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

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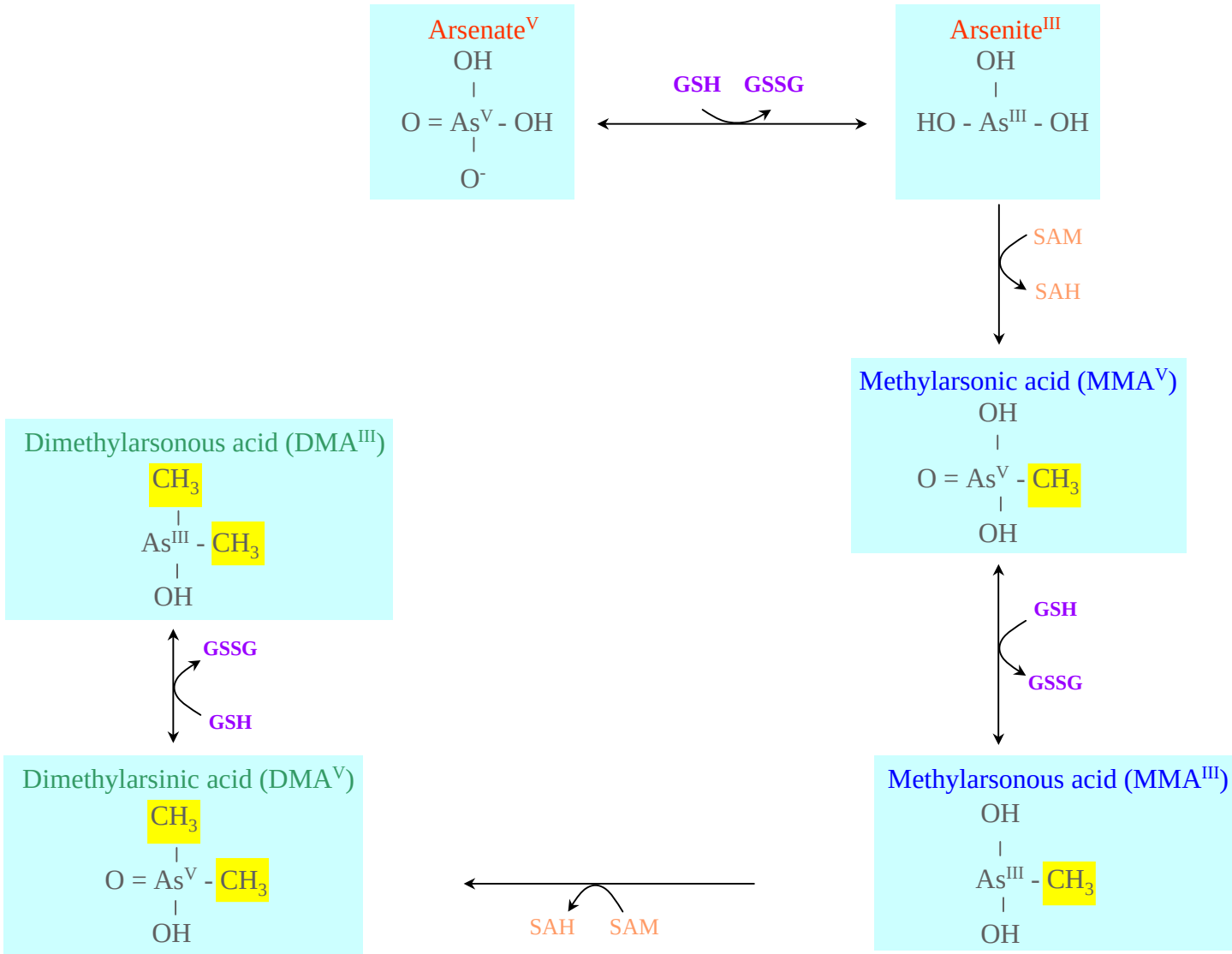
Arsenic in Groundwater: An International Problem

