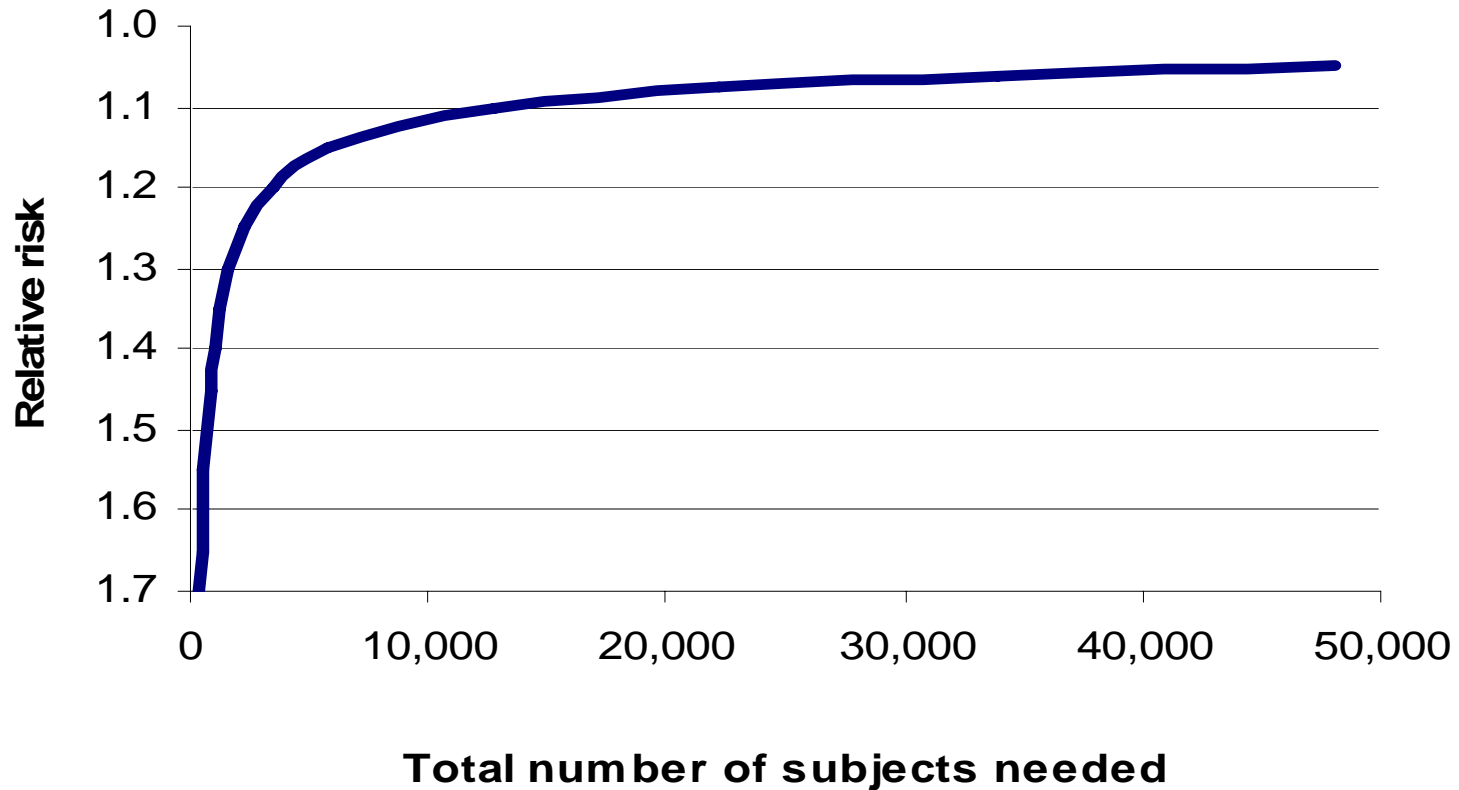


# Problems with low exposure studies

- Latency of arsenic caused cancer is 30 years or more, so assessing past (not current) exposure is important
- Migration is high in the US
- Multiple water sources
- Hair or nails only assesses exposure for about the last one year, can be external contamination
- Epidemiology is not sensitive: Detecting cancer risks at low exposures (i.e. detecting RRs of 1.1) requires incredibly large studies

**Figure 4. Number of subjects needed in a lung and bladder cancer case-control study in order to detect various levels of relative risk with 80% statistical power**  
(2 controls per case;  $z = 1.645$  with an alpha of 0.05; proportion of controls exposed = 40%)



