Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Ecological studies						
Taiwan						
Tseng *et al*. (1968)	40 421 residents from 37 villages (SW)	Prevalence ≥ 20 years of age	Median arsenic concentrations of wells in village of residence (μg/L) < 300 300–600 > 600	428	Prevalence (per 1000) 2.6 10.1 21.4	Prevalence based on clinical examination of all households. Excludes villages with wells no longer in use or with variations in arsenic concentration (range, 1–1820 μg/L; most wells contained 400–600 μg/L arsenic)
Chen *et al*. (1985)	4 neighbouring townships on the SW coast	Mortality 1968–82	Areas hyperendemic (21 villages), endemic (25 villages) and not endemic (38 villages) for Blackfoot disease, corresponding to high, medium and low exposure	46 men 49 women	SMR (95% CI) 534 (379–689) 652 (469–835)	Mortality rates in all Taiwan as standard
Chen *et al*. (1988a)	Region endemic for Blackfoot disease (SW)	Mortality 1973–86	Median arsenic concentrations of well-water (μg/L) < 300 300–600 > 600	 Men Women Men Women Men Women	<u>Age-standardised mortality rates per 100,000</u> 1.6 1.6 10.7 10.0 28.0 15.1	Age-standardized to the 1976 world standard population
Wu *et al*. (1989)	42 villages in region endemic for Blackfoot disease (SW)	Mortality 1973–86	Median arsenic concentrations of well-water in village of residence (μg/L) in 1964–66 < 300 300–600 > 600 < 300 300–600 > 600	19 men 17 women Men Women 	Age-adjusted mortality rates per 100,000 2.03 14.01 32.41 ($p < 0.001$) 1.73 14.75 18.66 ($p < 0.001$)	Age-standardized to the 1976 world standard population

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Chen & Wang (1990)	314 precincts and townships	Mortality 1972–83	Average arsenic concentrations	NS Men Women	Increase (β) in mortality rate per 100 000 per 0.1 μg/L increase: β (SE) = 0.9 (0.2) β (SE) = 1.0 (0.2)	Multiple regression adjusted for age and indices of urbanization and industrialization. Mortality rates standardized to the 1976 world standard population
Guo *et al*. (1998)	243 townships, 11.4 million residents	Incidence 1980–87	Arsenic concentration in wells Exposure categories: > 50, 50–89, 90–169, 170–329, 330–640 and > 640 μg/L	952 men 595 women	Risk difference of 0.34/100 000 ($p < 0.01$) associated with a 1% increase in arsenic concentrations > 640 μg/L Relative risk of highest versus lowest exposure category: 14.21 in men; 19.25 in women No excess risk for other categories	Rates standardized using the 1976 world standard population. Model assumes that same number of individuals use each well.
Tsai *et al*. (1999)	Four townships (SW)	Mortality 1971–94	Area endemic for Blackfoot disease		Age- and sex-adjusted SMR (95% CI)	
				66 men	4.8 (3.7–6.2) 5.97 (4.6–7.6)	Local standard National standard
				68 women	5.7 (4.4–7.2) 6.8 (5.3–8.6)	Local standard National standard

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Guo *et al*. (2001)	243 townships, 11.4 million residents	Incidence 1980–89	Concentration of arsenic in well-water: Exposure categories (μg/L) arsenic	2369 (1415 men, 954 women) 764 BCC	Rate difference association with a 1% increase in residents with categories of arsenic (μg/L):	Cancers identified through National Cancer Registry. Models include age and urbanization index. Models assume same number of individuals use each well. BCC, basal-cell carcinoma SCC, squamous-cell carcinoma *$p < 0.05$ **$p < 0.01$
			Intercept	Men Women	0.779 –0.002	
			50–89	Men Women	0.004 –0.012	
			90–169	Men Women	–0.017 0.018	
			170–329	Men Women	0.006 0.004	
			330–640	Men Women	–0.024 0.016	
			> 640	Men Women	0.128** 0.027	
			Intercept	Men 736 SCC Women	0.821 1.488	
			50–89	Men Women	0.024 –0.006	
			90–169	Men Women	–0.026 0.006	
			170–329	Men Women	0.073** 0.016	
			330–640	Men Women	–0.100** –0.064*	
			> 640	Men Women	0.155** 0.212**	
				182 melanoma	No increase associated with melanoma	

