



Environment and Cardiovascular Disease: Opportunities for Prevention in the Strong Heart Study Communities

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Strong Heart Study: Team Science



Collective effort

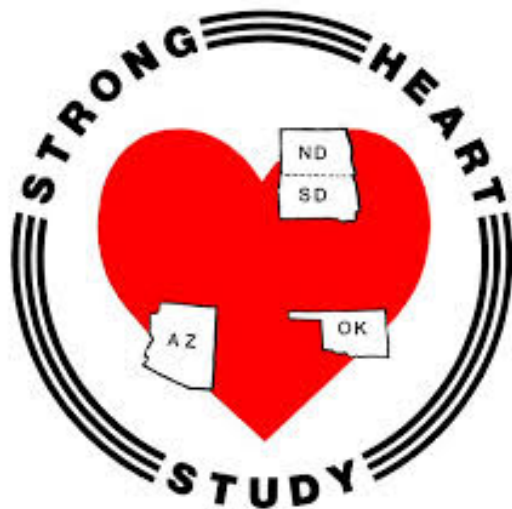


Strong Heart Study

Population-based prospective cohort study funded since 1988 by the National Heart, Lung and Blood Institute and the Indian Health Service

N = 7,600 adults

13 tribes and communities





Arizona



N/S
Dakota



Oklahoma

Study Population

Original Strong Heart Study
4,549 adults 45-74 y



Visit 1
1989-91

Visit 2
1993-95

Visit 3
1998-99

64% baseline
response rate

89%

retention rate

88%

Ongoing Surveillance: Morbidity & Mortality

Visit 3 pilot
1998-99

Visit 4
2001-03

Visit 5
2006-09

Visit 6
2014-16

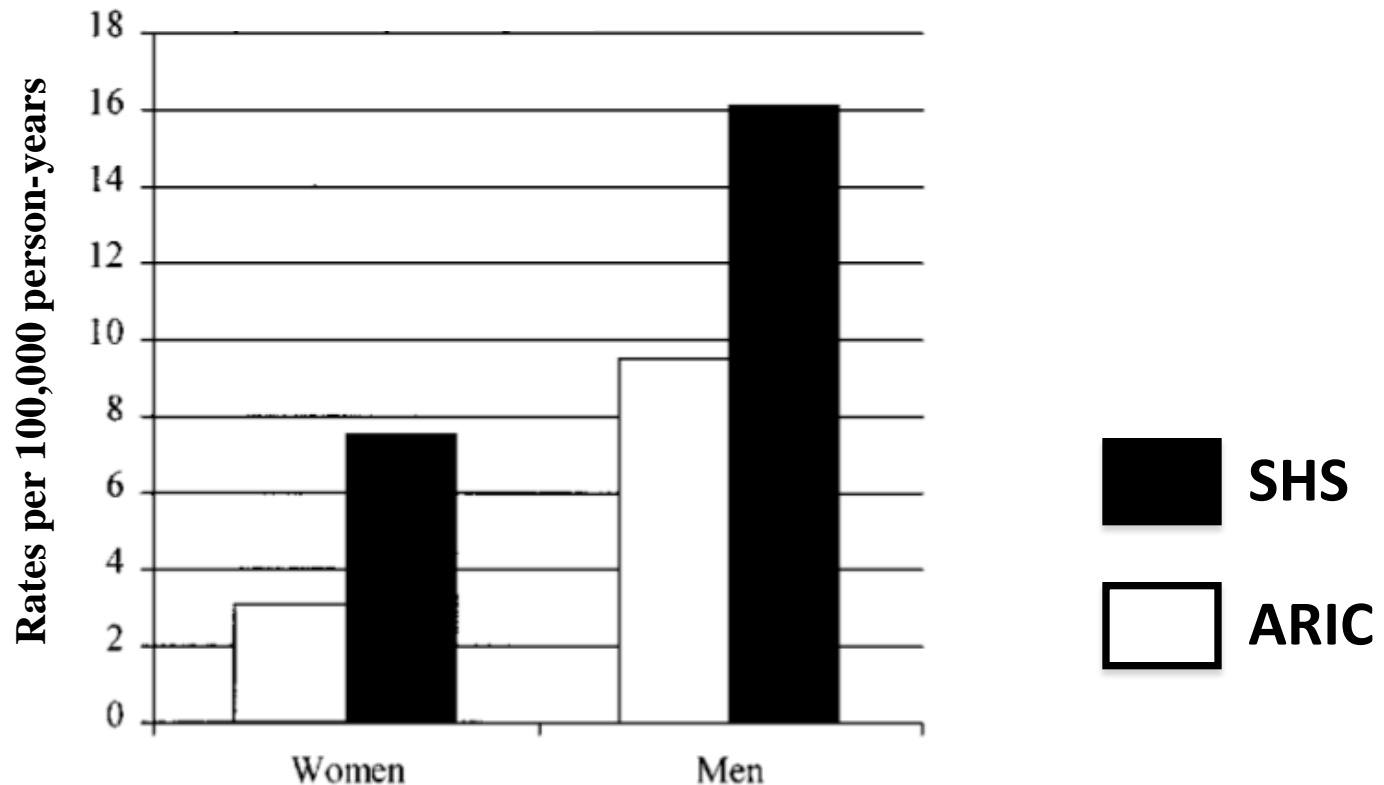
Strong Heart *Family* Study
3,050 participants ≥ 14 y