# Important issues when designing studies of arsenic related health effects

**Is there enough statistical power?**

**Can we accurately assess past exposure?**

# Some other health effects of ingested arsenic

Non-malignant pulmonary disease

Reproductive effects

Cognitive developmental effects

Susceptible subpopulations

- Genetics

- Metabolism

- Children

- Other



# DOES INGESTED ARSENIC CAUSE NON-MALIGNANT LUNG DISEASE?

108 people with arsenic-caused skin lesions

Number with chronic cough

33 (31%)

OR = 3.2 (1.7-6.1)

150 people without arsenic-caused skin lesions

18 (12%)



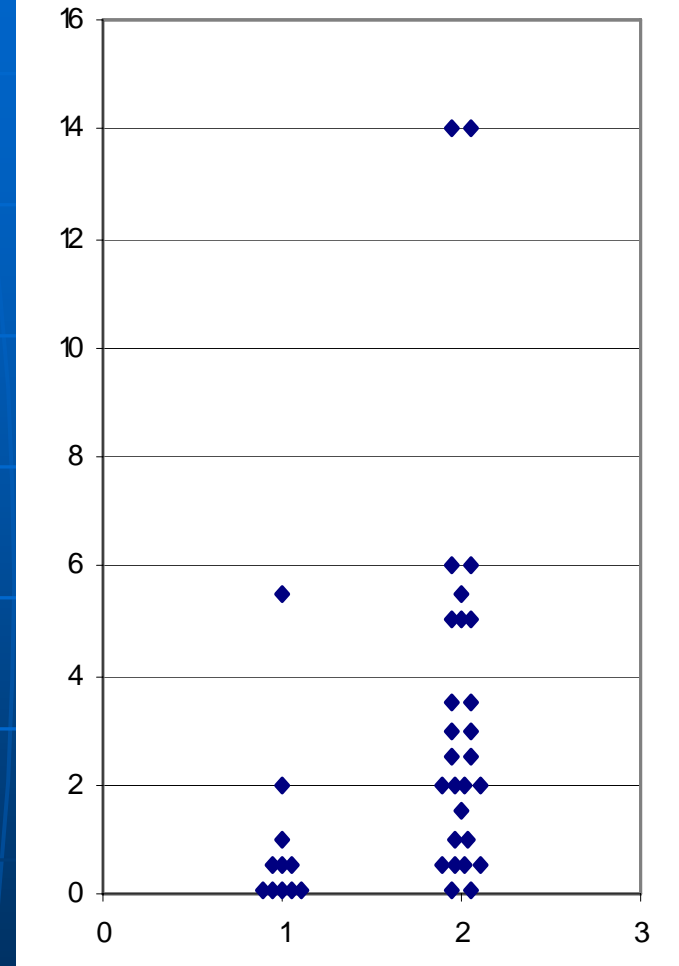
# Bronchiectasis

Those with chronic cough



Lung CT scans

Average bronchiectasis severity scores



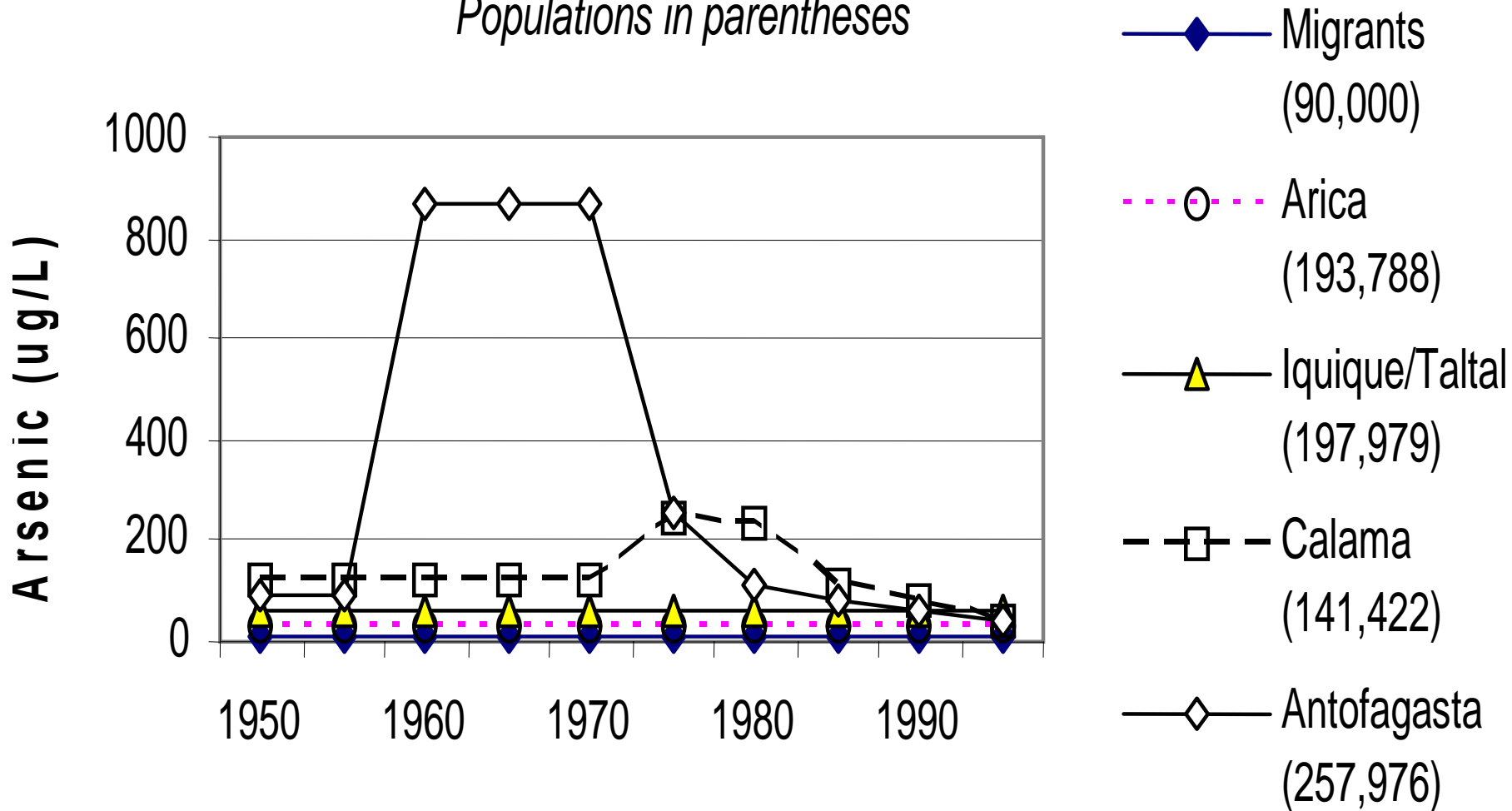
No skin lesions (n = 11)

With skin lesions (n = 27)

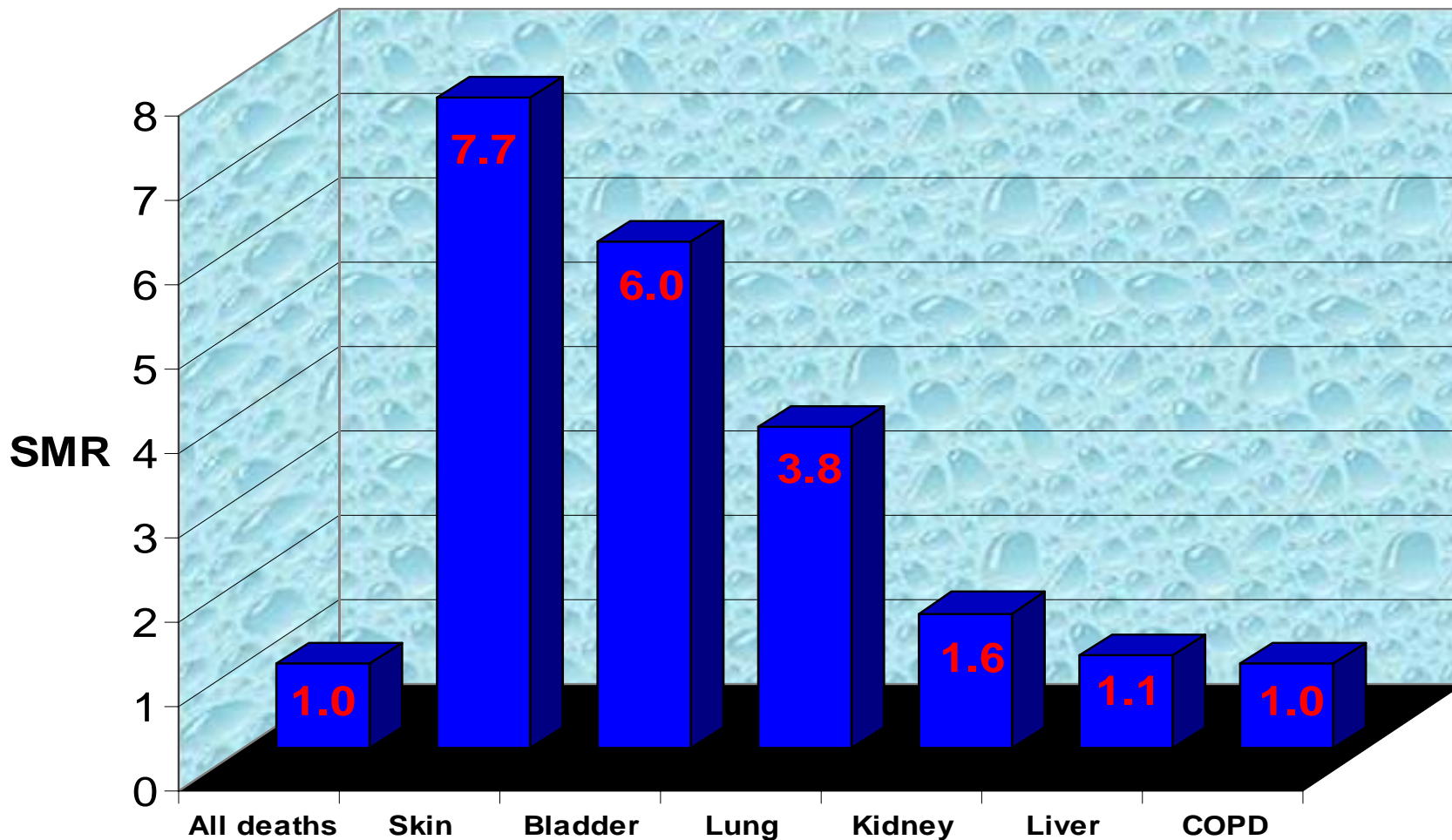
Guha-Mazumder, DN; Steinmaus, C; Bhattacharya, C; von Ehrenstein, O; Ghosh, N; MBBS; Gotway, M; Sil, A; Balmes, J; Haque, R; Hira-Smith, M; Smith, AH. Increased Risk of Bronchiectasis in Persons with Skin Lesions Due to Arsenic in Drinking Water in West Bengal, India (In press, Epidemiology)