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Guo *et al*. (2001) (contd)			Three categories of township: (1) No well with arsenic > 40 µg/L; (2) Some wells > 40 µg/L but none > 640 µg/L; (3) More wells > 640 µg/L than between 320 and 640 µg/L		Dose–response relationship between basal-cell and squamous-cell skin cancer in both men and women and in all age categories (except for basal-cell < 30 years of age, which had few subjects). No consistent increase in melanoma incidence by exposure category	
Mexico						
Cebrián *et al*. (1983)	Two rural populations in Lagunera region; 2486 residents	Prevalence (time frame not specified)	Town of El Salvador de Arriba: high exposure to arsenic (410 µg/L); town of San Jose del Vinedo: low exposure (5 µg/L)	4	High exposure: 1.4% (4 cases in 57 households and 296 individuals); low exposure: 0% (0 cases in 68 households and 318 individuals)	Epidermoid or basal-cell carcinomas detected on physical exam of every 3rd household
Chile						
Zaldívar (1974)	City of Antofagasta	Incidence of cutaneous lesions of chronic arsenic poisoning, 1968–71	Concentration of arsenic fell from 580 µg/L in 1968–69 to 8 µg/L in 1971		Incidence rates: Men: 145.5/100 000 in 1968–69, 9.1/100 000 in 1971; women: 168.0/100 000 in 1968–69 and 10.0/100 000 in 1971	
Rivara *et al*. (1997)	Regions II and VIII	Mortality 1976–92	Exposed group: Antofagasta in region II (arsenic concentration in drinking-water, 40–860 µg/L; 1950–92) Unexposed group: region VIII, no arsenic contamination (reference)	NS	SMR (95% CI) 3.2 (2.1–4.8)	
Smith *et al*. (1998)	Region II, northern Chile	Mortality 1989–93, age ≥ 30	Annual average arsenic concentrations ranging 43–569 µg/L in 1950–94	20 men 7 women	SMR (95% CI) 7.7 (4.7–11.9) 3.2 (1.3–6.6)	Age-standardized to the national rates of Chile in 1991

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
USA						
Berg & Burbank (1972)		Mortality 1950–67	Trace metals in water supplies from 10 basins throughout the USA; concentration of arsenic in water, Oct. 1962–Sept. 1967		No correlation	
Morton *et al*. (1976)	Lane County, OR	Incidence 1958–71	Mean arsenic concentration in municipal water system and single-family systems	3039	Correlation of arsenic content in drinking-water: squamous-cell carcinoma: 0.151 for men and –0.20 for women; basal-cell carcinoma: –0.064 for men and 0.10 for women	Non-melanoma cases identified by review of pathology reports
Wong *et al*. (1992)	Four counties in Montana	Incidence 1980–86	Two contaminated counties (copper smelter and copper mines); two control counties	Around 2300 in the 4 counties	Age-adjusted skin cancer incidence higher in control counties	Overall incidence rates for exposed counties within range observed for other US locations
Cohort studies						
Taiwan						
Chen *et al*. (1988b)	Four townships (SW)	Mortality 1968–83, all ages	Diagnosis of Blackfoot disease as a surrogate for high exposure to arsenic	7	SMR 28.46 ($p < 0.01$) (national standard) 4.51 ($p < 0.05$) (local standard)	871 people who developed Blackfoot disease after 1968 were followed for 15 years. National standard used for the age- and sex-standardized rates of the general Taiwanese population.
Hsueh *et al*. (1997)	Three villages in Putai township (SW)	Incidence 1989–92, age, ≥ 30 years	Duration of residence in area endemic for Blackfoot disease (years) ≥ 33 34–43 44–53 > 53	 1 4 8 20	Relative risk (95% CI) 1.0 5.01 (0.5–48.1) 4.9 (0.6–41.6) 6.8 (0.9–53.7) (p for trend = 0.07)	654 subjects (275 men and 379 women) without skin cancer followed with dermatological examinations. Total of 2239 person–years. Relative risk adjusted for age, sex and level of education

