

Arsenic as a Human Health Hazard: Highlights of Recent Epidemiologic Findings

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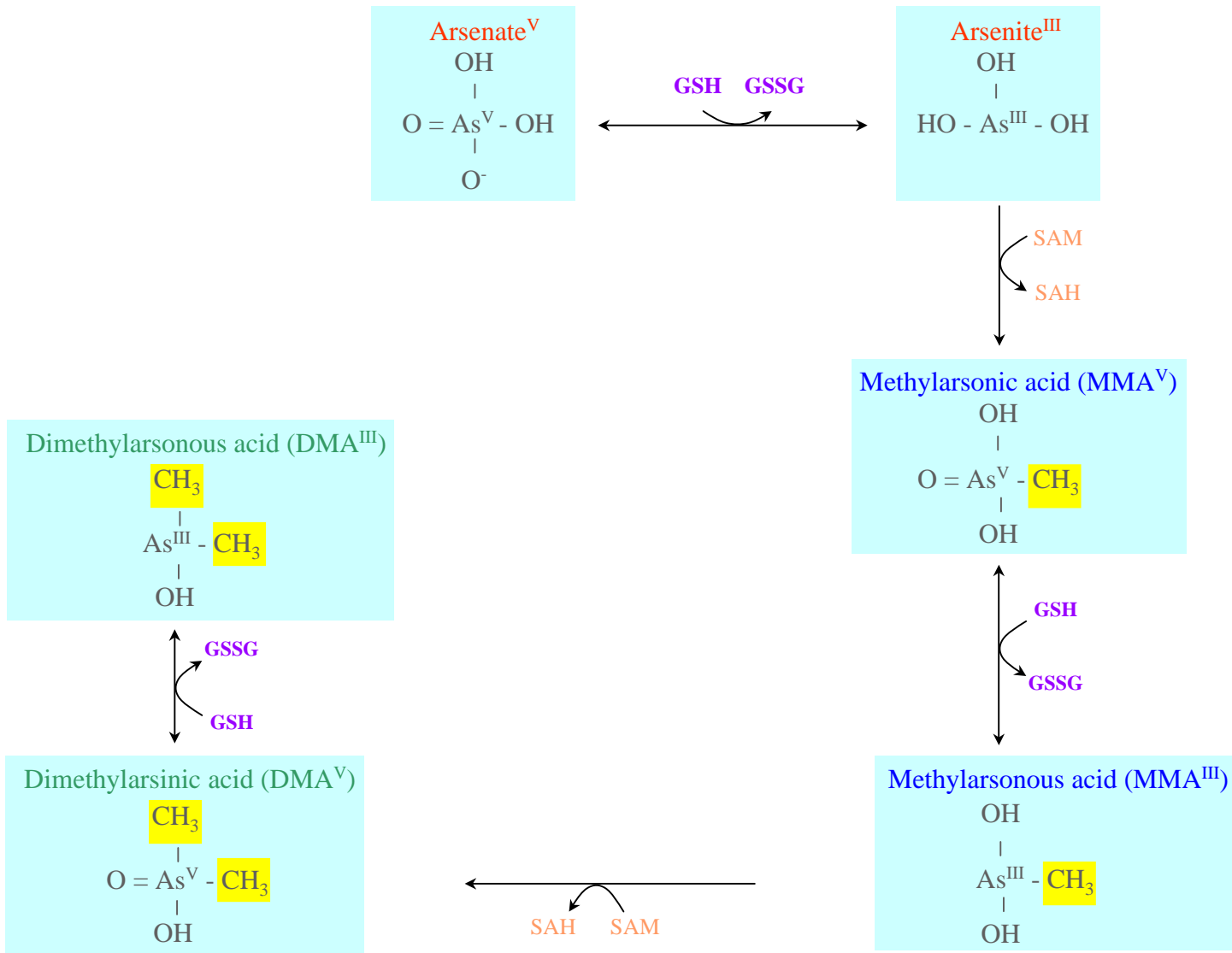
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Arsenic in Groundwater: An International Problem

- Taiwan
- China
- Chile
- Argentina
- Mexico
- United States
- India
- Bangladesh
- Nepal
- Vietnam
- Cambodia
- Mongolia

Arsenic metabolism: **detoxification**(?) by mono- and dimethylation.



Arsenic Metabolites in Human Urine

LD₅₀
(Toxicity)

- As⁺³ Arsenite 8 mg/kg
- As⁺⁵ Arsenate 22 mg/kg

Mammalian Metabolites

- MMA⁺³ Monomethylarsonous Acid 2 mg/kg
- MMA⁺⁵ Monomethylarsonic Acid 916 mg/kg
- DMA⁺⁵ Dimethylarsinic Acid 648 mg/kg