- 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

		LD_{50} (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	

Hughes, M.F. Toxicology Letters, 2002

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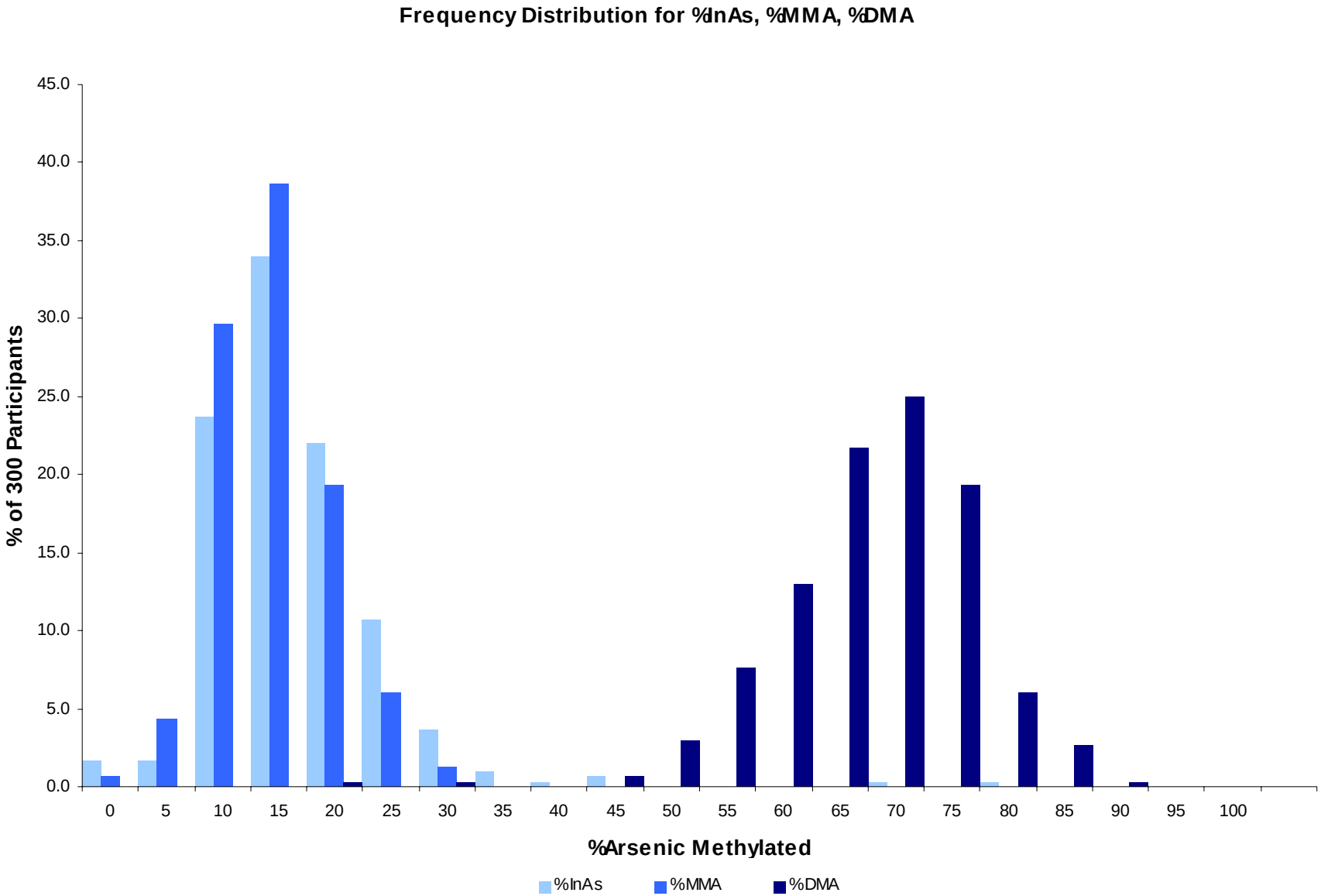
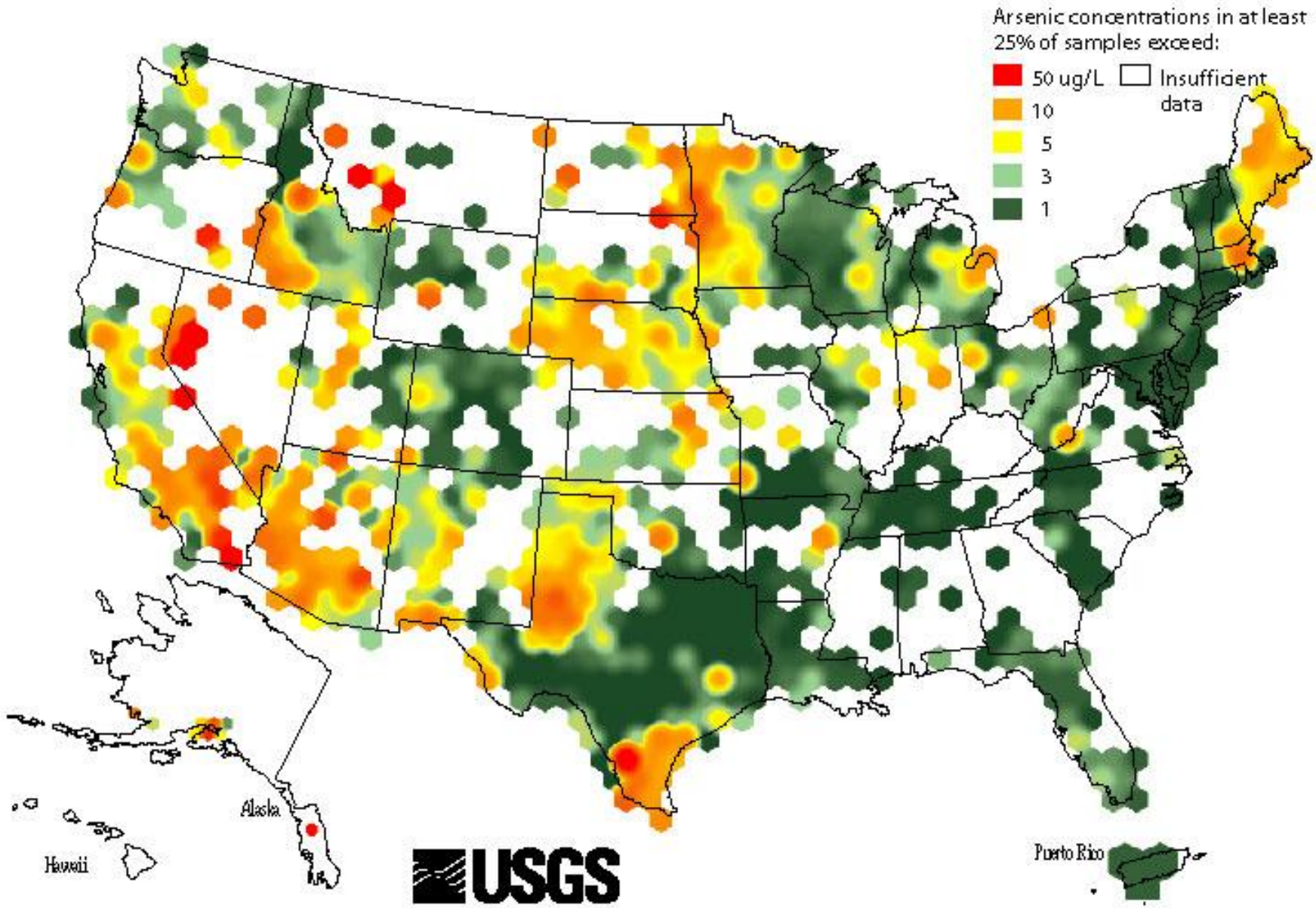