Continuous funding critical to maintain sustainable research projects

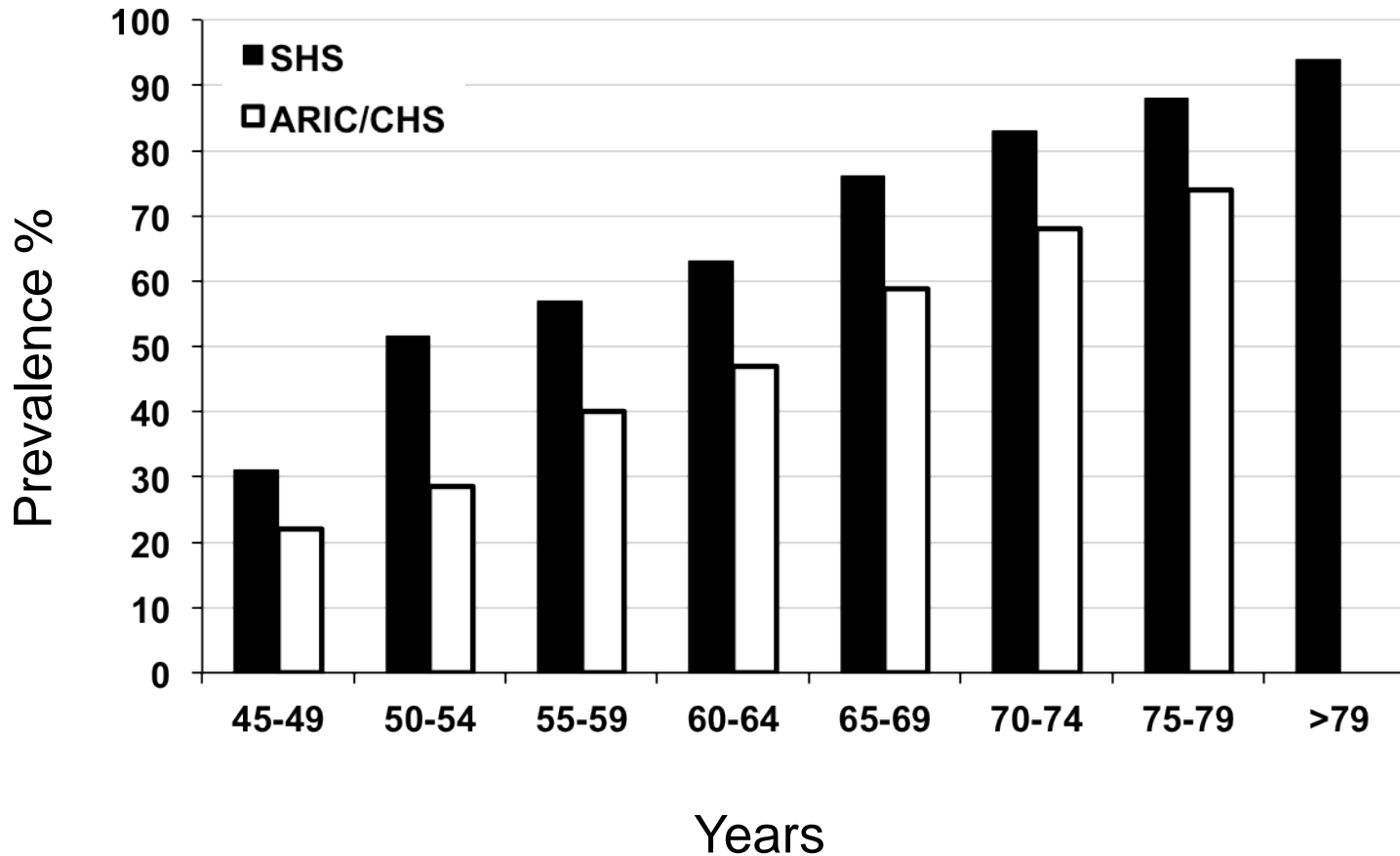
Rising Tide of Cardiovascular Disease in American Indians : The Strong Heart Study