Fish Metabolites

- AsB Arsenobetaine ~10,000 mg/kg
- AsC Arsenocholine

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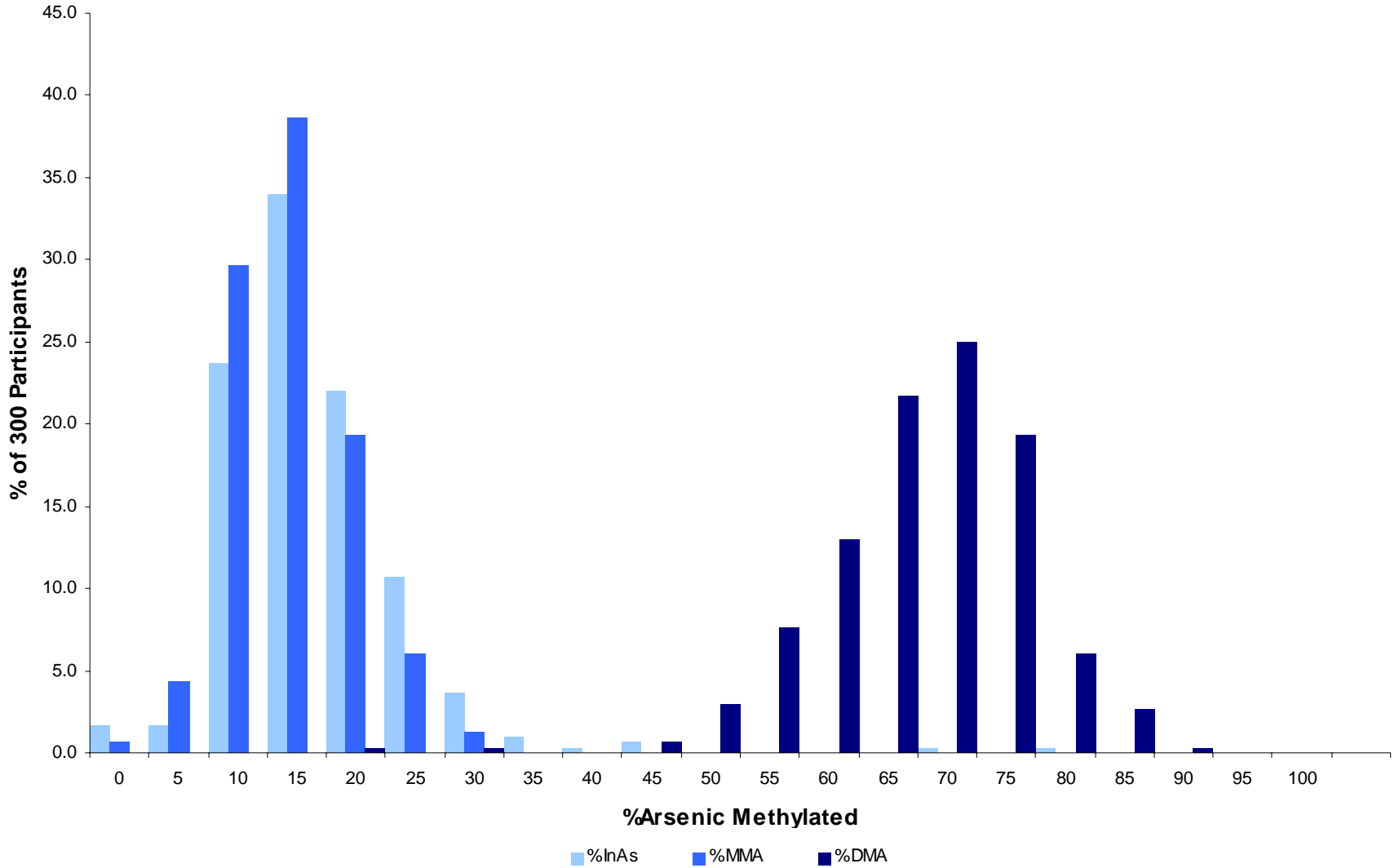
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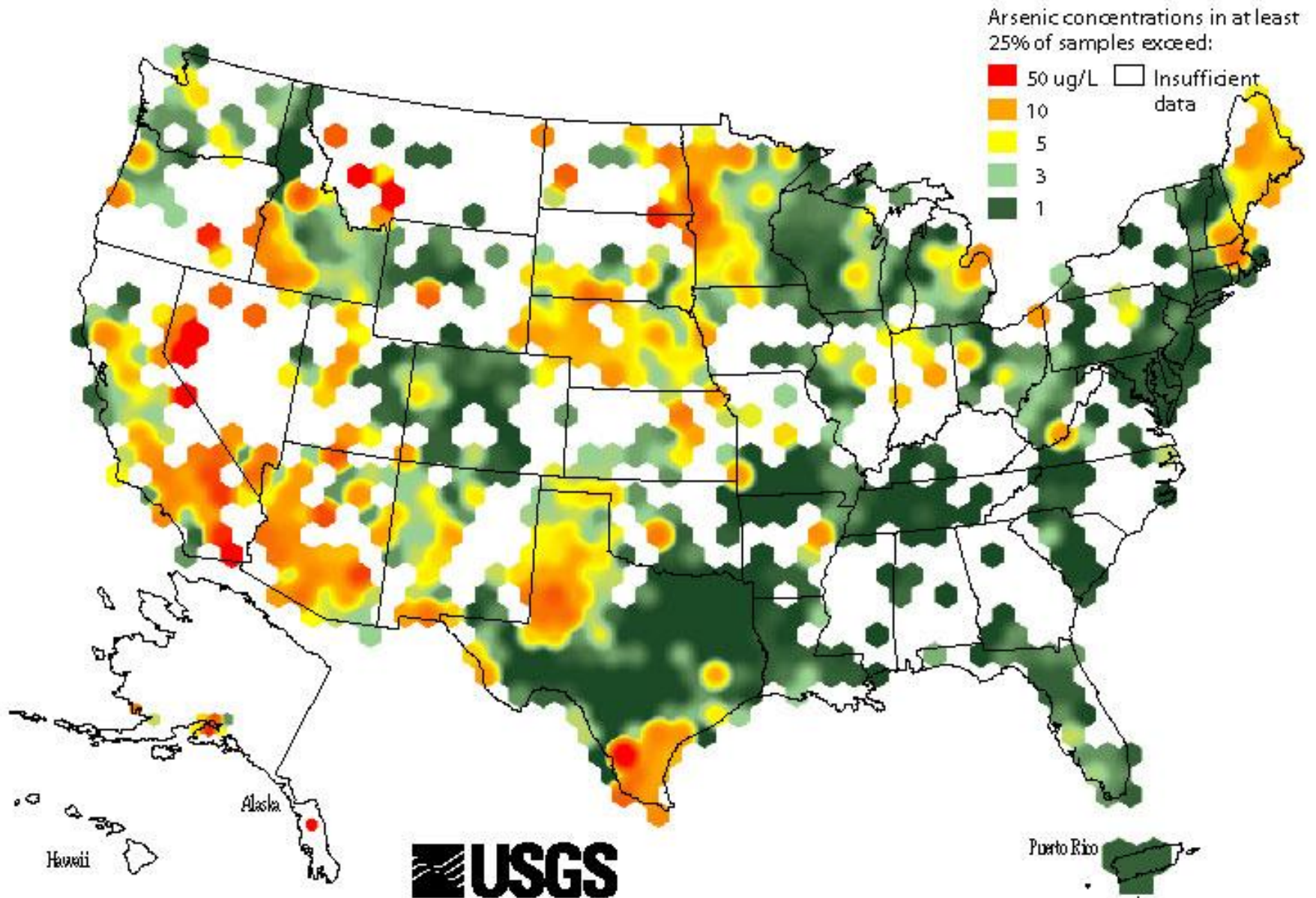
Frequency Distribution for %InAs, %MMA, %DMA