**Figure 2. Arsenic concentrations by year in all major population centers in Regions I and II**

*Populations in parentheses*



# Cancer standardized mortality ratios (SMRs) in Region II, Chile, 1989-93





# MORTALITY FOR **MEN** AGED 30 AND OVER IN REGION II OF CHILE, 1989-1993

Age Group	30-39	40-49	50-59	60-69	70-79	SMR	p value
<b>LUNG</b>							
Observed	14	48	142	177	129		
Expected	1.2	8.1	28.5	61.8	32.1		
O/E	11.7	5.9	4.9	2.9	4.0	3.8	p<0.001
<b>SKIN</b>							
Observed	0	1	3	7	3		
Expected	0	0.2	0	0.7	0.8		
O/E	0	5.0	-	10.0	3.8	7.7	p<0.001
<b>COPD</b>							
Observed	4	4	18	34	34		
Expected	0.8	2.8	9.6	33.1	45.5		
O/E	5.0	1.4	1.9	1.0	0.7	1.0	p=0.926

# MORTALITY FOR **WOMEN** AGED 30 AND OVER IN REGION II OF CHILE, 1989-1993

Age Group	30-39	40-49	50-59	60-69	70-79	SMR	p value
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## LUNG

Observed	5	23	21	41	47		
Expected	1.2	3.0	8.0	16.0	13.3		
O/E	4.2	7.7	2.6	2.6	3.5	3.1	p<0.001