Barbara V. Howard, Elisa T. Lee, Linda D. Cowan, Richard B. Devereux, James M. Galloway, Oscar T. Go, William James Howard, Everett R. Rhoades, David C. Robbins, Maurice L. Sievers and Thomas K. Welty
Circulation 1999;99:2389-2395

Coronary Heart Disease (45-64 y)



Prevalence of Atherosclerosis Plaque

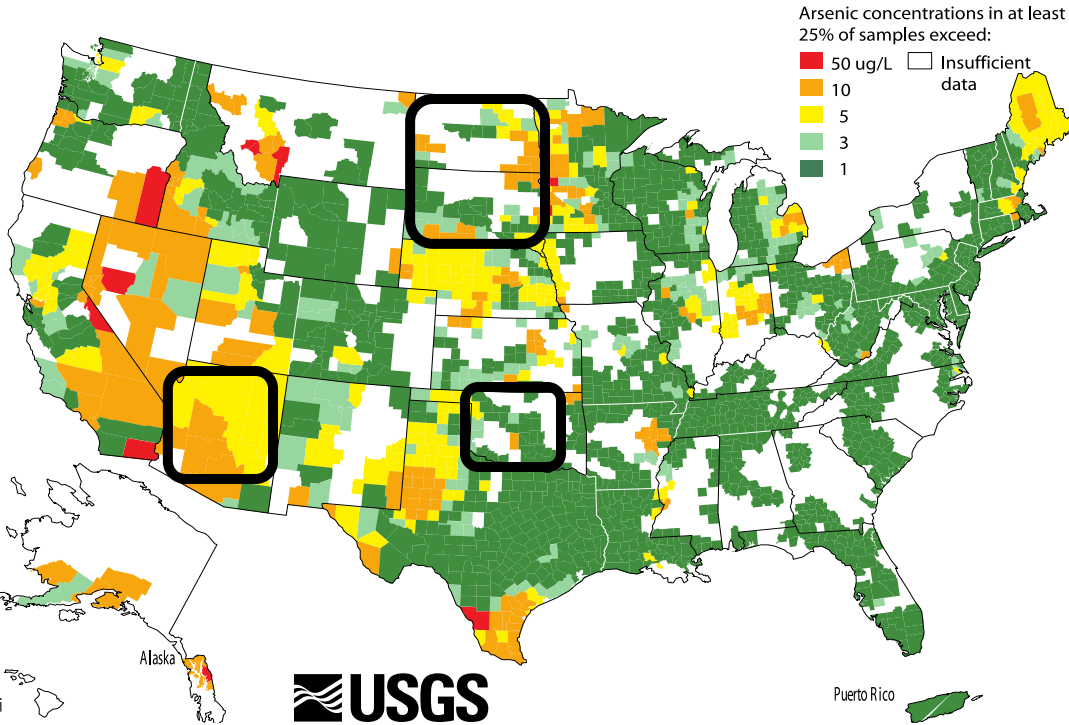


Tribally owned community water systems (CWS) with arsenic > 10 µg/L in year 2000

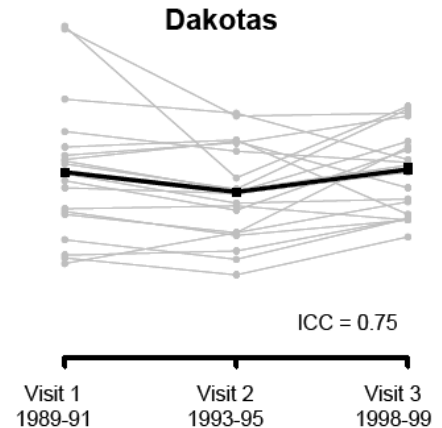
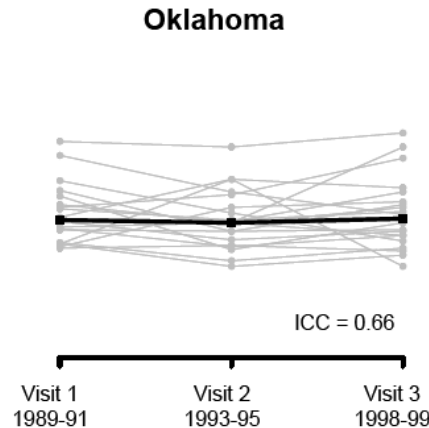
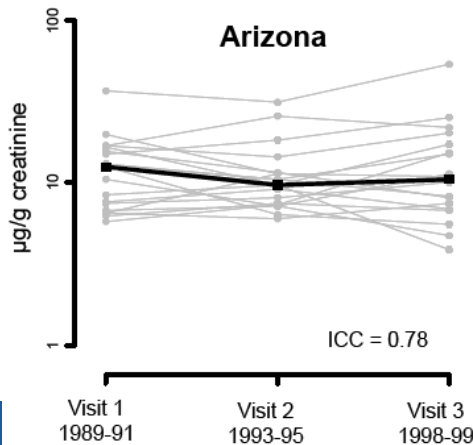
