital, pack–year and industries with $P < 0.05$
Boffetta *et al.* (2003) Pooled analysis France Italy, Spain, Switzerland 1980–83	Larynx (161) and hypopharynx (148)	1010 male cases with histologically confirmed epidermoid carcinomas from Turin, Varese, Pamplona, Calvados, Zaragoza, and Geneva	2176 population-based controls from the same centres, chosen census lists, electoral roles, or population registries	Occupational histories collected by interview	Larynx/ hypopharynx Shoe makers/ repair Shoe finishers Larynx Only Shoe finishers 1–10 yr 11–20 yr 21+ yr	 15 7 3 4 0	 1.2 (0.6–2.6) 3.2 (0.8–13.9) 4.4 (1.0–18.8) 4.6 2.7 0.0	Adjusted for age, centre, alcohol, and smoking

CI, confidence interval; OR, odds ratio; yr, year or years

Table 2.5 Case–control studies on cancer of the bladder in shoe workers or workers exposed to leather dust

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Cole *et al.* (1972) Population-based Massachusetts, USA	Bladder and lower urinary tract	461 histologically confirmed cases of transitional or squamous cell carcinoma	485 controls selected from the same sex and age from residents lists for the area	Lifetime work history collected by interview	Men: leather products	79	2.0 (1.4–2.9)	Age and smoking	
					Finishing & associated	44	2.7 (1.6–4.5)		
					Contact with finished	13	1.7 (0.9–3.4)		
Silverman *et al.* (1983) Population-based Detroit, USA 1977–78	Bladder and lower urinary tract	303 male, histologically confirmed transitional or squamous cell carcinoma cases identified by 60/61 hospitals in the region	296 controls selected through random-digit dialling or random selection from Health Care Finance Administration lists selected to be similar in age to cases	Lifetime work history collected by interview	Leather & leather products manufacture & repair	4	0.5 (0.1–1.6)	Unadjusted	
					Shoe repairman and bootblack	3	0.7 (0.2–3.3)		
Schoenberg *et al.* (1984) Population-based New Jersey, USA 1978–79	Bladder (188)	658 male, histologically confirmed carcinoma cases	1258 controls selected through random-digit dialling or random selection from Health Care Finance Administration lists selected to be similar in age to cases	Lifetime work history collected by interview	Leather worker	19	1.8 (0.9–3.5)	Age and smoking	
					Leather products	6	1.2 (0.4–3.6)		
					Shoe repair/ bootblack	9	1.9 (0.7–5.1)		
					Leather materials	34	1.9 (1.1–3.2)		

Table 2.5 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Marrett *et al.* (1986) Population-based 10 areas, USA 1978–79	Bladder	2982 histologically confirmed carcinoma cases	5782 controls selected through random-digit dialling or random selection from Health Care Finance Administration lists selected to be similar in age to cases	Lifetime work history collected by interview	Leather dust < 5 yr 5–14 yr 15+ yr	42 21 6 13	1.4 (0.9–2.1) 1.6 (0.9–2.8) 0.8 (0.3–1.9) 1.4 (0.7–3.0)	Unadjusted	
Silverman *et al.* (1989) Population-based 10 areas, USA 1977–78	Bladder	2100 histologically confirmed white male carcinoma cases. 75% of cases were interviewed.	3874 white male controls selected through random-digit dialling (84% interviewed) or random selection from Health Care Finance Administration lists (83% interviewed) selected to be similar in age to cases	Lifetime work history collected by interview	Leather-processing workers	13	1.2 (0.6–2.7)	Smoking	Further adjustment for age, area, education and other factors had no effect
Schumacher *et al.* (1989) Population-based Utah, USA 1977–83	Bladder (188)	417 (332 men and 85 women) cases identified by the Utah cancer registry	877 (685 men and 192 women) controls selected by random-digit dialling or randomly from Health Care Finance Administration lists, frequency-matched on sex and age	Lifetime occupational histories obtained by interview	Men: Ever Leather industry < 10 yr ≥ 10 yr > 45 yr before diagnosis Men: leather dust Women: leather dust	 2 1	1.4 (0.5–4.0) 1.4 (0.5–4.6) 1.2 (0.1–13.4) 3.0 (0.6–13.8) 0.8 (0.1–5.1) 2.3 (0.03–179)	Age, smoking, religion, education	