Recent Findings from Taiwan

- People with a relatively high proportion of MMA in urine had ~5-fold higher risk for skin and bladder cancer (Yu et al, 2000).
- There is a dose-response relationship between the ratio of MMA/DMA in urine and the risk for skin and bladder cancer (Chen et al, 2003).
- Those with very heavy As exposure (> 20 mg/L-yrs) had a 3-fold higher risk for carotid atherosclerosis (Wang et al, 2002), as well EKG findings of a prolongation of the QT interval (Wang et al, 2003).

As in the United States



Recent Findings from New Hampshire

- Among smokers, an elevated odds ratio for bladder cancer was observed for those in the upper quartile of As exposure (toenail As) (Karagas et al, 2004).
- Arsenic exposure is associated with decreased DNA repair *in vitro* and in people residing in New Hampshire and Mexico (Andrew et al, 2006).
- Bladder cancer mortality, long known to be particularly high in northern New England, is associated with the use of private wells (Ayotte et al, 2006).

Recent Findings from Chile

For those born in Antofagasta, during the high arsenic exposure period (1958-1971) with probable exposure *in utero* and early childhood, the standardized mortality ratios were 6.1 for lung cancer (CI 3.5-9.9, $p < 0.001$) and 46.2 for bronchiectasis (CI 21.1-87.7, $p < 0.001$) (Smith et al, 2006).



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Transplacental carcinogenicity of inorganic arsenic in the drinking water: induction of hepatic, ovarian, pulmonary, and adrenal tumors in mice

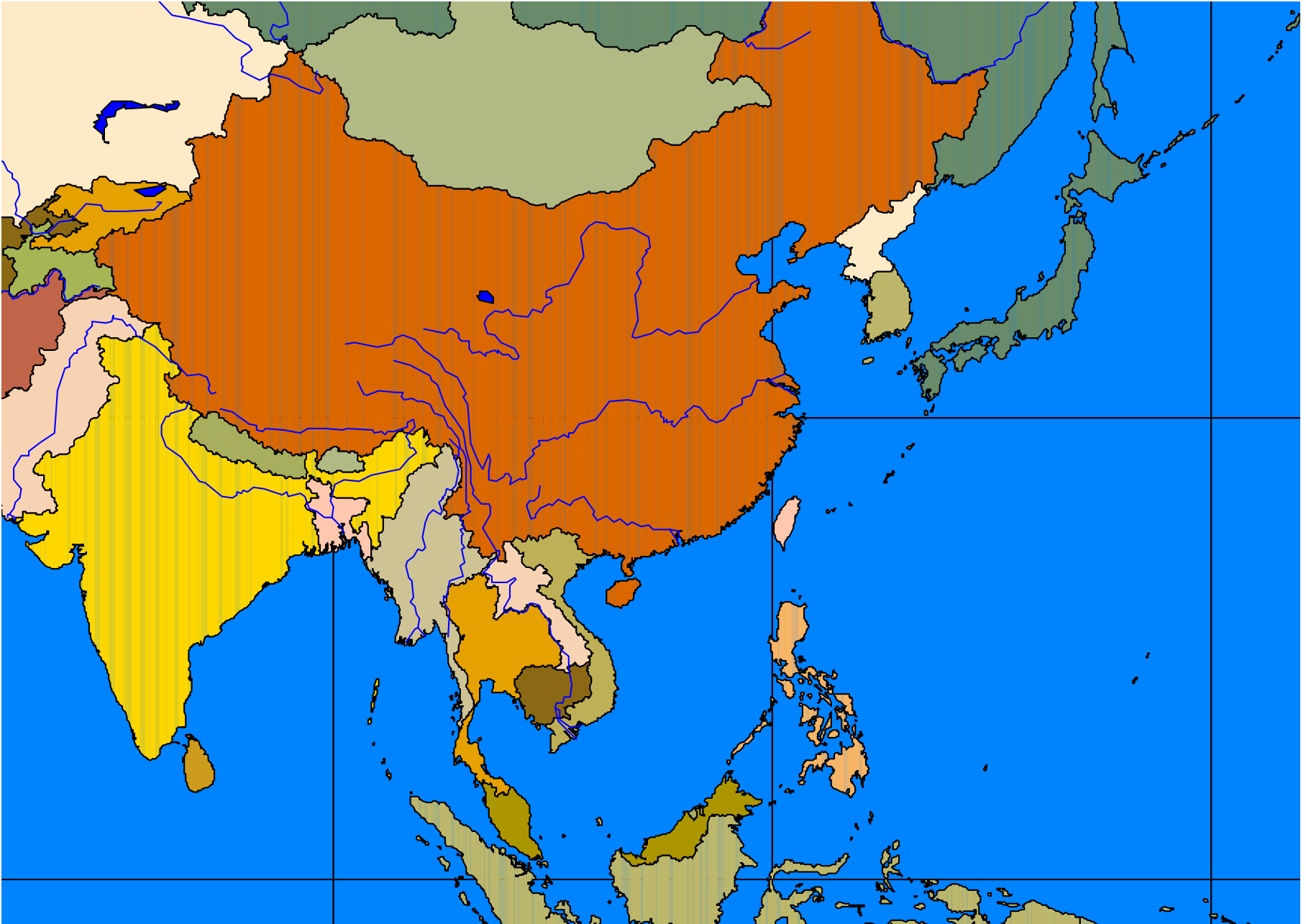
Michael P. Waalkes,^{a,*} Jerrold M. Ward,^b Jie Liu,^a and Bhalchandra A. Diwan^c