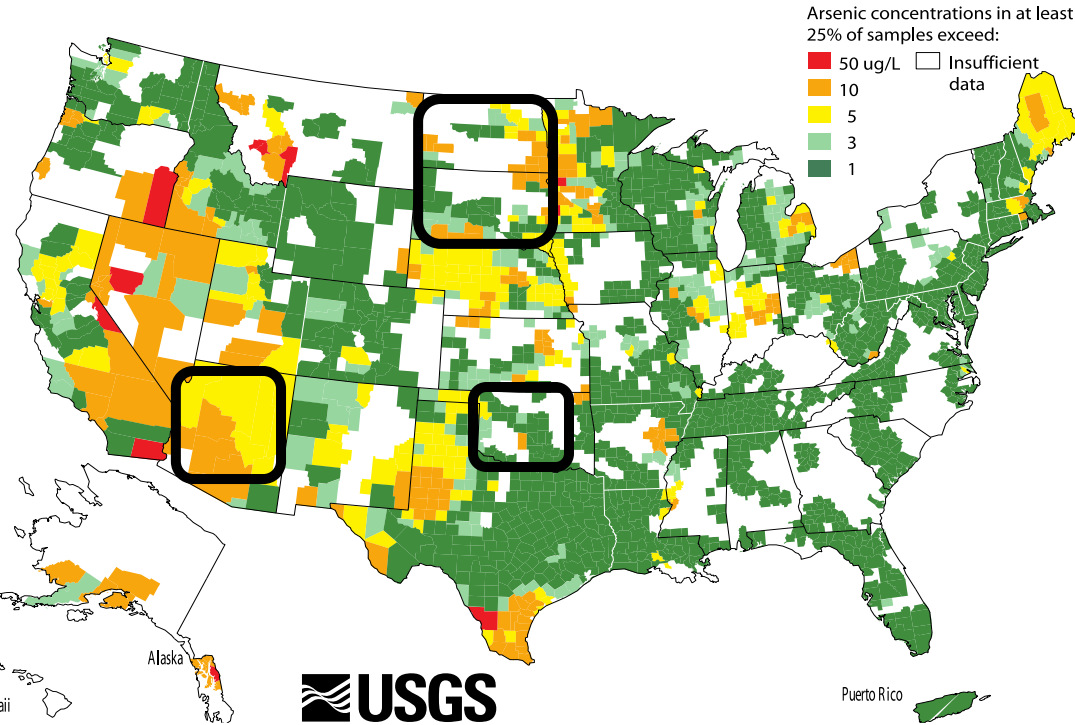
US EPA Region	Comm. Water Systems		Population	
	No.	% As >10µg/L	No.	% As >10µg/L
1 (Ct, Ma, Me, Nh, Ri, Vt)	1	0	41,000	0
2 (Nj, Ny)	7	0	8,425	0
3 (Dc, De, Md, Pa, Va, Wv)	--	--	--	--
4 (Al, Fl, Ga, Ms, Nc, Sc, Tn)	15	0	19,326	0
5 (Il, In, Mi, Wi, Oh)	79	4	87,687	3
6 (Ar, La, Nm, Ok , Tx)	47	23	60,413	35
7 (Ia, Ks, Mo, Ne)	8	0	4,468	0
8 (Co, Mt, Nd , Sd , Ut, Wy)	104	8	87,342	4
9 (Az , Ca, Nv, Hi, islands)	192	30	201,391	26
10 (Id, Or, Wa)	82	12	45,918	10
Navajo Nation	95	14	116,227	13
Total	630	16	672,197	15