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Hsueh *et al*. (1997) (contd)			Duration of consumption of artesian well-water (years)			
			0	1	1.0	
			1–15	1	1.2 (0.4–19.7)	
			16–25	8	3.9 (0.5–32.1)	
			> 25	23	8.9 (1.1–72.9) (p for trend < 0.05)	
			Average concentration of arsenic in drinking-water (mg/L)			
			0	1	1.0	
			0.01–0.70	12	3.3 (0.4–35.8)	
			0.71–1.10	13	8.7 (1.1–65.5) (p for trend < 0.05)	
			Unknown	7	4.8 (0.6–40.4)	
			Cumulative exposure to arsenic (mg/L–years)			
			0	1	1.0	
			0.1–10.6	2	2.8 (0.3–31.9)	
			10.7–17.7	5	2.6 (0.3–22.9)	
			> 17.7	18	7.6 (0.95–60.3) (p for trend = 0.06)	
			Unknown	7	5.1 (0.6–44.4)	
			Level of serum β-carotene (μg/mL)	16 cases (61 controls)	OR (95% CI)	OR adjusted for age, sex, cumulative exposure to arsenic, serum cholesterol and triglyceride levels, cigarette smoking and alcohol drinking Incidence 14.74/1000 person–years
			≤ 0.14		1.0	
			0.15–0.18		0.4 (0.1–2.9)	
			> 0.18		0.01 (0.0–0.4) (p for trend < 0.01)	

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Case–control studies						
USA						
Karagas *et al*. (2001)	New Hampshire	Incidence 1993–96	Concentration of arsenic in toenails (μg/g)		OR (95% CI)	OR adjusted for age and sex
					Squamous-cell carcinoma	284 cases, 524 controls
			0.009–0.089	155	1.0	
			0.090–0.133	64	0.9 (0.6–1.3)	
			0.134–0.211	33	0.98 (0.6–1.6)	
			0.212–0.280	14	1.1 (0.55–2.2)	
			0.281–0.344	5	1.0 (0.3–3.0)	
			0.345–0.81	13	2.1 (0.9–4.7)	
					Basal-cell carcinoma	587 cases, 524 controls
			0.009–0.089	281	1.0	
			0.090–0.133	156	1.01 (0.8–1.4)	
			0.134–0.211	92	1.06 (0.7–1.5)	
			0.212–0.280	22	0.7 (0.4–1.3)	
			0.281–0.344	10	0.8 (0.3–1.8)	
			0.345–0.81	26	1.4 (0.7–2.8)	
Nested case–control study						
Taiwan						
Hsueh *et al*. (1995)	Three villages in Putai Township (SW)	Prevalence	Duration of residence in area endemic for Blackfoot disease (years)		OR (95% CI)	OR adjusted for age and sex; 1081 residents (468 men, 613 women) underwent a physical examination.
			≤ 45	2	1.0	
			46–49	11	5.2 (1.1–25.8)	
			≥ 50	53	8.5 (1.96–37.2)	
					p for trend < 0.05	
			Duration of drinking artesian well-water (years)			
			≤ 13	2	1.0	
			14–25	15	5.1 (1.03–24.98)	
			≥ 26	52	6.4 (1.4–27.9)	
					p for trend < 0.05	

Table 2.8. Summary of epidemiological studies of arsenic in drinking-water and skin cancer

Reference	Location	End-point	Exposure	No. of cases	Study outcome	Comments
Hsueh *et al*. (1995) (contd)			Average exposure to arsenic (ppm)			
			0	2	1.0	
			0–0.70	20	3.5 (0.7–17.0)	
			> 0.71	30	5.0 (1.1–23.8)	
			Cumulative exposure to arsenic (ppm–years)			
			≤ 4	1	1.0	
			5–24	22	8.9 (1.1–73.8)	
			≥ 25	28	13.7 (1.7–111.6)	
			Chronic hepatitis B carrier and liver function status:			
			Non-carrier with normal liver function	41	1.0	
			HBsAg carrier with normal liver function	13	0.95 (0.52-2.16)	
			Non-carrier with liver dysfunction	3	2.73 (0.69-10.88)	
			HBsAg carrier with liver dysfunction	4	6.61 (1.75-25.03) *p* for trend < 0.05	

SMR, standardized mortality ratio; CI, confidence interval; NS, not specified; OR, odds ratio