Frequency Distribution for %InAs, %MMA, %DMA
% of 300 Participants
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
%Arsenic Methylated
%InAs
%MMA
%DMA

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 bronciectasis (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

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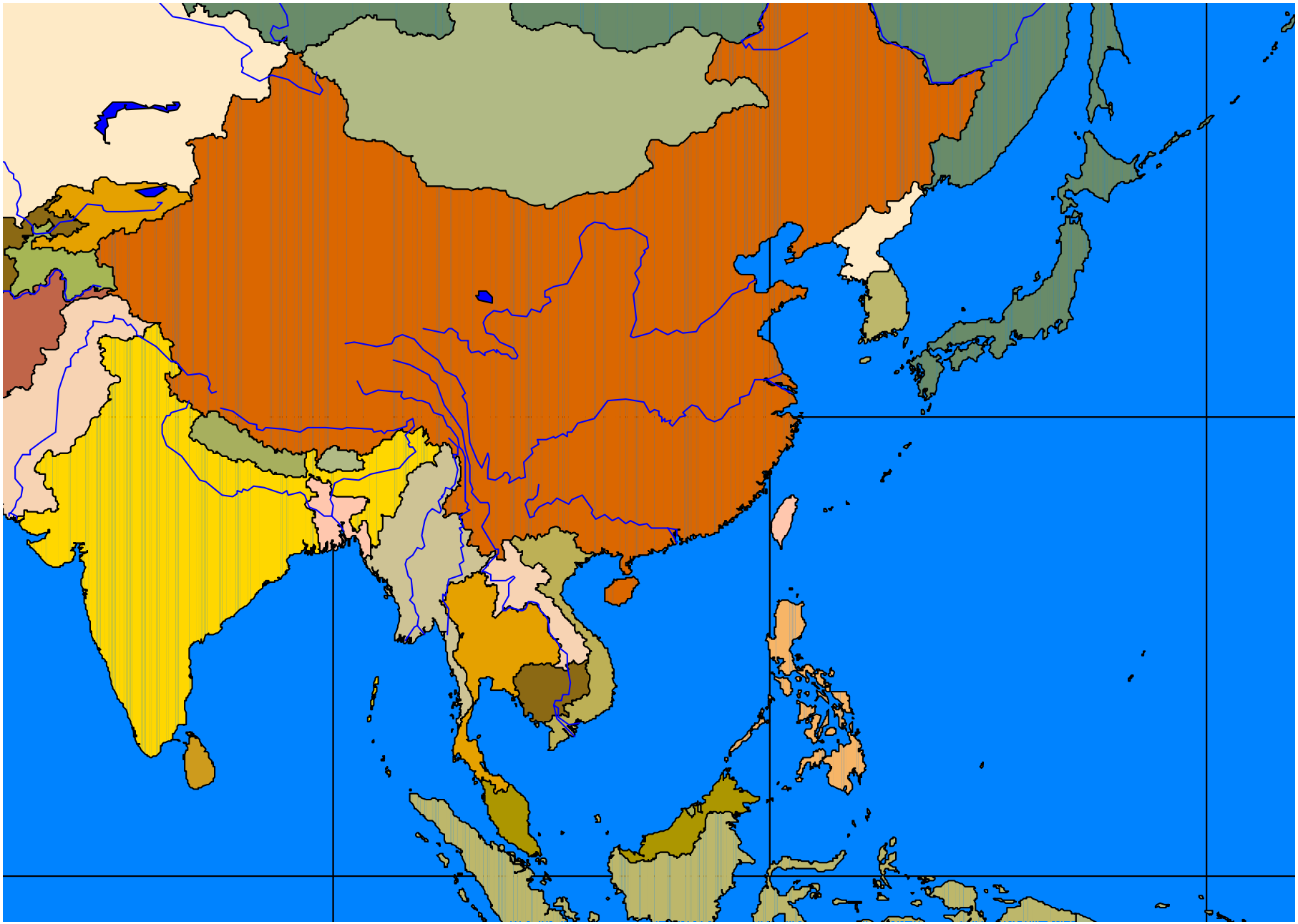
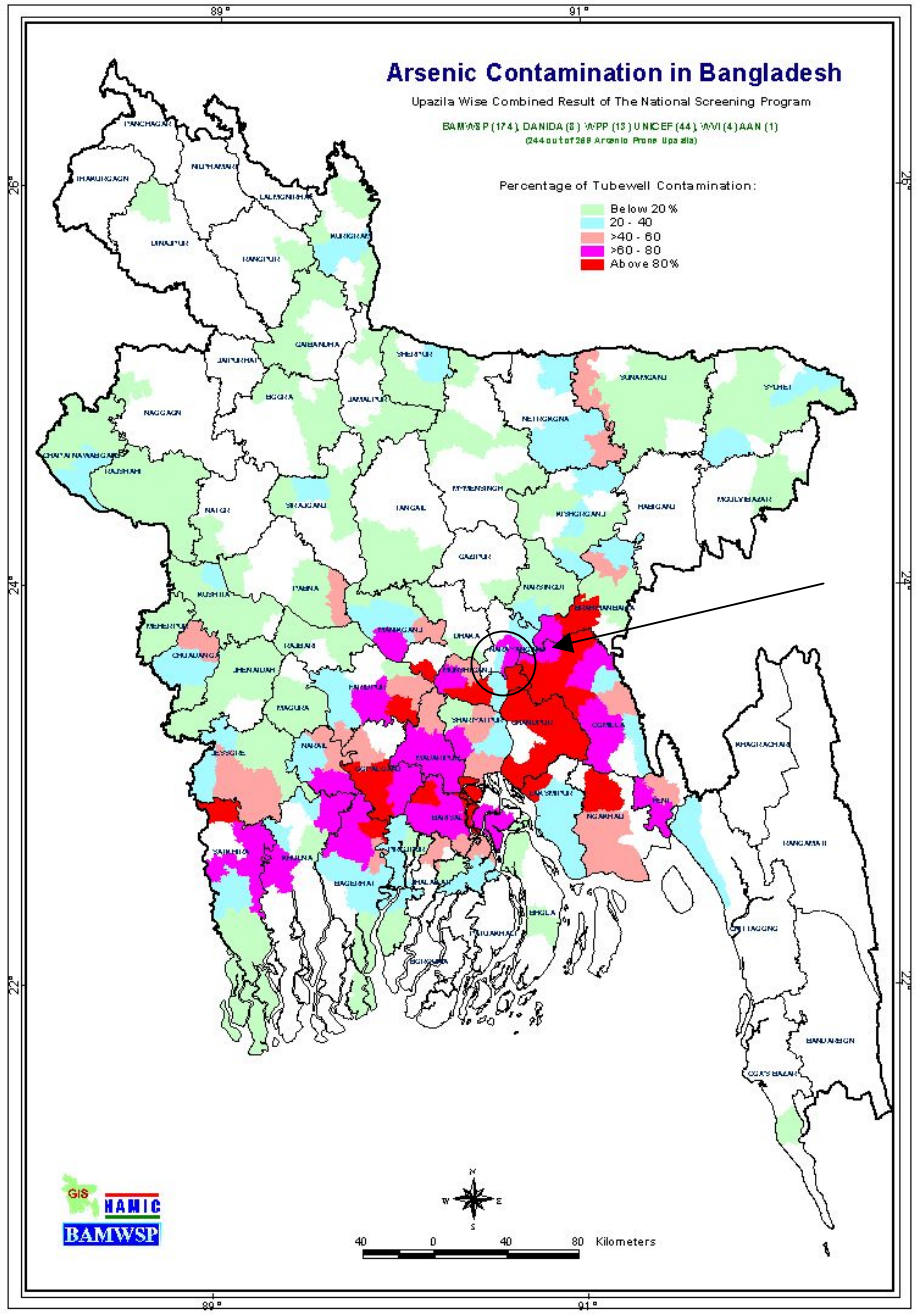
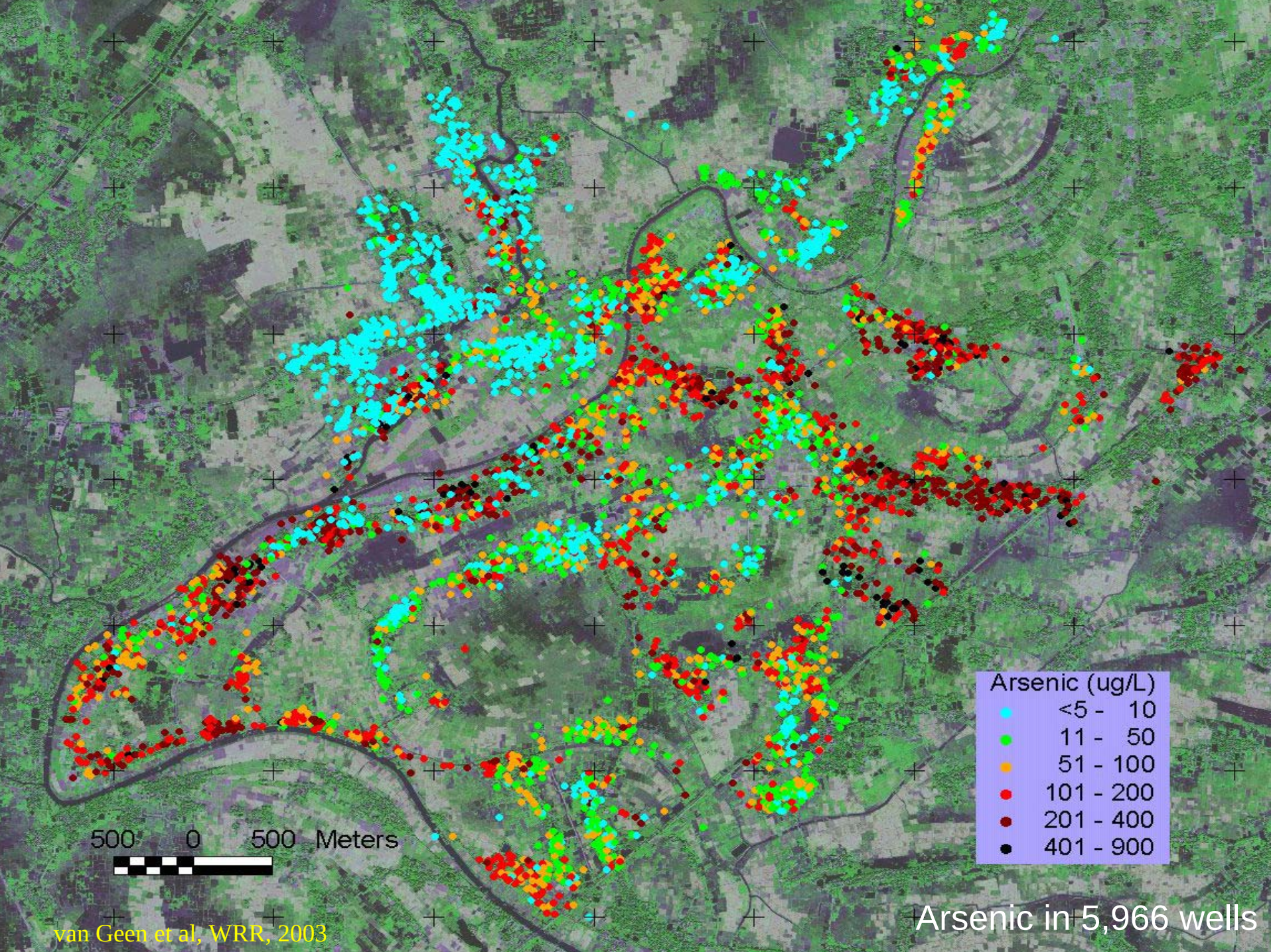
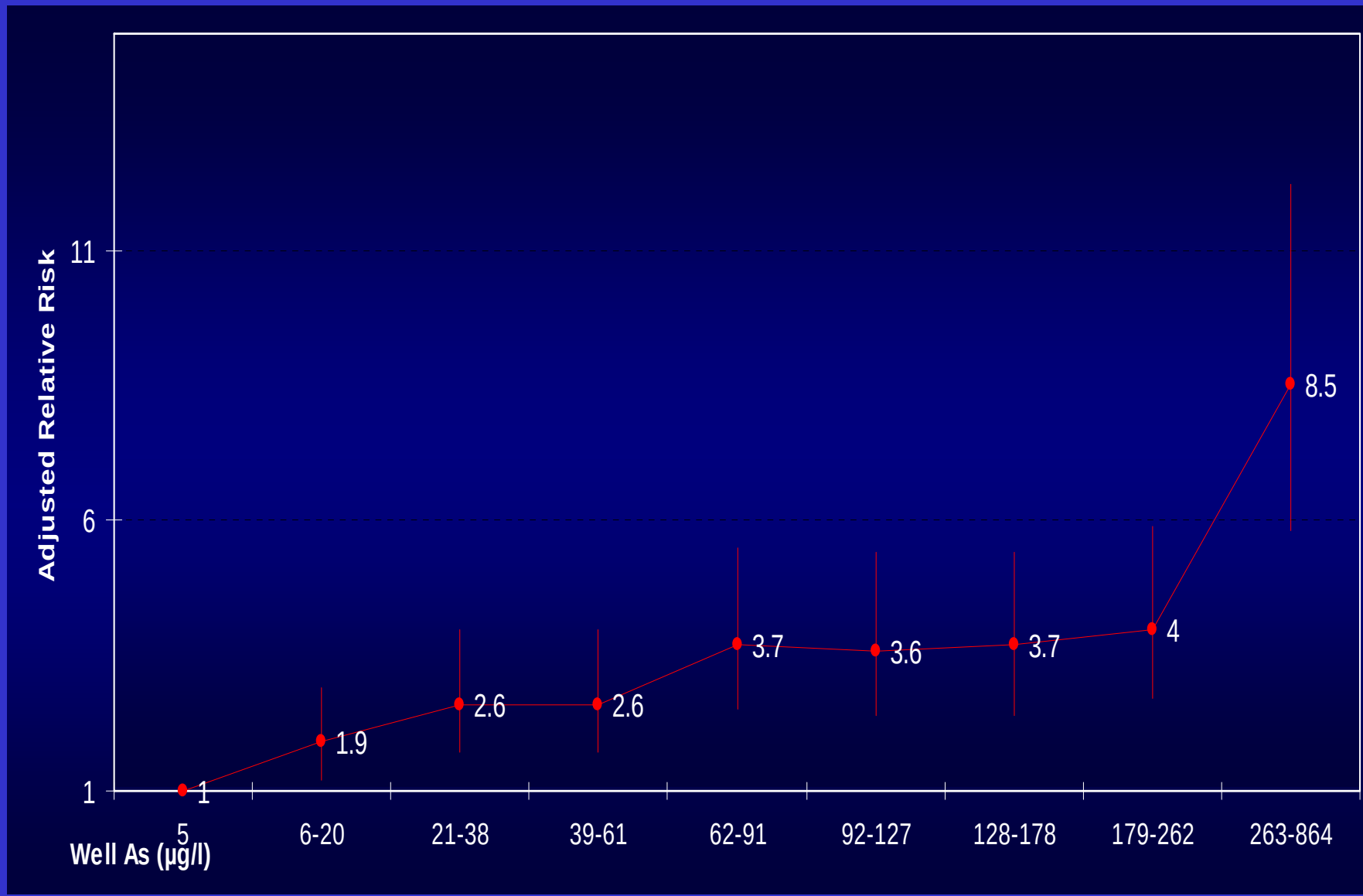