**16% of tribally owned community water systems above > 10 µg/L vs.
4% for the overall US population**

Arsenic exposure disproportionately affects rural areas in the US, including American Indian communities

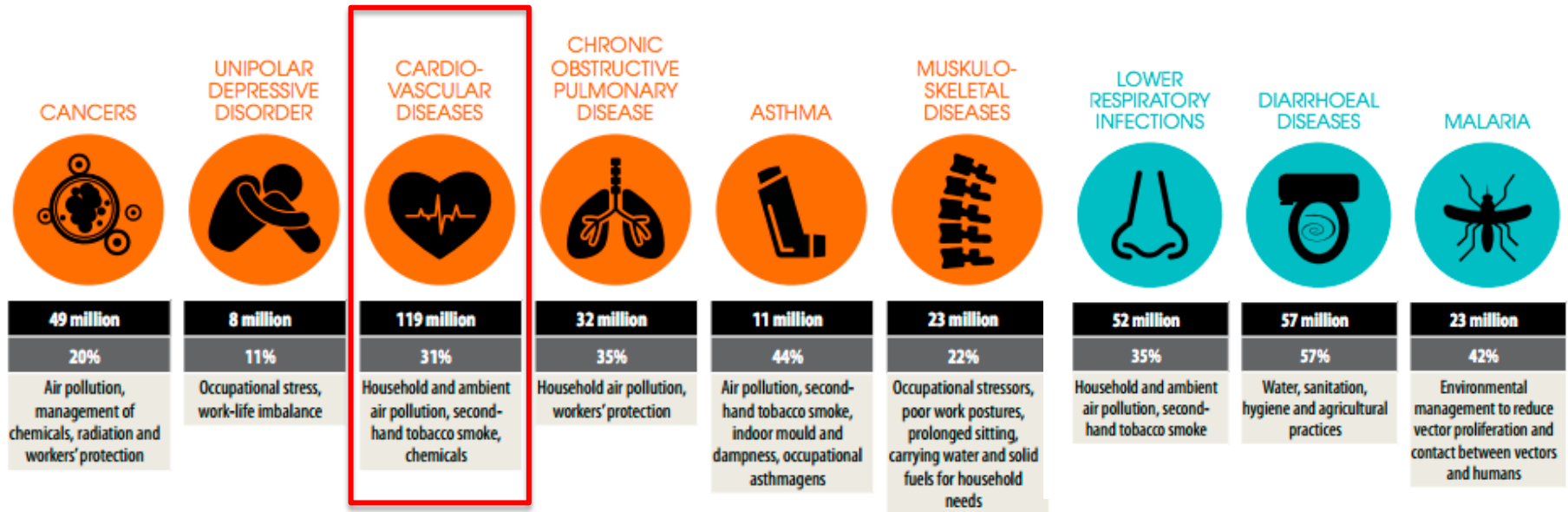


Arsenic exposure disproportionately affects rural areas in the US, including American Indian communities