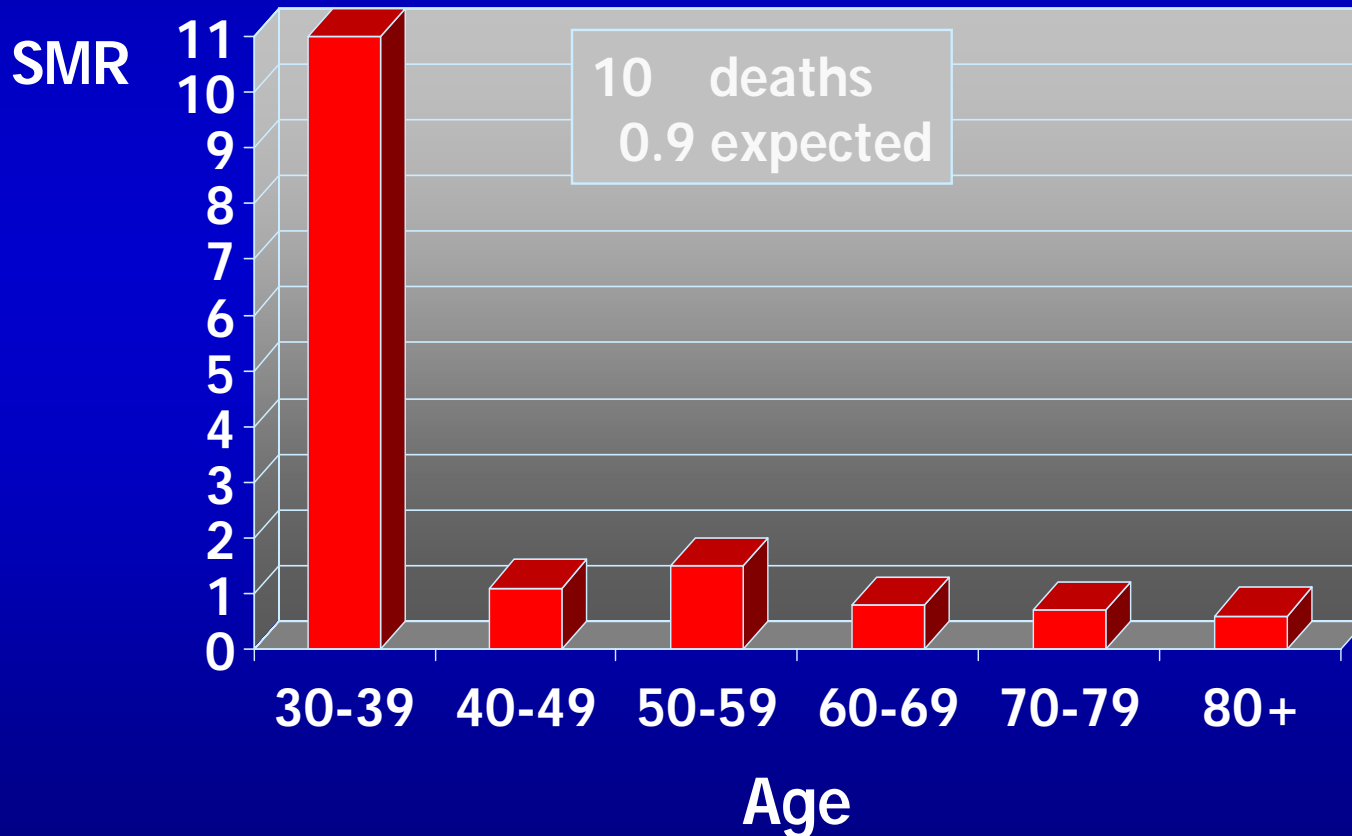
## SKIN

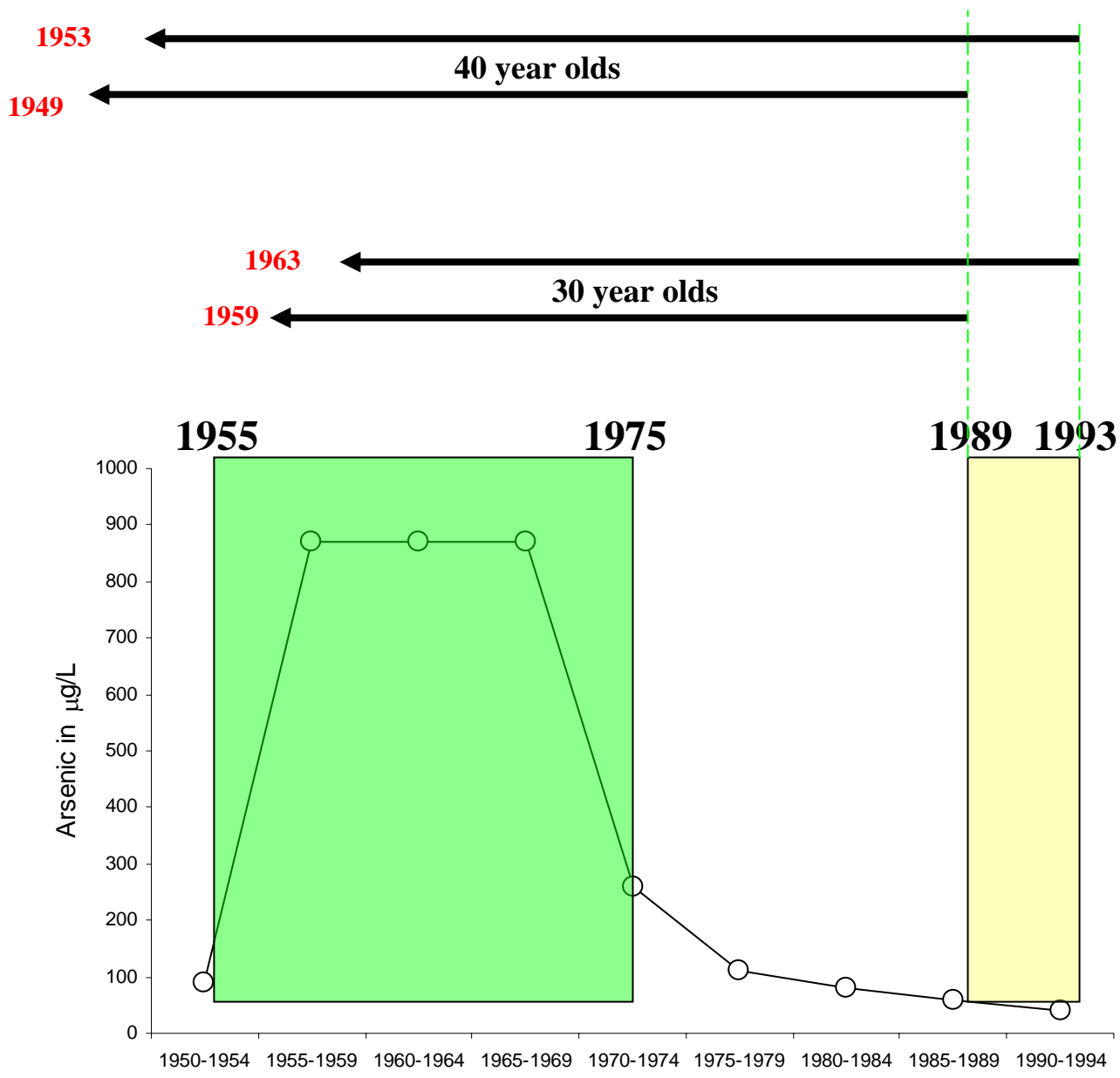
Observed	0	0	1	3	0		
Expected	0	0	0.3	0.3	0.2		
O/E	0	0	3.3	10	0	3.2	p=0.016

## COPD

Observed	6	1	6	7	16		
Expected	0.1	1.9	6.2	16.4	29		
O/E	60.0	0.5	1.0	0.4	0.6	0.6	p<0.001

# MORTALITY FROM COPD, REGION II, CHILE, MEN AND WOMEN COMBINED





Subjects age 30-40 during 1989-1993 were in utero or young children at the time of peak exposures in Antofagasta, Region II.