Arsenic Contamination in Bangladesh
Upazila Wise Combined Result of The National Screening Program
BAMWSP (174), DANIDA (8), WPP (13), UNICEF (44), WVI (4), AAN (1)
(244 out of 268 Arsenic Prone Upazila)
Percentage of Tubewell Contamination:
Below 20 %
20 - 40
>40 - 60
>60 - 80
Above 80%
89°
91°
26°
24°
22°
GIS
NAMIC
BAMWSP
N
W
E
S
40
0
40
80
Kilometers

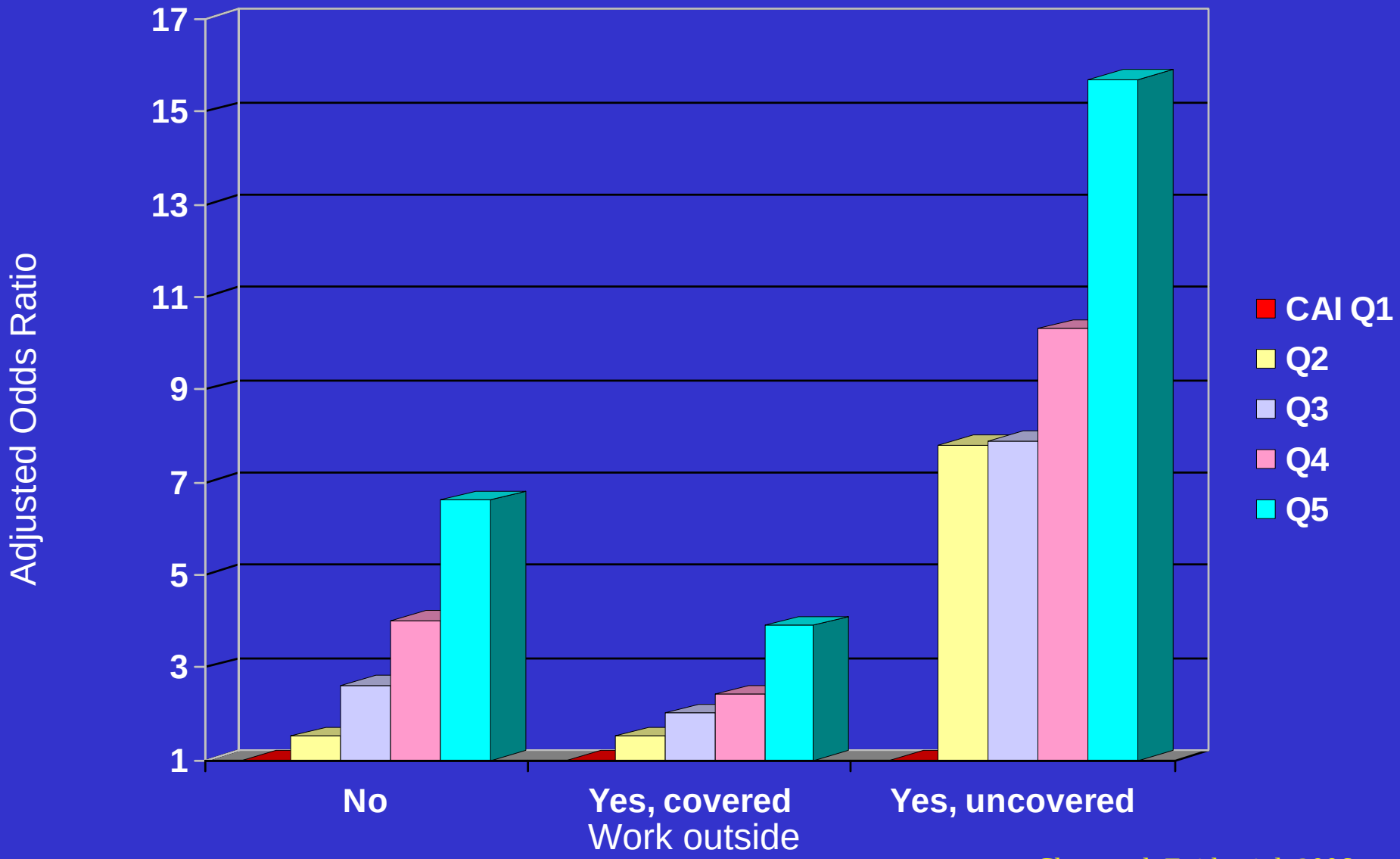

Arsenic (ug/L)
<5 - 10
11 - 50
51 - 100
101 - 200
201 - 400
401 - 900
500 0 500 Meters
van Geen et al, WRR, 2003
Arsenic in 5,966 wells