ICC = Intraclass correlation coefficient

Environment and the burden of disease



31% of the burden of disease from fatal CVD globally could be avoided if all environmental risks were removed (household and ambient air pollution, secondhand tobacco smoke, and chemicals)
(World Health Organization, 2016)

Elevated Concentrations of U and Co-occurring Metals in Abandoned Mine Wastes in a Northeastern Arizona Native American Community

Johanna M. Blake,[†] Sumant Avasarala,[‡] Kateryna Artyushkova,[§] Abdul-Mehdi S. Ali,^{||} Adrian J. Brearley,^{||} Christopher Shuey,[⊥] Wm. Paul Robinson,[⊥] Christopher Nez,[#] Sadie Bill,[#] Johnnye Lewis,[∇] Chris Hirani,[○] Juan S. Lezama Pacheco,[◆] and José M. Cerrato^{*;‡}



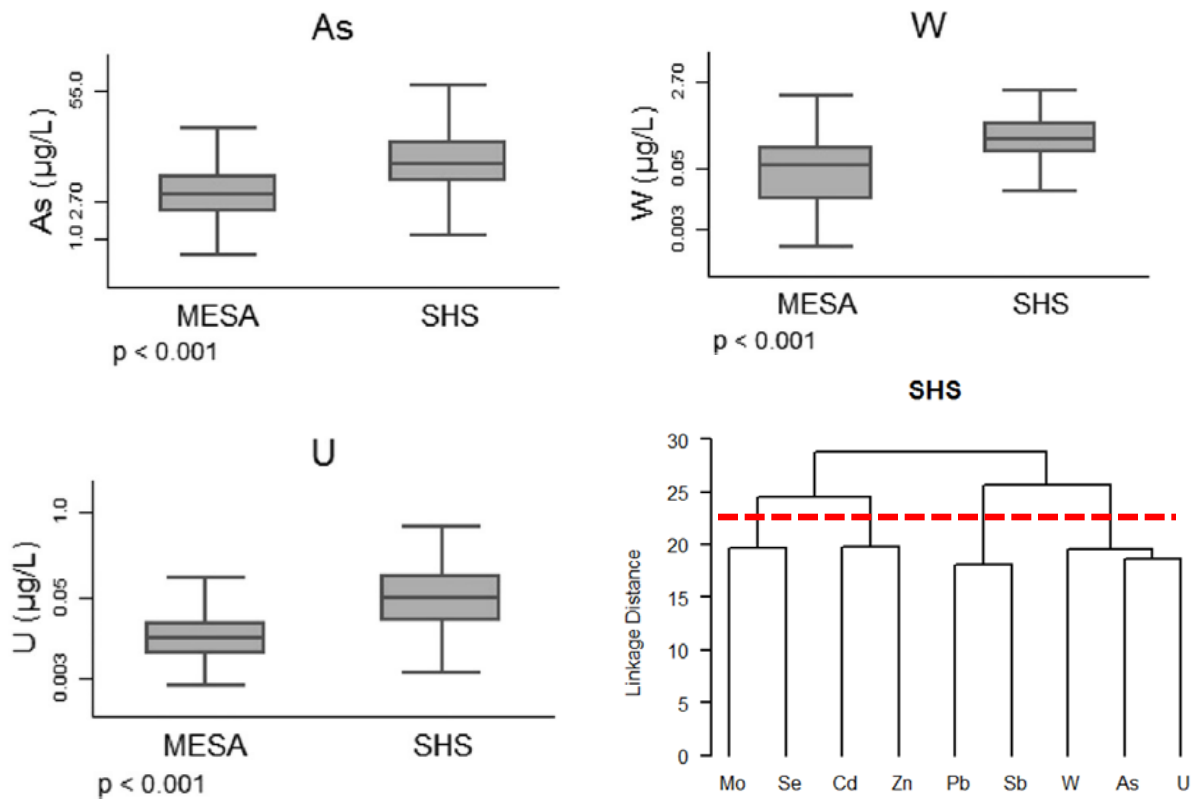
**Abandoned
Uranium Mine
Waste
(Northeastern
Arizona)**