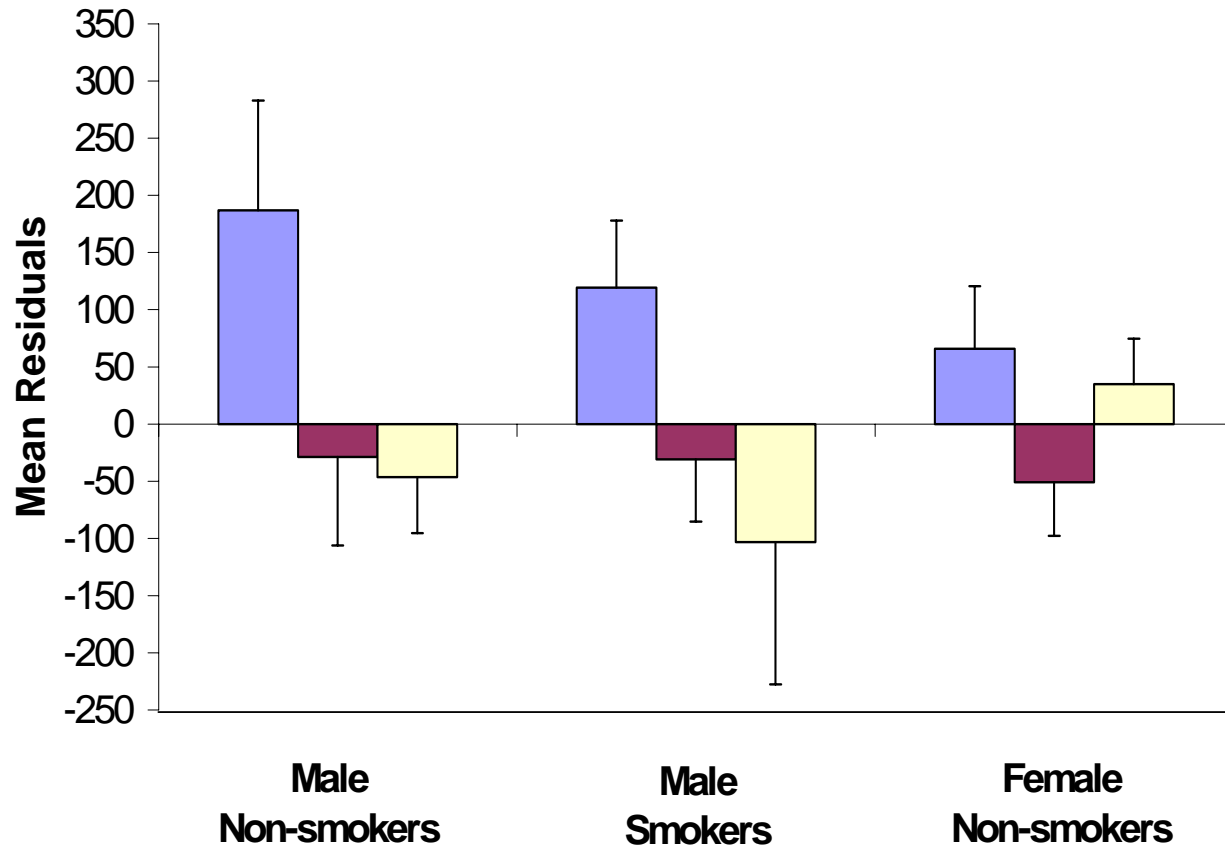
# FOR SUBJECTS BORN DURING THE PERIOD OF PEAK ARSENIC EXPOSURE

**Mortality from 1989-2000 in Antofagasta compared to the rest of Chile for subjects born from 1958-1970**

	O	E	SMR	95% CI	P
Lung Cancer	16	2.63	6.1	3.5 - 9.9	0.000
Bronchiectasis	9	0.19	46.2	21.1 - 87.7	0.000
Other COPD	7	0.92	7.6	3 - 15.6	0.000
All other deaths	488	449.71	1.1	1.0 - 1.2	0.039

# FEV1

Arsenic (ug/L) 0-99 100-399 400+



# Reproductive effects

**TABLE 4.** Multivariable Model Results\* for Birthweight Differences According to Selected Maternal and Infant Characteristics and Location

Characteristic	Adjusted Birthweight Difference (gm) (N = 813)	
	Difference	95% CI
Town		
Valparaíso <sup>h</sup>		
Antofagasta	-57	-123 to 9

**Results:** The final study group consisted of 424 infants from Antofagasta and 420 from Valparaíso. After controlling for confounders, results of the multivariable analysis indicated that Antofagasta infants had lower mean birth weight (-57 g; 95% confidence interval = -123 to 9).

**Conclusion:** This study suggests that moderate arsenic exposures from drinking water (<50 µg/L) during pregnancy are associated with reduction in birth weight, similar in magnitude to that resulting from other environmental exposures such as environmental tobacco smoke and benzene.