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



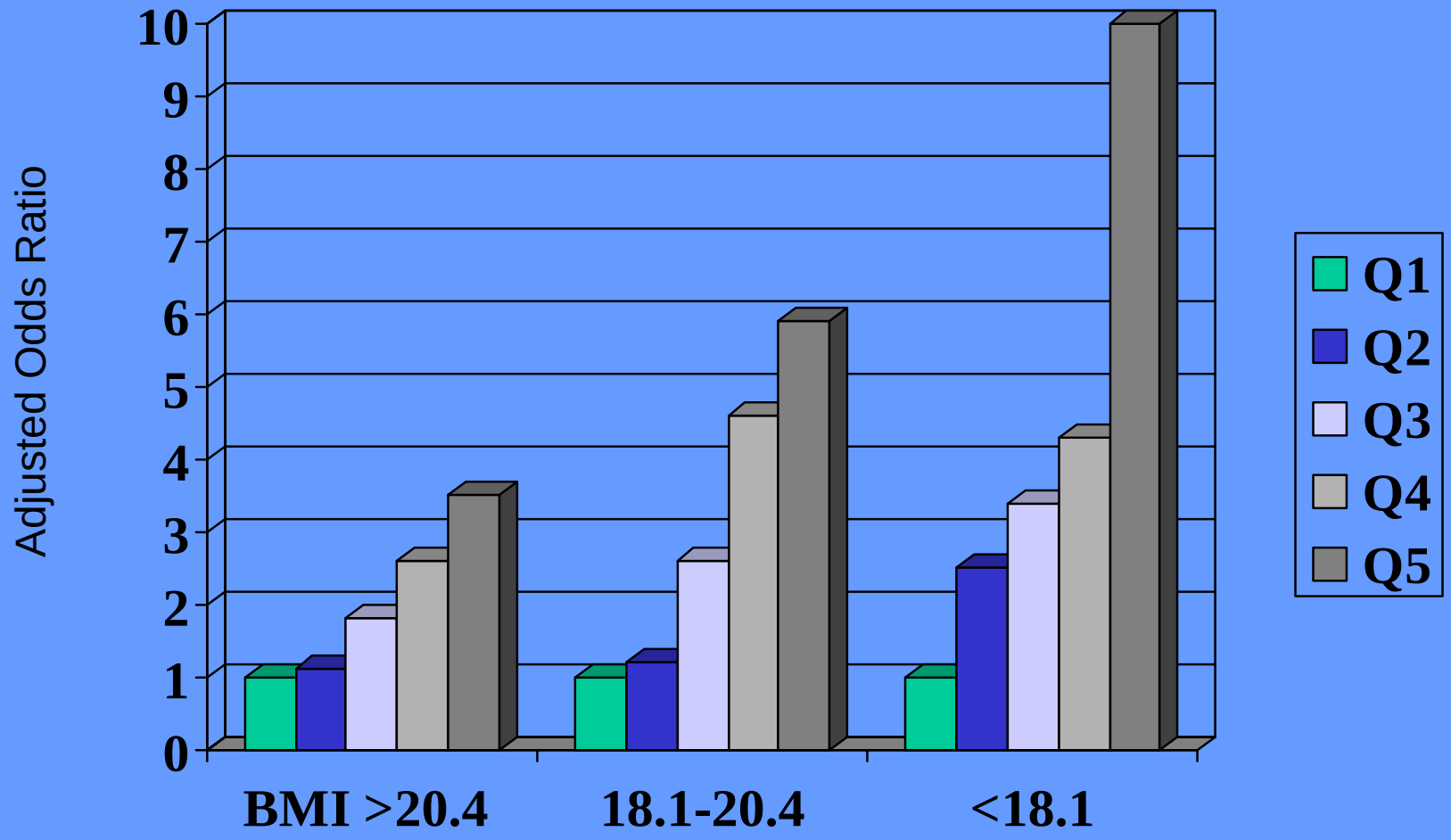
Ahsan et al, AJE, 2006

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



Chen et al, Epidemiol, 2006

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 (μg/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.

Chen et al, in review

Blood Arsenic and Risk of Skin Lesions

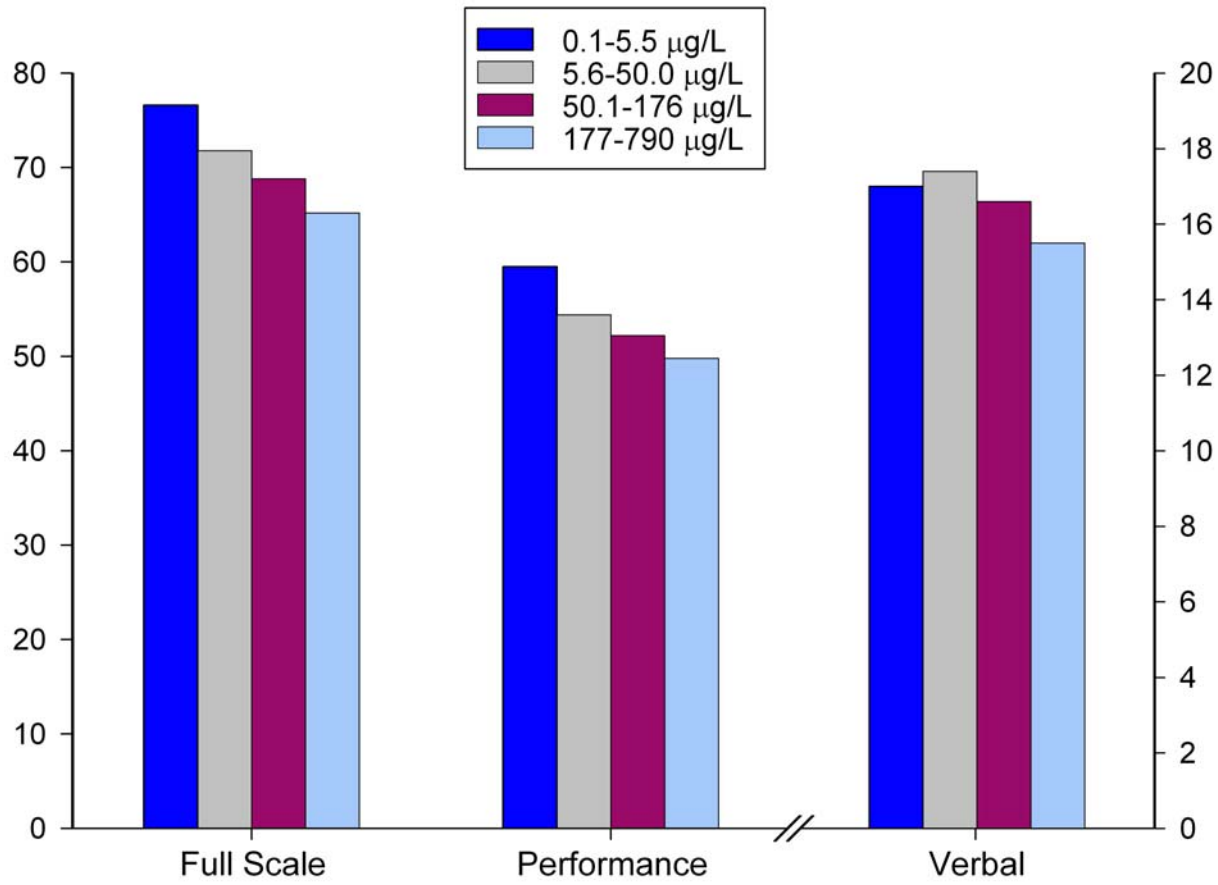
Blood Arsenic Level (µg/L)	Total N	Adjusted Hazard Ratios (95% CI)
< 5.8	222	1.0
5.8-7.9	225	1.24 (0.64-2.38)
8.0-10.9	218	1.94 (1.02-3.69)
11-15.9	221	2.37 (1.26-4.49)
16.0-63.9	222	3.71 (1.94-7.09)