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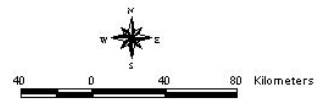
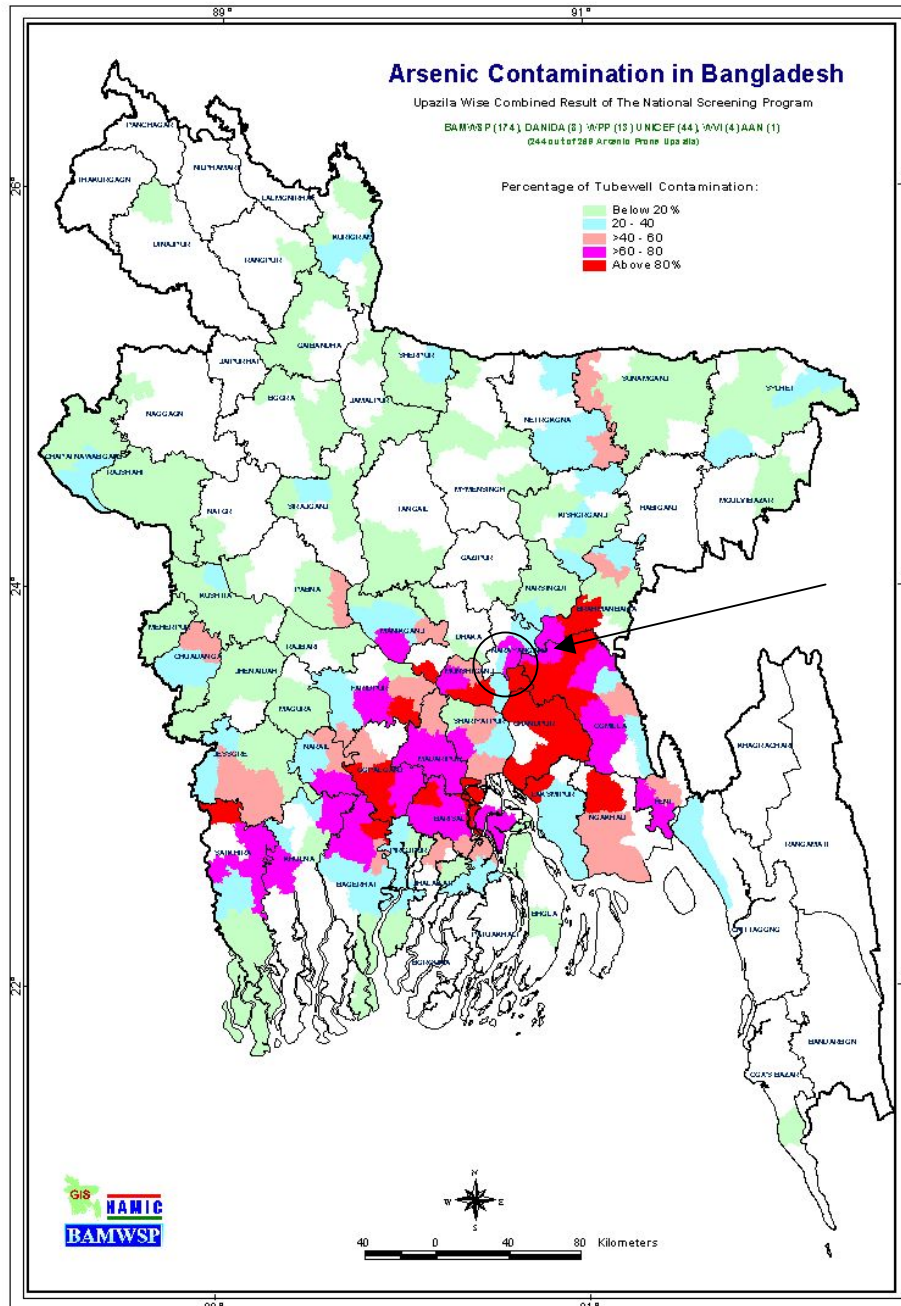
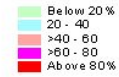