Table 2.5 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Siemiatycki *et al.* (1994) Population-based case-control study Montreal, Canada 1979–86	Bladder	484 cases among male residents of the Montreal area	1879 cancer cases from the same large study (all sites, excluding kidney) and 533 population controls from random-digit dialling	Extensive interview review by exposure assessment team	Leather workers: < 10 yr ≥ 10 yr Shoe makers: < 10 yr ≥ 10 yr Leather dust: Substantial Non-substantial	 12 14 5 1 8 5	 1.0 (0.5–1.9) 0.7 (0.4–1.3) 2.0 (0.7–5.6) 0.3 (0.0–2.0) 0.7 (0.3–1.5) 0.6 (0.2–1.5)	Age, ethnicity SES, smoking, and coffee consumption	
Teschke *et al.* (1997) Population-based Canada 1990–92	Bladder (188)	All incident cases (n = 105) with histologically confirmed primary malignant tumours age ≥ 19 yr	Controls (n = 139) selected randomly from 5-yr age and sex strata of provincial voters list; frequency-matched for age and sex	Occupational histories were obtained by interview	Shoe and leather workers	2	0.4 (0.1–2.6)	Age, sex, and smoking	
't Mannetje *et al.* (1999b) Re-analysis of 11 population-based studies Germany, France, Italy, Greece, Denmark, Spain, 1976–96	Bladder	700 incident female cases, age 30–79 yr	2425 population-based or hospital controls individually or frequency-matched on age group and geographic area	Lifetime occupational history	Shoe makers and leather goods makers	7	0.4 (0.2–1.1)	Age, smoking, and study centre	

Table 2.5 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Kogevinas *et al.* (2003) Re-analysis of 11 population-based studies Germany, France, Italy, Greece, Denmark, Spain, 1976–96	Bladder	3346 incident male cases, age 30–79 yr	6840 population-based or hospital controls individually or frequency-matched on age group and geographic area	Lifetime occupational history	Leather workers	48	1.3 (0.9–1.9)	Age, smoking, and study centre	Authors reported that risks were higher in studies conducted in 1990s vs 1980s
Samanic *et al.* (2008) Hospital-based Spain 1998–2000	Bladder carcinoma or in situ (1880–1889) (2337)	1219 incident cases (1067 men, 152 women, 84% participation) from 18 hospitals, age 21–80 yr	1465 controls (1105 men, 166 women, 88% participation) from the same hospitals with unrelated diseases and matched on sex, age, race/ethnicity, and hospital	Computer Assisted Interview (CAPI)	Leather, tanning and finishing Overall < 10 yr ≥ 10 yr	 28 10 18	 0.8 (0.4–1.3) 0.9 (0.4–2.2) 0.7 (0.3–1.4)	Age, region, smoking, other high-risk occupation	

CI, confidence interval; OR, odds ratio; yr, year or years; SES, socioeconomic status

Table 2.6 Other case–control studies with results for shoe workers or workers exposed to leather dust

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Mikoczy *et al.* (1996) Nested case–control study Sweden 1900–89	Pancreas, lung, soft tissue sarcoma	68 cases occurred among a cohort of 2487 workers from 3 Swedish tanneries	178 controls, 3 per case, matched on age and selected using incidence-density sampling from the same cohort	Exposure assigned by an occupational hygienist and long-term employees based on work histories	Leather dust: Pancreas Lung Soft tissue sarcoma	 8 8 NR	 7.2 (1.4–35.9) 0.7 (0.2–2.1) 3.8 (0.3–48.0)	Age, sex, and plant	All 4 pancreas cases & 1/11 controls exposed to vegetable dust No "noteworthy" associations reported for stomach, kidney, or bladder
Costantini *et al.* (2001) Multicentre (12 areas) population-based study Italy 1991–93	Lymphatic and haematopoietic cancers	Incident cases age 20–74 diagnosed during 1991–93. Composed of 811 male and 639 female NHL cases, 193 male and 172 female Hodgkin disease cases, and 383 male and 269 female leukaemia cases	1779 controls randomly selected from the general population frequency-matched on sex and age group	Interview at home to collect detailed occupational history and exposure to solvents and pesticides	Shoe makers and leather goods makers: Men– NHL and CLL Hodgkin disease All leukaemia	 30 3 7	 1.0 (0.5–1.9) 1.2 (0.3–4.0) 0.9 (0.3–2.2)	Age	Detailed results not presented for women