**Table 3. Pregnancy outcomes and infant mortality in relation to pre- and postnatal arsenic exposure.**

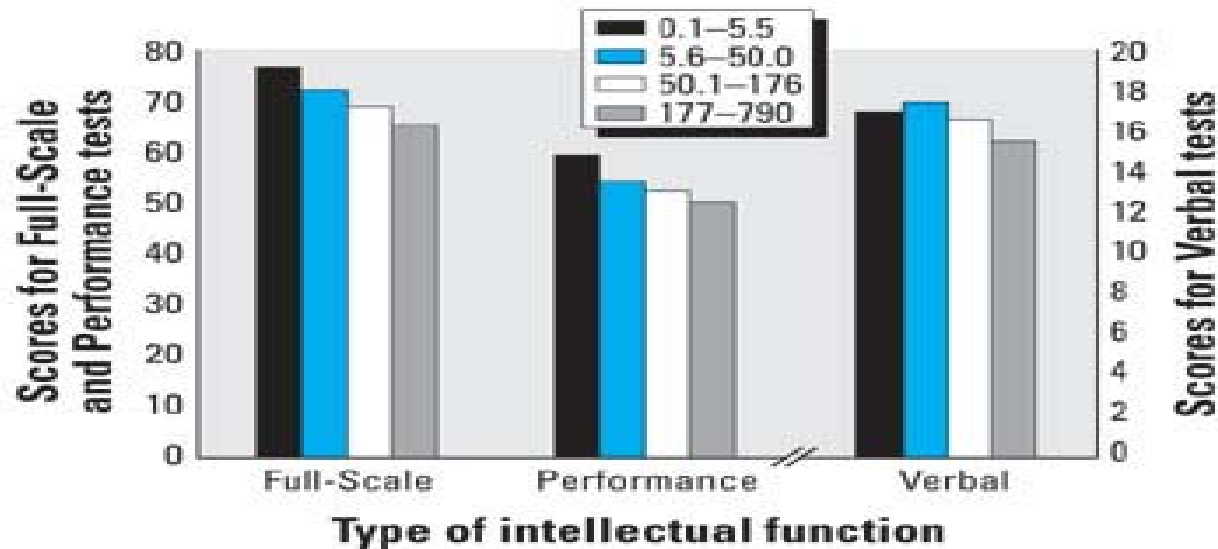
Arsenic	Spontaneous Abortion				Stillbirth				Neonatal Death				Infant Mortality <sup>§</sup>			
	N = 660 <sup>1</sup>		OR (95% CI)		N = 558 <sup>2</sup>		OR (95% CI)		N = 540 <sup>3</sup>		OR (95% CI)		N = 540 <sup>3</sup>		OR (95% CI)	
	no	yes	unadj.	adj.*	no	yes	unadj.	adj.*	no	yes	unadj.	adj.*	no	yes	unadj.	adj.*
0-49	46	23	1	1	39	8	1	1	39	7	1	1	38	15	1	1
50-199	55	2	0.73 (0.17, 3.1 9)	0.82 (0.18, 3.7 4)	51	1	0.97 (0.12, 7.9 4)	0.82 (0.1, 7.3)	50	1	1.11 (0.13, 9.2 5)	0.83 (0.10, 7.1 7)	49	2	1.04 (0.23, 4.6 8)	0.68 (0.14,3.29)
≥ 200	11	5	0.90 (0.33, 2.4 2)	0.97 (0.35, 2.7 2)	92	9	<b>4.86</b> <b>(1.82,</b> <b>12.9)</b>	<b>6.32</b> <b>(2.11,</b> <b>19.0)</b>	88	4	2.53 (0.73, 8.8 4)	2.09 (0.58, 7.5 7)	88	4	1.16 (0.38, 3.5 7)	1.18 (0.36,3.87)



# Cognitive Effects

## Water Arsenic Exposure and Children's Intellectual Function in Araihasar, Bangladesh

Gail A. Wasserman et al., Environmental Health Perspectives 112, Sept 2004



**Figure 1.** Adjusted scores by quartiles of water As for Full-Scale, Performance, and Verbal raw scores. In each case, adjustments were made for maternal education and intelligence, type of housing, child height and head circumference, and access to television.

**Table 4. Intellectual function test scores and arsenic concentrations in urine in the second and third tertile vs. the lowest tertile.**

Test	2 <sup>nd</sup> tertile **	95% CI	3 <sup>rd</sup> tertile * #	95% CI	p-value for trend**
Vocabulary	-1.01	(-2.87, 0.85)	-2.07	(-3.95, -0.18)	<b>0.015</b>
Digit Span	-0.086	(-0.65, 0.48)	-0.0009	(-0.576, 0.57)	0.50
Object Assembly	-0.89	(-2.24, 0.46)	-1.31	(-2.68, 0.08)	<b>0.03</b>
Coding	-1.81	(-5.14, 1.52)	-1.70	(-5.08, 1.68)	0.16
Picture Completion	-0.49	(-1.30, 0.31)	-0.85	(-1.67, -0.029)	<b>0.04</b>
Block Design	0.65	(-1.51, 2.81)	-0.72	(-2.91, 1.47)	0.26
Full Scale	-3.50	(-11.4, 4.43)	-6.79	(-14.8, 1.26)	<b>0.05</b>
Peg Board	0.88	(-0.44, 2.20)	0.56	(-0.77, 1.89)	0.2
Colored progress. matrices	0.0057	(-1.43, 1.44)	-0.77	(-2.22, 0.69)	0.15
TSR	1.68	(0.008, 3.35)	0.92	(-0.476, 2.61)	0.15

\*adjusted for age using indicator variables for each age, sex, maternal and paternal education (no formal education, primary, secondary and higher), father's occupation (unemployed, farming, daily wage, service, business), number of rooms in house, type of house building material (mud, brick, mixed material), child's BMI, mother's age. Age groups: Pegboard and TSR: 5 – 15 years, all others 6 – 15 years.

\*\* test for trend across tertiles, one-sided. #Cut-off points: CPM and pegboard: 44.2 µg/L, 86.1 µg/L; all others: 43.6 µg/L, 82.6 µg/L.

Note: effects not present with drinking water arsenic concentrations