Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Enterline *et al*. (1987b) 8 copper smelters in US, 1949-1980	6078 male white workers in 8 US copper smelters who worked for at least 3 years between 1 January 1946 to 31 December 1976	Employment records abstracted. Arsenic exposure estimated but details of methods unclear. Some smoking information obtained.	Lung	Arsenic time-weighted exposure ($\mu g/m^3$ year) <100 100-249 250-999 1000+	 12 18 22 18	Relative risk 0.58 0.85 1.21 1.6 [a]p=0.28	Age Calendar-year Latency period	Dose-response driven primarily by ore plant. Interaction with SO_2 explored.
Ades and Kazantzis (1988) London, UK 1970-1982	4393 men born before 1940, who worked for at least one year before 1970 at a zinc-lead-cadmium smelter and followed through 1982. Matched case-control pairs from the cohort were used for the analysis. Controls were age and employment date matched.	Exposure was assessed based on the measurements by a plant hygienist. Arsenic present as impurity in the ores at 0.4% average. Exposure to arsenic graded as 0 (background), 1-3 (low, medium, high levels). From 1981-83 arsenic levels averaged 1-3$\mu g/m^3$ in sinter and 4-7$\mu g/m^3$ in furnace.	Lung	Exposure level 0 (Background) 1 (Low) 2 (High)	 66 134 2	Relative risk 1.25 1.36 2.05 Per 10 years employment. Baseline not clear, not adjusted for other exposures.		Multiple exposures. Arsenic and lead correlated and either equally strongly associated with lung cancer risk. Exposures in early 1980s at 1-7$\mu g/m^3$

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Sobel *et al*. (1988), Michigan, US, 1919-82	611 workers who had worked for at least one month in an arsenical exposure area and did not leave the company prior to 1940. The study was an extension of a previous study by Ott *et al*.	Job classification and arsenic exposure measurement by industrial hygienist by area monitoring data and interviews conducted by veteran manufacturing personnel	Buccal cavity and pharynx Digestive system Respiratory system Prostate Bladder Kidney Brain and CNS Leukemia Haemopoeitic system	<u>Cancer type</u> All cancer Buccal cavity and pharynx Digestive system Respiratory system Prostate Bladder Kidney Brain and CNS Leukemia Haemopoeitic system Other sites	 64 0 14 35 2 1 0 1 1 4 3	<u>SMR (95% CI)</u> 138 (106-176) 0 (0-246) 106 (58-177) 225 (156-312) 65 (8-236) 72 (1-403) 0 71 (2-398) 57 (1-317) 148 (40-379) 93 (19-273)		
				<u>Respiratory cancer</u> *By duration of exposure (years)* <1 1-4 5+	 21 9 5	 214 (133-328) 218 (100-417) 313 (101-729)		
				By follow-up interval 1940-73 1974-82	 26 9	 333 (218-488) 116 (53-220)		
				By period of first arsenic exposure <1930 1930-39 1940-49 1950-56	 19 8 6 2	 358 (215-559) 242 (104-476) 126 (46-274) 91 (11-328)		
				<u>All cancer</u> *By follow-up interval* 1940-73 1974-82	 47 17	 181 (133-241) 83 (48-132)		

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Järup *et al*. (1989) Stockholm, Sweden 1928-1967 to 1981	Cohort included 3916 male workers employed for at least 3 months from 1928 to 1967. Data on work history and causes of death were obtained till December 31, 1981.	Air arsenic concentrations estimated by industrial hygienist based on measurements, amount of raw As handled, changes in production methods, and information on sick leave owing to etches and gas injuries caused by arsenic.	Lung	Intensity of exposure (mg/m^3)				
				<10 years of exposure		SMR SMR_{adj}		
				<0.1	11	330 330		
				0.1-<0.3	11	407 343		
				0.3+	18	422 412		
				Total	40	388 371		
				10-29 years of exposure				
				<0.1	5	122 125		
				0.1-<0.3	5	285 317		
				0.3+	31	565 566		
				Total	41	361 357		
				>30 years of exposure				
				<0.1	1	90 57		
				0.1-<0.3	5	565 294		
				0.3+	17	448 251		
				Total	23	397 216		
				Dose category (mg years/m^3)		SMR_0 (95% CI) SMR_1 SMR_2		
				<0.25	14	271 (148-454) 272 269		
				0.25 to <1	13	360 (192-615) 384 366		
				1 to <5	17	238 (139-382) 230 249		
				5 to <15	15	338 (189-558) 350 352		
				15 to <50	29	461 (309-662) 468 456		
				50 to <100	6	728 (267-1585) 742 750		
				100+	12	1137 (588-1986) 1152 1164		
				Total	106	372 (304-450) 379 379		

Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Kusiak *et al*. (1991) Ontario, 1977-86	54,128 men who worked in Ontario mines observed between 1955-1986. Except for uranium miners, only miners who attended the chest clinic in 1955 or later or who had been employed in a dusty job for a minimum of two weeks in mines in Ontario after 1954 and a minimum of 60 months in jobs with dust exposure in mining anywhere included in the study.	Regional values of four typical geographically distinct regions from summary studies. Chemical analytical data from a geochemical database. Weighted arsenic exposure of each employee based on the years of exposure and the level of arsenic in that mine was assessed.	Lung	<u>Mean index of exposure (% As-y)</u> *By exposure to arsenic before 1946, lagged by 20 years* 0.00 0.05 0.20 0.59 1.56 5.76 *By exposure to arsenic after 1945, lagged by 20 years* 0.00 0.05 0.19 0.60 3.00	 106 21 43 75 47 15 78 34 43 99 53	<u>SMR</u> 98 99 146 170 163 252 125 126 116 152 117		Exposure estimates based on measurements in the ores. No indication of radon and arsenic interaction.

Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Enterline *et al*. (1995) Tacoma, Washington, 1940-1964	2802 men who worked for one or more years during 1940-1964 at a copper smelter in Tacoma, Washington; mortality follow-up 1941-1976 updated until 1986; includes estimates of exposure for period 1977-1984	Air arsenic measurements from company annual reports starting in 1938 and urinary arsenic measurements identified at the department and individual levels from 1948. Urinary arsenic levels were converted to air levels.	Respiratory system	Cumulative exposure ($\mu g/m^3$ year)		SMR		Different methods of exposure assessment and follow up were used at different time intervals. When environmental arsenic was measured, measurement of low exposure areas was not taken into account.
				Total cohort				
				<750	22	154.0		
				750-1,999	30	175.5		
				2,000-3,999	36	209.7		
				4,000-7,999	36	211.7		
				8,000-19,999	39	252.0		
				20,000-44,999	20	284.0		
				45,000+	5	315.7		
				Hired <1940				
				<750	2	65.0		
				750-1,999	5	68.2		
				2,000-3,999	22	246.2		
				4,000-7,999	15	149.9		
				8,000-19,999	28	255.1		
				20,000-44,999	14	251.7		
				45,000+	5	338.7		
				Hired ≥1940				
				<750	20	178.4		
				750-1,999	25	256.0		
				2,000-3,999	14	170.1		
				4,000-7,999	21	300.2		
				8,000-19,999	11	244.4		
				20,000-44,999	6	405.5		
				45,000+	0	-		
			Buccal cancer					
				<750	2	186.7		
				750-1,999	2	154.8		
				2,000-3,999	5	366.2		
				4,000-7,999	3	220.3		
				8,000-19,999	0	-		
				20,000-44,999	0	-		
				45,000+	0	-		

Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Enterline *et al*. (1995) (contd)			*Colorectal cancer*					
				<750	5	118.2		
				750-1,999	9	169.8		
				2,000-3,999	12	199.3		
				4,000-7,999	13	205.0		
				8,000-19,999	10	158.2		
				20,000-44,999	3	97.7		
				45,000+	1	137.0		
			Kidney cancer					
				<750	0	-		
				750-1,999	2	162.5		
				2,000-3,999	1	78.2		
				4,000-7,999	3	232.2		
				8,000-19,999	2	165.6		
				20,000-44,999	3	538.0		
				45,000+	0	-		
			Bone cancer					
				<750	0	-		
				750-1,999	0	-		
				2,000-3,999	0	-		
				4,000-7,999	1	470.0		
				8,000-19,999	4	1969.8		
				20,000-44,999	0	-		
				45,000+	0	-		

Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Bulbulyan *et al*. (1996) Voskresensk, Moscow, Russia, 1965-1990	Fertilization plant workers employed at least 2 years between 1945-1985 in production or other services, 2039 men, 2957 women, 84193 person years from 1965 to 1990, 320 lost to follow up	Arsenic exposure burden, Industrial hygiene survey No arsenic measurements	Stomach cancer (151), Lung cancer (162)	Cumulative exposure level (unit-year) *Stomach cancer* Unexposed ≤19 20-34 35-49 ≥50 *Lung cancer* Unexposed ≤19 20-34 35-49≥50	 55 3 3 6 7 28 6 7 2 4	Relative risk (95% CI) 1.0 0.6 (0.2-1.9) 0.8 (0.2-2.4) 1.7 (0.7-4.0) 1.9 (0.9-4.2) 1.0 1.9 (1.2-4.5) 2.8 (1.2-6.5) 0.9 (0.2-3.6) 1.4 (0.5-4.2)		Model estimates for arsenic index only. Findings insignificant without significant trend.
Qiao *et al*., (1997) Yunnan, China, 1973-1993	6000 tin miners: 1. At least 40 years old 2. Confirmed history of at least 10 years underground and/or smelting experience 3. Current or retired YTC workers 4. No proven active or verified history of previous malignancy (except non melanoma skin cancer) 5. Consenting	At the time of the study entry cohort was interviewed by a standardized questionnaire. Working level months (WLM) for each job prior to the date of entry at initial screening for both cases. Index of Arsenic Exposure Months (IAEM) which was calculated as a time weighted arsenic exposure (mg/m^3 × months)	Skin	Cumulated arsenic exposure (IAEM) 1st quartile 2nd quartile 3rd quartile 4th quartile	% of lung cancer cases[b] 2.1 18.7 45.2 34.0	Relative risk (95% CI) 1 3.15 (1.23-8.05) 5.55 (2.21-13.91) 4.94 (1.95-12.54)	Age	Not adjusted for radon.

Table 2.2. Cohort studies of arsenic exposure and cancer

Reference, study location, period	Cohort description	Exposure assessment	Organ Site (ICD code)	Exposure Categories	No. of cases/ deaths	Relative risk or SMR (95% CI)	Adjustment for potential confounders	Comments
Lubin *et al.* (2000) Montana copper smelter, 1938-63	8014 white males employed ≥ 12 months before 1957 at a Montana copper smelter	Employment records with information on work area, year started and year ended from the start of employment through September 30, 1977 Airborne arsenic measured in light, medium and heavy areas with time weighted average airborne arsenic concentration	Lung Cancer	<u>Airborne arsenic exposure (years)</u> *Light and unknown* 1-4 5-14 15-24 25-34 ≥35 *Medium* 0 1-4 5-9 ≥10 *Heavy* 0 1-4 5-9 ≥10	 63 49 39 51 50 117 79 12 44 201 30 4 15	<u>Relative risk (95% CI)</u> 1 0.95 (0.6-1.4) 1.22 (0.8-1.9) 1.86 (1.2-2.9) 1.98 (1.3-3.1) 1 1.39 (1-1.9) 1.3 (0.7-2.4) 3.01 (2.0-4.6) 1 1.11(0.8-1.6) 1.4 (0.5-3.8) 3.68 (2.1-6.4)	Age calendar year Work status Duration of exposure	

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Englyst *et al*. (2001), Sweden 1958--1987	3979 primary copper and lead smelter workers first employed for at least 1 year during 1928-1979, and also included in a blood lead register started in 1950. 15 lost to follow up, 3523 were alive and 456 were deceased at end of study on 31 December 1987. From this original cohort, Lead Subcohort 1 (710 workers of lead department and also employed at other works) and Lead Subcohort 2 (383 workers of lead department never employed at As or Nickel plant or roaster or where exposure to carcinogen was known.	Arsenic exposure via inhalation assessed based on detailed information in company occupational records and spot air sampling by company health service. At the end of 1940s concentration of airborne arsenic was 0.35-1.5 mg/m^3 at roasters and lower at As department. Exposure to As among workers in As department was estimated close to Swedish occupational exposure limit of 500$\mu g/m^3$ from 1940 to 1975 and 50$\mu g/m^3$ from 1975 to 1987. Blood lead samples were obtained once or more each year.	Malignant neoplasm (140-209); Gastrointestinal (150-154); Respiratory (160-162); Lung (1620-1621); Kidney (180); Renal pelvis, ureter, bladder (181); Brain, nervous system (193); Lymphoma, myeloma (200-203); Leukemia (204-207)	**Lead sub cohort 1** Malignant neoplasm Gastrointestinal Respiratory tract Lung Kidney Renal pelvis, ureter, bladder Brain, nervous system Lymphoma, myeloma Leukemia **Lead sub cohort 2** Malignant neoplasm Gastrointestinal Respiratory tract Lung Kidney Renal pelvis, ureter, bladder Brain, nervous system Lymphoma, myeloma Leukemia				Findings not reported specifically for arsenic. All but one of 10 lung cancer cases in sub cohorts had significant arsenic exposure.

[a]Test of heterogeneity
[b]Presented as % of lung cancer cases.
SMR_{adj} = Conventional SMRs adjusted to the lowest intensity/shortest duration exposure group
SMR_0 = No latency period
SMR_1 = 10 years minimum latency period
SMR_2 = 10 years minimum latency period, exposure lagged 5 years