Table 2.6 (continued)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of cases	OR (95%CI)	Adjustment for potential confounders	Comments
Terry *et al.* (2005) Population-based USA & Canada 1986–89	Leukaemia	811 incident cases from a multisite study	637 controls recruited through random-digit dialling with frequency-matching on age, sex, race, and region	Telephone interview to gather information on employment and duration in 27 occupations	Leather/shoe industry or shoe repair (1+ yr) All leukaemia AML		 0.7 (0.3–1.5) 0.6 (0.3–1.5)	Age, sex, race, region, smoking, education, proxy response	Overall 84% response from cases, 34% from proxies. Overall 66% reponse rate with 13% surrogate respondents
Forand (2004) USA 1981–87	Leukaemia (204–208)	36 incident cases during 1981–90 among men 65 yr or older, residing in the town of Union and deceased as of August 1997	144 controls (all men) were matched by death certificate for year of death and year of birth (± 1 yr)	Occupation and employer determined from death certificates	Employment in boot & shoe industry AML Leukaemia	 13 4	 1.5 (0.7–3.1) 1.2 (0.3–4.3)	Matching on date of birth and death	

AML, acute myeloid leukaemia; CI, confidence interval; CLL, chronic lymphocytic leukaemia; NHL, non-hodgkin leukaemia; NR, not reported; OR, odds ratio; yr, year or years

the prevalence of leather work in the source population.]

Results of descriptive studies from the United Kingdom and the Nordic countries are presented in Table 2.1. High relative risks were observed, particularly when presenting results for adenocarcinoma (Acheson *et al.*, 1970a, 1982). Relative risks in more recent studies are somewhat lower, but still significantly elevated (Acheson *et al.*, 1982; Olsen, 1988; Andersen *et al.*, 1999).

A large excess was reported in the pooled English and Florence cohorts, based on 12 and one cases observed, respectively (Fu *et al.*, 1996). The risk of sinonasal cancer was associated with probable exposure to leather dust in the English cohort (Fu *et al.*, 1996), and the excess was reported to be greatest in the finishing area in the earlier report on the English cohort (Pippard & Acheson, 1985). Results for sinonasal cancer were not reported for the Russian and American shoe-manufacturing cohorts (Bulbulyan *et al.*, 1998; Lehman & Hein, 2006). The US cohort study reported there was 'no evidence of any significant level of exposure to leather dust.' No sinonasal cancer cases were reported in any of the three proportionate mortality ratio (PMR) studies. There were 2.2 and 1.9 expected cases in the studies of Decouflé & Walrath (1983) and Walrath *et al.* (1987), respectively. Expected numbers were not reported for Garabrant & Wegman (1984), see Table 2.2.

Fourteen sinonasal case–control studies and one pooled re-analysis of seven European studies were reviewed. Twelve of the 14 studies observed evidence of an excess of sinonasal cancer, although sometimes based on very small numbers. The largest odds ratios were observed in the Italian studies, with odds ratios in the range of 3.5 (95%CI: 0.6–2.3) (Magnani *et al.*, 1993) to 121 (95%CI: 17.3–844) for heavy leather dust exposure (Merler *et al.*, 1986). In addition, two studies reported an infinite risk (Cecchi *et al.*, 1980 with seven cases and zero controls; Bimbi *et al.*, 1988 with three cases and zero controls). Excesses were also observed in studies from Sweden (Hardell *et al.*, 1982), Japan (Shimizu *et al.*, 1989), Germany (Bolm-Audorff *et al.*, 1989, 1990), and France (Luce *et al.*, 1992, 1993). The only non-positive studies were from the USA (Brinton *et al.*, 1984) and Canada (Teschke *et al.*, 1997), the only North American studies. The pooled re-analysis of European case–control studies observed increased risks associated with leather dust exposure among both men (OR, 1.9; 95%CI: 1.1–3.4) and women (odds ratio [OR], 2.7; 95%CI: 0.8–9.4), see Table 2.3.

Relative risks (RR) for adenocarcinoma were consistently high in descriptive (Acheson *et al.*, 1970b, 1982) and case–control studies (Cecchi *et al.*, 1980; Merler *et al.*, 1986; Comba *et al.*, 1992a; 't Mannetje *et al.*, 1999a). However, smaller excess risks were also observed in the few cases where squamous cell carcinoma results were presented (Shimizu *et al.*, 1989; Luce *et al.*, 1992, 1993; 't Mannetje *et al.*, 1999a).

