

Slides for Issue 3. Integrating Epidemiological Studies



Joyce S. Tsuji, Ph.D., DABT, Fellow ATS

Stratification is Best for Interpreting Nonlinear Factors: As and CVD by Smoking Status

Exponent



* Hazard ratios for ischemic heart disease and other heart disease adjusted for sex, age, BMI, education, changes in urinary arsenic between visits Source: Chen et al. (2011) Prospective cohort mortality study of 11,746 people in Bangladesh



Meta-Analysis of Low-Level Arsenic Exposure* and Bladder Cancer: All Participants

Study Name	Subgroup within Study	Relative Risk and 95% Cl
Bates (1995)	19–<33 mg cumulative 33–<53 mg ≥53 mg	
Karagas (2004)	0.060–0.086 µg/g toenail 0.087–0.126 µg/g 0.127–0.193 µg/g 0.194–0.277 µg/g 0.278–0.330 µg/g 0.331–2.484 µg/g	
Lewis (1999)	<1,000–5,000 ppb-years (men) <1,000–5,000 ppb-yesrs (women)	
Meliker (2010)	1–10 µg/L >10 µg/L	
Steinmaus (2003)	6.4–82.8 mg cumulative >82.8 mg	
Bates (2004)	1.1–17 µg/L 18–80 µg/L >80 µg/L	
Kurttio (1999)	0.1–0.5 μg/L ≥5 μg/L	
Michaud (2004)	0.05–0.105 µg/g toenail 0.106–0.161 µg/g >0.161 µg/g	
Chen (2010)	10–49.9 μg/L 50–99.9 μg/L	
	SRRE = 1.07 (95% CI: 0.95–1.21) P-Heterogeneity = 0.543	0.1 0.2 0.5 1 2 5 10

Source: Mink et al. (2008); Tsuji et al., (2014)



Meta-Analysis of Low-Level Arsenic Exposure and Bladder Cancer: Never Smokers

Study Name	Subgroup within Study	Relative Risk and 95% Cl
Bates (1995)	19–<33 mg cumulative 33–<53 mg ≥53 mg	
Karagas (2004)	0.060–0.086 μg/g toenail 0.087–0.126 μg/g 0.127–0.193 μg/g 0.194–0.277 μg/g	
Lewis (1999)	<1,000–5,000 ppb-years (men) <1,000–5,000 ppb-yesrs (women)	
Meliker (2010)	1–10 µg/L >10 µg/L	
Steinmaus (2003)	6.4–82.8 mg >82.8 mg cumulative	
Bates (2004)	1.1–17 µg/L 18–80 µg/L >80 µg/L	
Kurttio (1999)	0.1–0.5 μg/L ≥5 μg/L	
	SRRE = 0.85 (95% CI: 0.66–1.08) P-Heterogeneity = 0.915	0.1 0.2 0.5 1 2 5 10

Source: Mink et al. (2008); Tsuji et al., (2014)



Direct and Indirect Water Intake from Rural Bangladesh and West Bengal, India

Reference (Location)	Mean Direct Water Intake (L/day)	Dietary/Cooking Water Intake (L/day)
Hossain et al. (2013) (West Bengal, India)	3.95 men 3.03 women	2.15 men 1.81 women
Al-Amin et al. (2011) (Central Bangladesh)	3	Not reported
Chowdhury et al. (2001) (West Bengal, India)	4 men 3 women 6-10 laborers	1
Milton et al. (2006) (NW Bangladesh)	3.53	6.7 used in cooking
Ohno et al. (2007) (NW Bangladesh)	3.1 men 2.9 women	3
Smith et al. (2006) (Central Bangladesh)	3	Not reported
Watanabe et al. 2004) (NW Bangladesh)	3	1.6 men 0.95 women



Total iAs Intake from Water and Diet in Bangladesh at 100 µg/L As in Water

Source	Parameter	Value
100 µg/L As in water x 5 L/day	iAs intake from water	500 µg/day
Mean for Dhaka (Williams et al. 2006)	iAs intake from rice (80% iAs, 90% bioavail)	52.2 µg/day
Mean for Bangladesh (Williams et al. 2006)	iAs intake from vegetables	8.9 µg/day
Williams et al. (2006)	Body weight	60 kg
Total intake rate from water, rice, and vegetables divided by body weight	Total iAs dose	9.4 µg/kg-day



Difference in Folate Status (Affects Internal As⁺³ Dose): Bangladesh vs. United States

	Bangladesh	United States
Folate source	Natural	Natural, fortified foods, supplements
Stability of form of folate (FAO 2001)	Natural folate is sensitive to oxidation by heat/storage	Folic acid is very stable to oxidation
Cooking/storage practices	Less food preservation ability. Prolonged cooking of curries and rice destroys folate (Gamble et al. 2005)	Better food storage and preservation— folic acid is highly stable (FAO 2001)
Folate bioavailability (FAO 2001)	50-75% for natural folate	Nearly 100% for folic acid
Betel nut use	Prevalent (reduces folate status; synergistic with smoking)	Rare
Median folate serum level (ng/mL)	HEALS cohort without skin lesions: 3.4 (Gamble et al. 2005)	U.S. 2005-2006: 12.2; <1% are < 3 (McDonald et al. 2008)



Dose-Response for Arsenic in Tap Water and IQ Test Scores for Children in Maine?