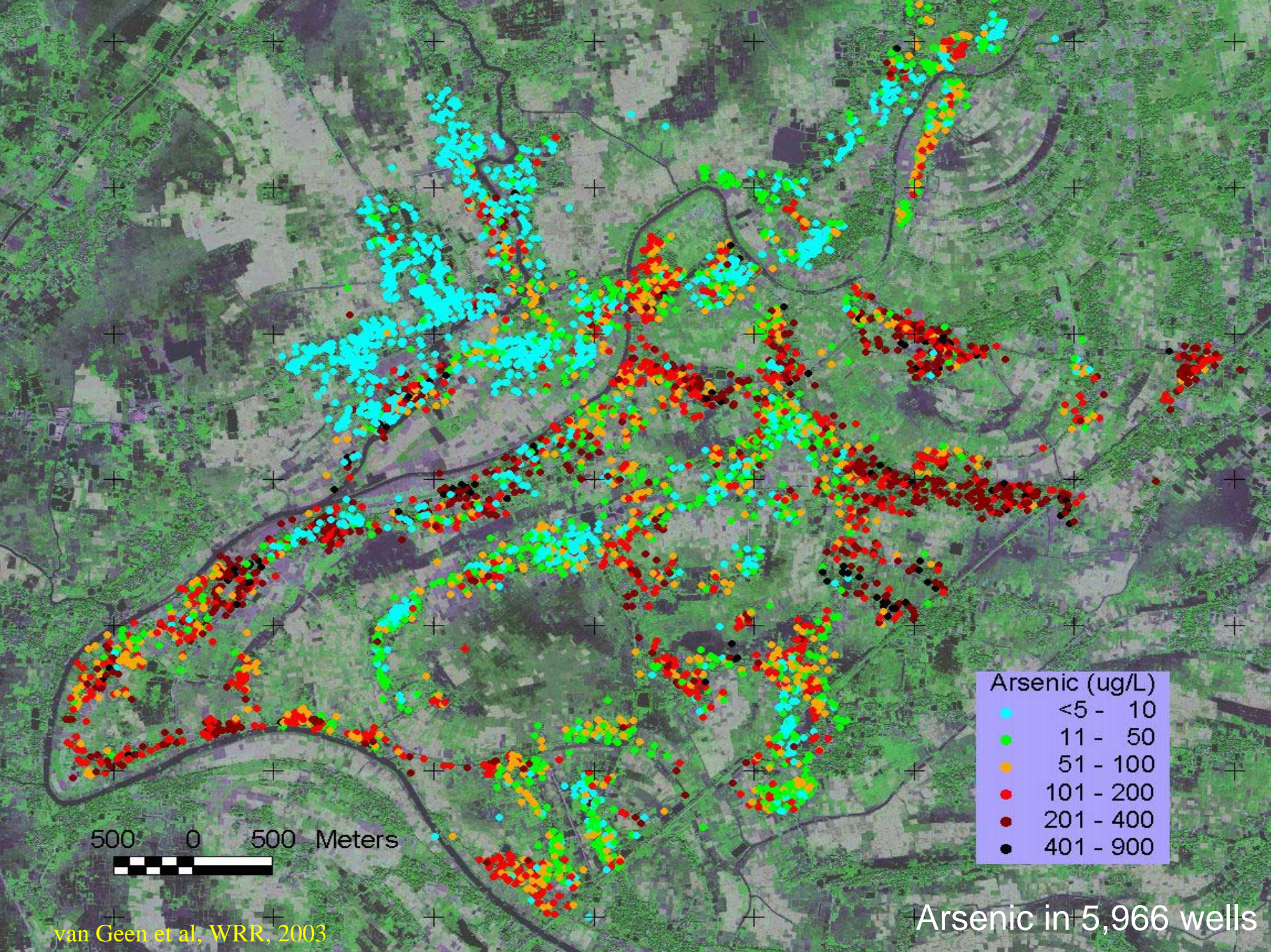
Arsenic Contamination in Bangladesh

Upazila Wise Combined Result of The National Screening Program

BAMWSP (174), DANIDA (3), WFP (13), UNICEF (44), WVI (4), AAN (1)
(244 out of 268 Arsenic prone Upazila)

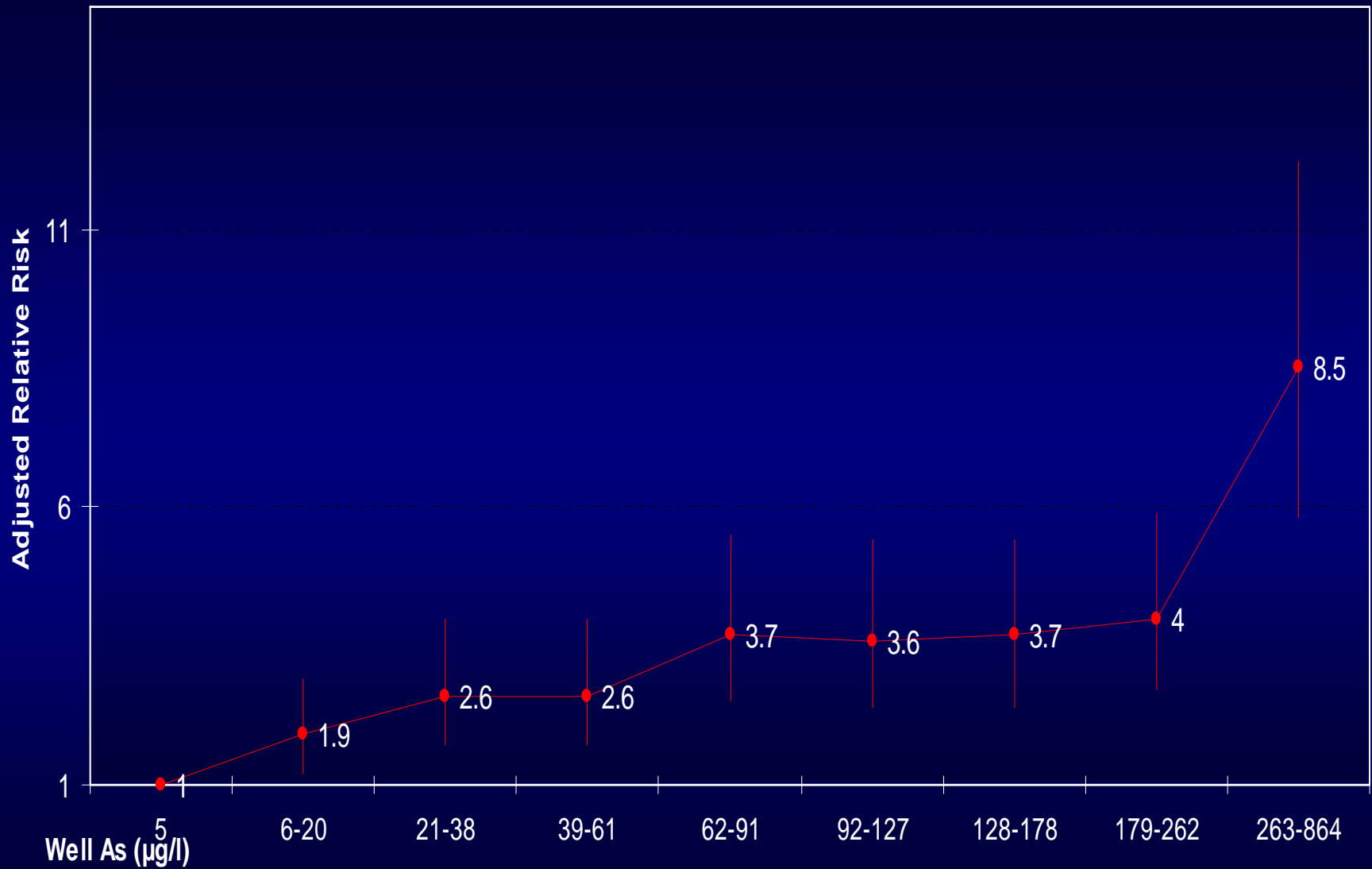
Percentage of Tubewell Contamination:



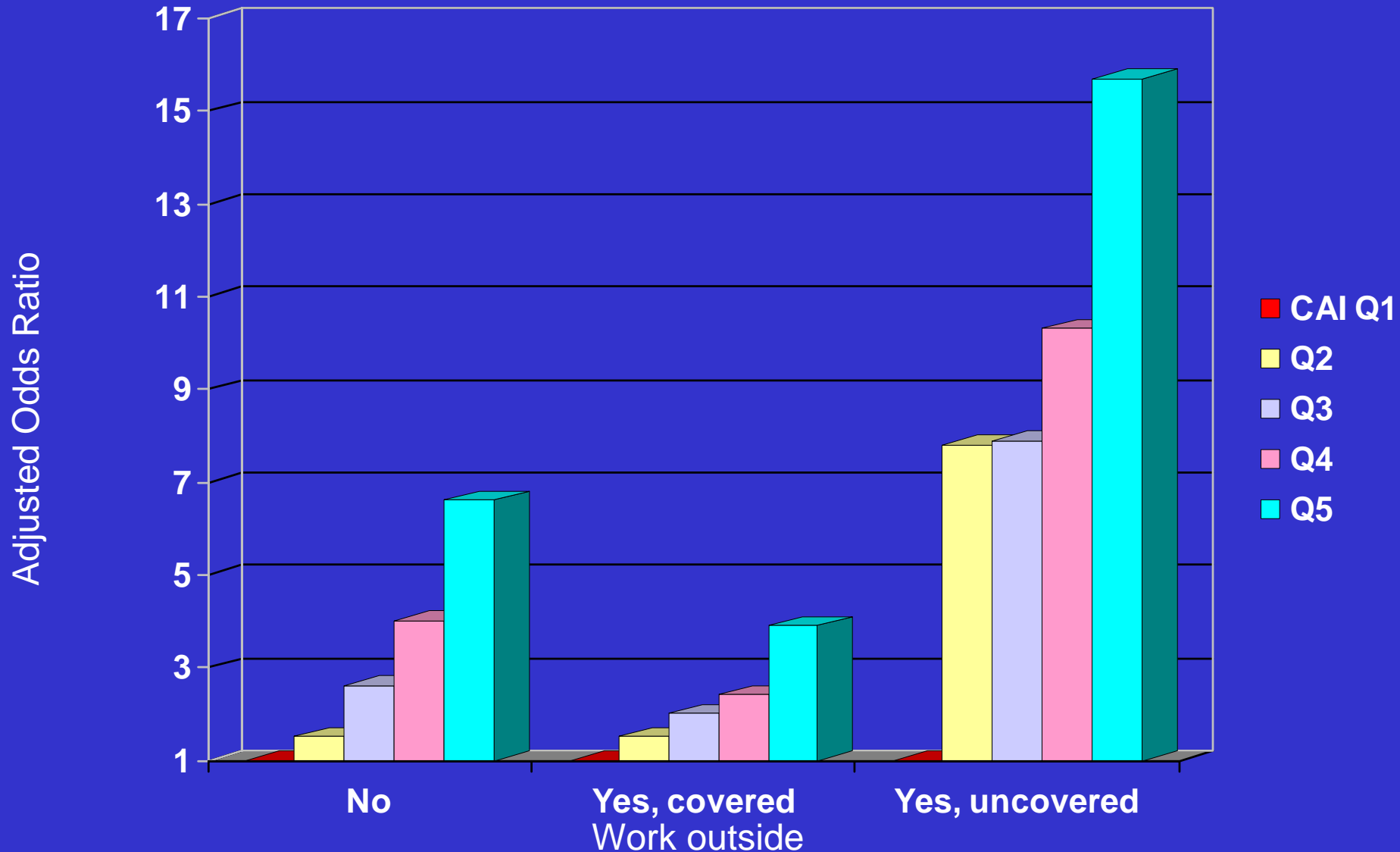


500 0 500 Meters

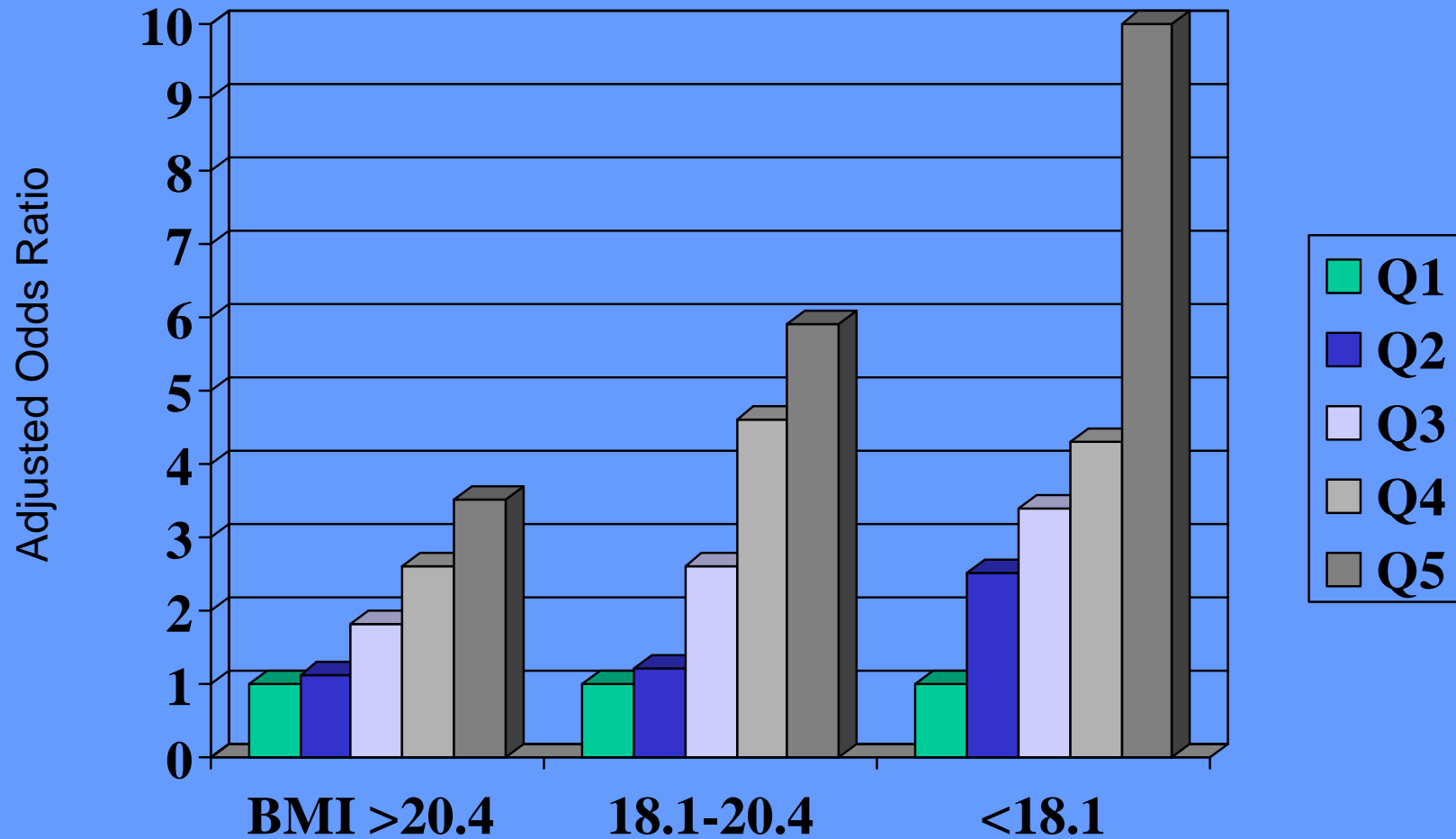
Dose-Response Relationship Between Water As Concentration and Risk for Skin Lesions



Influence of Sun Exposure on Effect of Arsenic on Risk of Skin Lesion in Men



Influence of Body Mass Index on Effect of Arsenic on Risk of Skin Lesions



Other Recent Findings from Bangladesh

- Blood folate concentrations are associated with the ability to methylate arsenic. Those who are folate deficient are poor methylators and are at increased risk for arsenic-induced skin lesions (Gamble et al, EHP, 2005).
- Folate supplementation decreases the proportion of MMA and inorganic As in urine, and increases the proportion of DMA (Gamble et al, AJCN, 2006).
- People with a higher proportion of MMA in their urine are at increased risk for skin lesions (Ahsan et al, in review).

Blood Selenium Level and Risk of Skin Lesions

Blood Selenium Level ($\mu\text{g/L}$)	Total N	Adjusted Hazard Ratios (95% CI)
< 131.8	222	1.0
131.9-144.3	222	0.71 (0.42-1.21)
144.5-156.3	221	0.54 (0.32-0.91)
156.4-169.8	222	0.54 (0.31-0.93)
169.9-262.6	221	0.53 (0.31-0.90)

*RRs were controlled for age, gender, BMI, and smoking status.

Blood Arsenic and Risk of Skin Lesions

Blood Arsenic Level ($\mu\text{g/L}$)	Total N	Adjusted Hazard Ratios (95% CI)
< 5.8	222	1.0
5.8-7.9	225	1.24 (0.64-2.38)
8.0-10.9	218	1.94 (1.02-3.69)
11-15.9	221	2.37 (1.26-4.49)
16.0-63.9	222	3.71 (1.94-7.09)

*RRs were controlled for age, gender, BMI, and smoking status.