In reviewing trends from Northamptonshire, the United Kingdom, Acheson *et al.* (1982) noted that the majority of cases had been employed in the departments with the most dusty operations, and that they had much higher risk compared to other operatives (RR, 4.5; 95%CI: 2.8–6.8). The retrospective cohort study of workers employed in the British boot and shoe industry also observed the highest risks among workers employed in the jobs with the highest exposure to leather dust (Pippard & Acheson, 1985). This was also observed in the update of the British cohort for the pooled analysis (Fu *et al.*, 1996). An increased risk among workers with the highest leather dust exposure was also observed in case–control studies that reported results for leather dust exposure (Merler *et al.*, 1986; Luce *et al.*, 2002). Most other case–control studies did not provide details regarding leather dust exposure, although Loi *et al.* (1989) did report that four of five leather workers were milling-machine operators, a group thought to have high leather dust exposure. In a pooled analysis of European

studies 't Mannetje *et al.* (1999a) observed an excess of adenocarcinoma (OR, 3.0; 95%CI: 1.3–6.7) as well as a possible increase for squamous cell carcinoma (OR, 1.5; 95%CI: 0.7–3.0).

2.2 Other respiratory cancers

None of the cohort or PMR studies reported results for the pharynx alone (Table 2.2). Among the three US PMR studies, Decouflé & Walrath (1983) and Walrath *et al.* (1987) observed slightly more cases than expected, but Garabrant & Wegman (1984) observed slightly less cases than expected. Tarvainen *et al.* (2008) observed an excess of oral and pharyngeal cancer among shoe makers in Finland based on only two cases. Gustavsson *et al.* (1998) observed an excess risk of squamous cell cancer associated with leather dust for both oral (OR, 2.2; 95%CI: 0.5–8.7) and pharyngeal (OR, 2.8; 95%CI: 0.8–10.2) cancer. Laforest *et al.* (2000) found no association between exposure to leather dust and squamous cell carcinoma of the hypopharynx. Boffetta *et al.* (2003) did not report separate results for the pharynx, but observed an excess of carcinomas of the larynx and hypopharynx among shoe finishers, but not shoe makers or repairers, see Table 2.4.

No excesses of cancer of the larynx were observed in the updated English or Italian cohorts or the three PMR studies (Table 2.2). Results for cancer of the larynx were not reported in the Russian or US cohorts. Gustavsson *et al.* (1998) observed an excess risk of squamous cell carcinoma of the larynx associated with leather dust exposure (OR, 2.1; 95%CI: 0.7–6.6). Laforest *et al.* (2000) found no association (OR, 0.9; 95%CI: 0.6–1.3) between exposure to leather dust and squamous cell carcinoma of the larynx. Boffetta *et al.* (2003) observed an excess of carcinoma of the larynx among shoe finishers (OR, 4.4; 95%CI: 1.0–18.8) that was not associated with duration of employment.

No excesses of lung cancer were observed in the updated English or Italian cohorts (Fu *et al.*, 1996). An excess was observed among men, but not among women in the Russian cohort (Bulbulyan *et al.*, 1998). The excess was limited to workers exposed to non-solvents who were also identified as having potential exposure to leather dust. An excess of lung cancer among both men and women was observed in the US cohort, which was not related to duration of employment (Lehman & Hein, 2006). Using indirect methods, the authors estimated that part, but not all, of the excess could be due to increased smoking rates among blue-collar workers. Although a small, but significant excess of lung cancer was observed among men (PMR, 1.2; $P < 0.05$) in Decouflé & Walrath (1983), no such excess was observed among women in the same study or among either sex in the other two PMR studies. In a pooled analysis of two German case–control studies, an excess risk for lung cancer among both male and female shoe workers was observed (Jöckel *et al.*, 2000). An excess was also observed in a a small Argentine case–control study (Matos *et al.*, 2000).

2.3 Leukaemia

Early studies reported in the previous *IARC Monograph* identified an unusually high prevalence of leukaemia and aplastic anaemia among shoe workers exposed to benzene in both Italy and Turkey (Aksoy *et al.*, 1974, 1976; Vigliani, 1976; Vigliani & Forni, 1976; Aksoy & Erdem, 1978). An excess was also identified in the Italian cohort study where benzene exposures were reported to be very high until 1963 when regulations were changed (Paci *et al.*, 1989; Fu *et al.*, 1996). An excess of leukaemia was observed among workers in the Russian cohort compared to the general population, and all five were in the highest solvent-exposed group (Bulbulyan *et al.*, 1998). All five of these cases were employed before 1960 when co-exposure to benzene was possible.