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

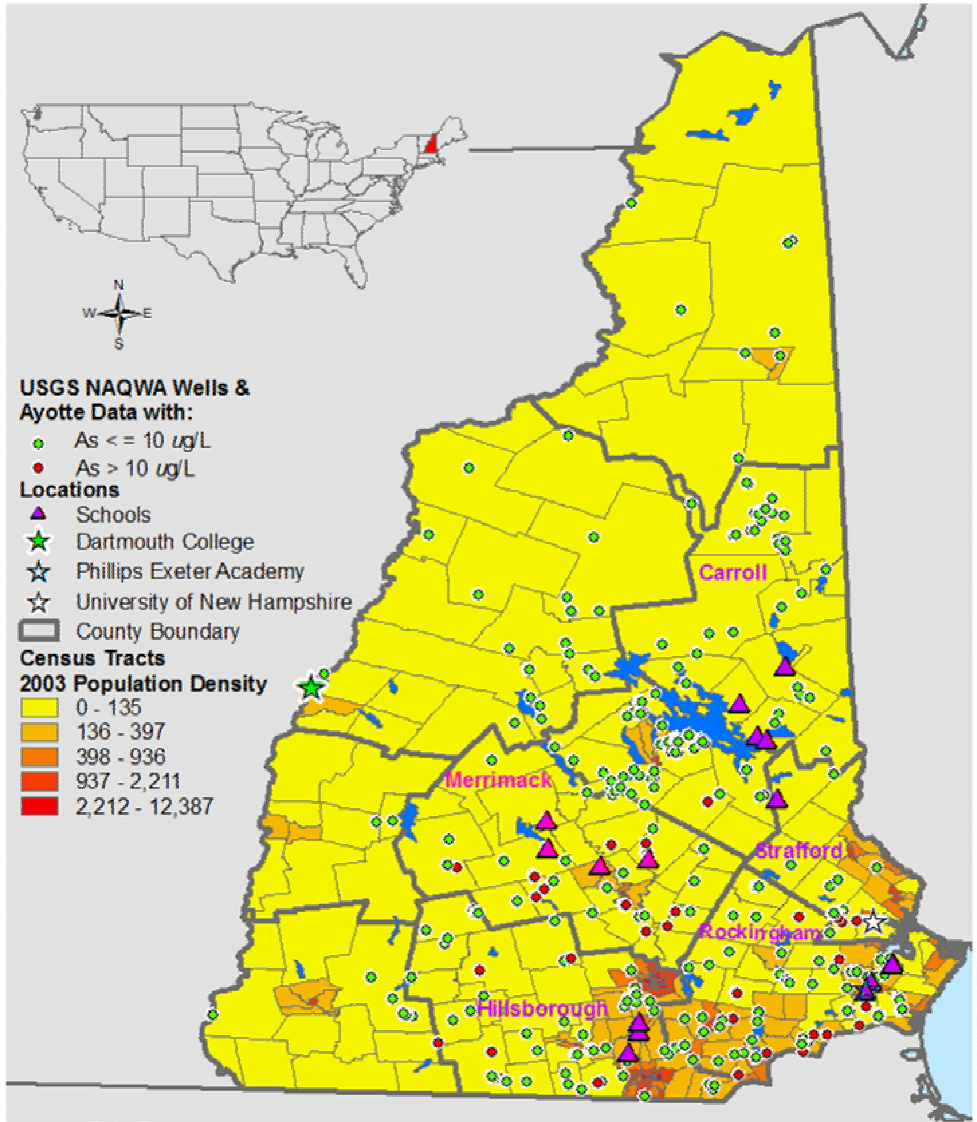
Hall et al, Toxicol, 2006

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

Kilometers
0 12.5 25 50