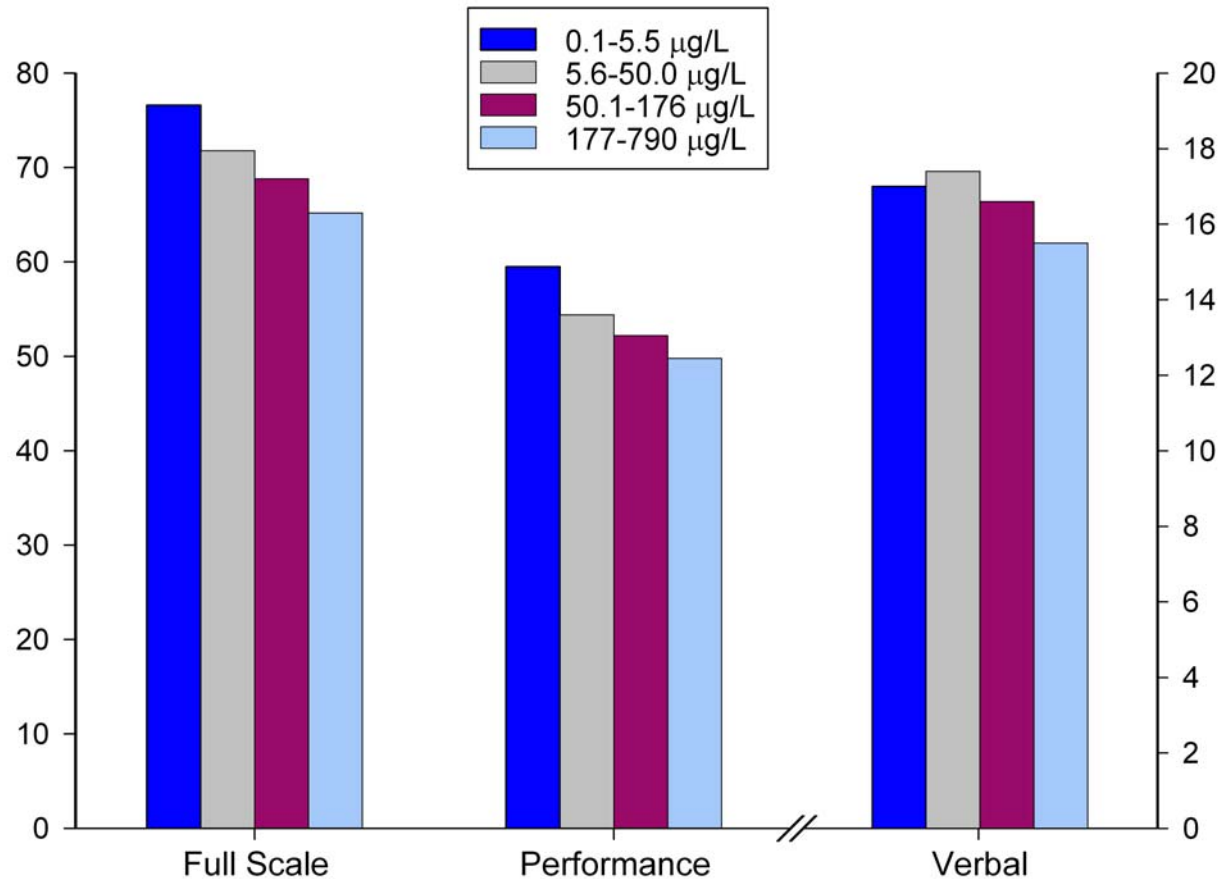


A Cross-Sectional Study of 10 year-old Children Exposed to a Wide Range of Arsenic Concentration in Drinking Water:
The Relationship Between Arsenic and Children Intelligence



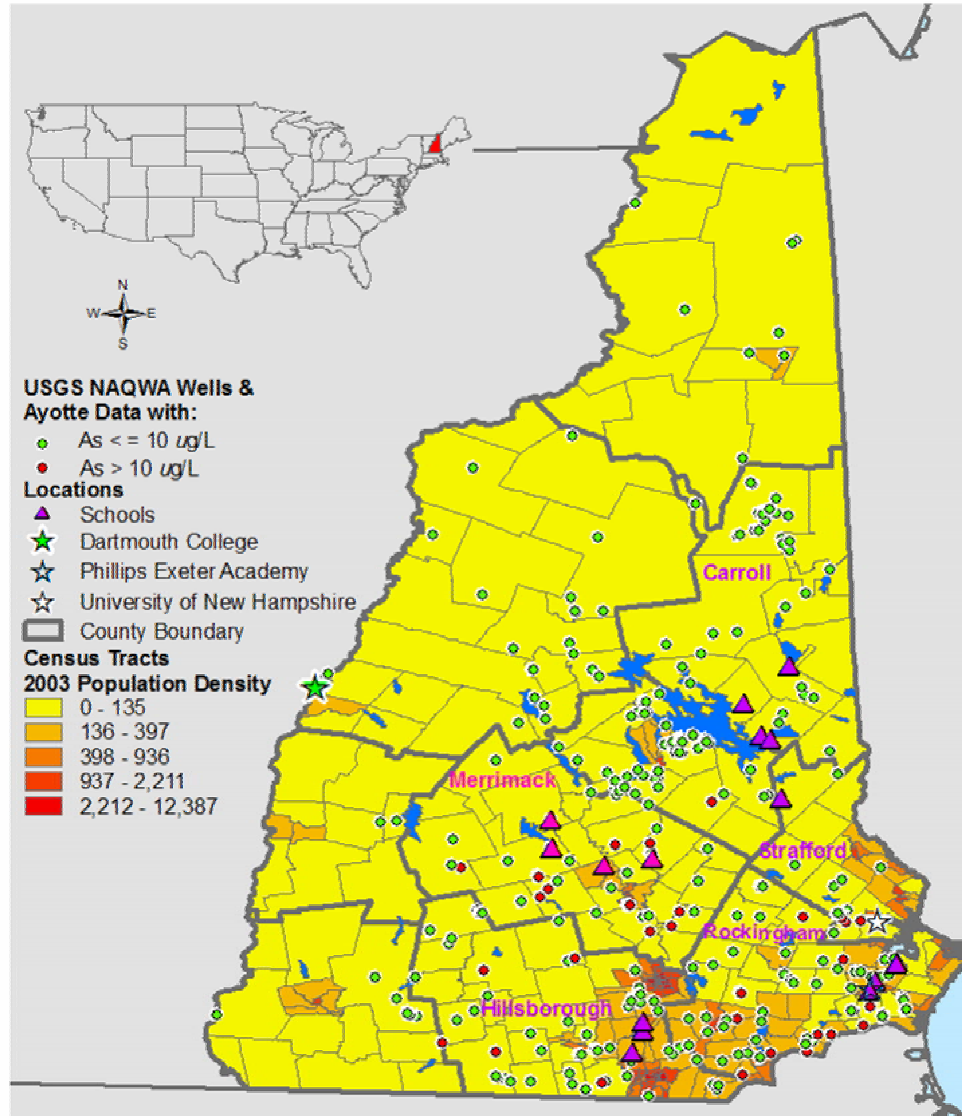


Relationship Between Water Arsenic Concentrations and Intellectual Function



New Hampshire

As in Wells, Selected Schools & Population Density



Data Source:
USGS NAQWA,
U.S. Census 2003 from ESRI
04/13/2005

0 12.5 25 50 Kilometers