No excess was observed in the updated English cohort (Fu *et al.*, 1996). No excess of leukaemia was observed in the US cohort study (Lehman & Hein 2006). However, benzene was not detected in industrial hygiene surveys for the US study and "company management asserted that benzene had never been present in the solvents used at either of the plants." No excesses were observed in the three US PMR studies. Andersen *et al.* (1999) also did not observe an excess in the Nordic Census to tumour registry linkage study. More recent case–control studies, including a large, multicentre Italian study with cases diagnosed during 1991–93, have not observed an excess risk for leukaemia associated with employment in the leather industries (Costantini *et al.*, 2001; Forand, 2004; Terry *et al.*, 2005).

2.4 Cancer of the bladder

An excess of cancer of the bladder was not observed in the updated British, Italian, or US cohorts (Fu *et al.*, 1996; Lehman & Hein, 2006). A significant excess of cancer of the bladder was observed among women shoe workers (PMR, 2; $P < 0.05$) in Decouflé & Walrath (1983). However, no excess was observed among men. No excess of cancer of the bladder among either sex in another PMR study was found (Walrath *et al.*, 1987). Pukkala *et al.* (2009) observed a slight excess in the Nordic Census to tumour registry linkage study (SIR, 1.08; 95%CI: 0.98–1.19).

Results for cancer of the bladder from 11 case–control studies are presented in Table 2.5. Two studies, both using broad definitions of leather work, observed strong evidence of an excess risk. Cole *et al.* (1972) observed an excess risk among leather-product workers. Schoenberg *et al.* (1984) observed an excess among men working with leather materials. Several studies observed very small excesses associated with leather work. Marrett *et al.* (1986) found a very weak association associated with leather dust. Schumacher *et al.* (1989) found very weak evidence of an excess risk associated with the leather industry, but not with leather dust. Kogevinas *et al.* (2003) observed a possible small excess among men from 11 European studies in a pooled re-analysis but 't Mannetje *et al.* (1999b) observed a decreased risk among women from the same studies. Other studies either observed no risk or a decreased risk for cancer of the bladder among leather workers. Silverman *et al.* (1983) did not observe an excess among either leather products workers or shoe repairers in Detroit, USA. Silverman *et al.* (1989) did not observe an excess among either leather processing workers from ten regions of the USA. Siemiatycki *et al.* (1994) and Teschke *et al.* (1997) found no evidence of an association with leather or shoe work. Samanic *et al.* (2008) also did not observe an excess for cancer of the bladder associated with leather industry workers in Spain. [The Working Group noted that the results of Silverman *et al.* (1983) and Marrett *et al.* (1986) were not adjusted for smoking.]

2.5 Other cancers

Excesses of other cancers have been observed in some studies, but no consistent pattern has emerged (Decouflé & Walrath, 1983; Garabrant & Wegman, 1984; Walrath *et al.*, 1987; Mikoczy *et al.*, 1996; Bulbulyan *et al.*, 1998).

2.6 Synthesis

There is consistent and strong evidence from both descriptive and case–control studies associating work in the boot and shoe industry with an increased risk of cancer of the nasal cavity and paranasal sinuses. Among those studies with histological classification of the tumours, very large excess risks were observed for sinonasal adenocarcinoma. When examined in case–control studies, the Brittish cohort study, and case series, this excess appears among workers with the highest leather dust exposure. There

is strong evidence that exposure to leather dust causes cancer of the nasal cavity and paranasal sinuses.

Clusters of leukaemia cases were reported among workers with benzene exposure in the shoe industries of Italy and Turkey in the 1970s. An excess was also observed in an Italian cohort study and among a subgroup of a Russian cohort where benzene exposure was likely to have occurred. A case–control study in Italy did not observe an excess in the industry after changes in industrial practices resulted in large reductions in benzene exposure. Benzene is already recognized as a cause of leukaemia, and is likely to be the explaination of the previous excess observed in the industry.

Several early studies reported an excess risk of bladder cancer among leather workers. Two case–control studies observed an association with the leather industry, but many more recent studies found little or no association with the leather industry when tanning was not considered. For other cancer sites, no consistent pattern of excess risk was observed or too little data was available to adequately assess causality with boot and shoe manufacturing.

3. Cancer in Experimental Animals

No data were available to the Working Group.

4. Other Relevant Data

See Section 4 of the *Monograph* on Wood Dust in this Volume.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of leather dust. Leather dust causes cancer of the nasal cavity and paranasal sinuses.

No data in experimental animals for the carcinogenicity of leather dust were available to the Working Group.

Leather dust is *carcinogenic to humans (Group 1)*.

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