Elevated **U** ($6,614 \text{ mg kg}^{-1}$)
Co-occurring metals:
(e.g. **As, V, Fe**)

<u>U in Water</u> (Spring)	<u>EPA MCL</u> for U
67-170 $\mu\text{g L}^{-1}$	> 30 $\mu\text{g L}^{-1}$

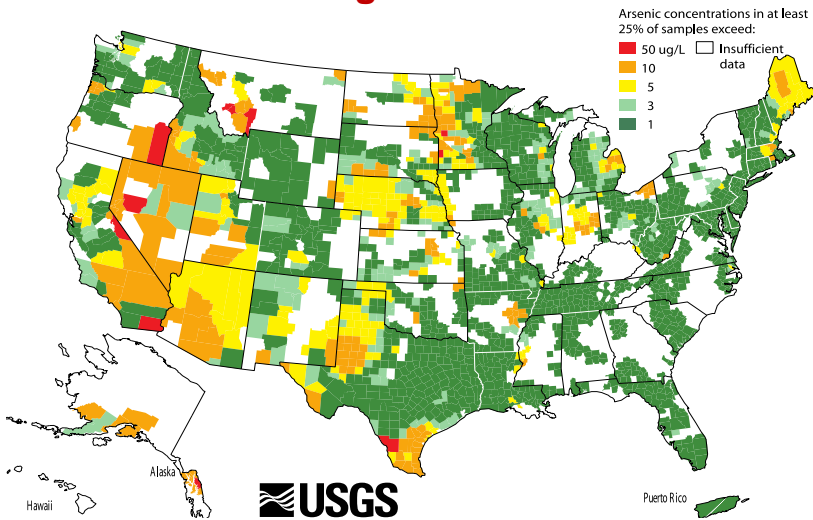
Metal mixtures in urban and rural populations in the US: The Multi-Ethnic Study of Atherosclerosis and the Strong Heart Study[☆]

Yuanjie Pang^{a,*}, Roger D. Peng^b, Miranda R. Jones^a, Kevin A. Francesconi^c,
 Walter Goessler^c, Barbara V. Howard^{d,e}, Jason G. Umans^{d,e}, Lyle G. Best^f,
 Eliseo Guallar^{a,g,h}, Wendy S. Post^{a,g,h}, Joel D. Kaufmanⁱ, Dhananjay Vaidya^h,
 Ana Navas-Acien^{a,g,j}



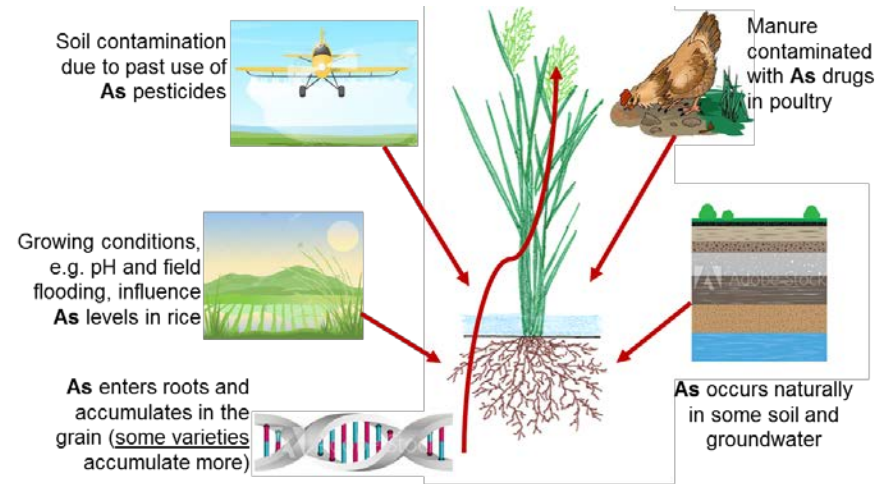
Arsenic is widespread in water and food

Arsenic in groundwater



US EPA standard in public water is 10 µg/L

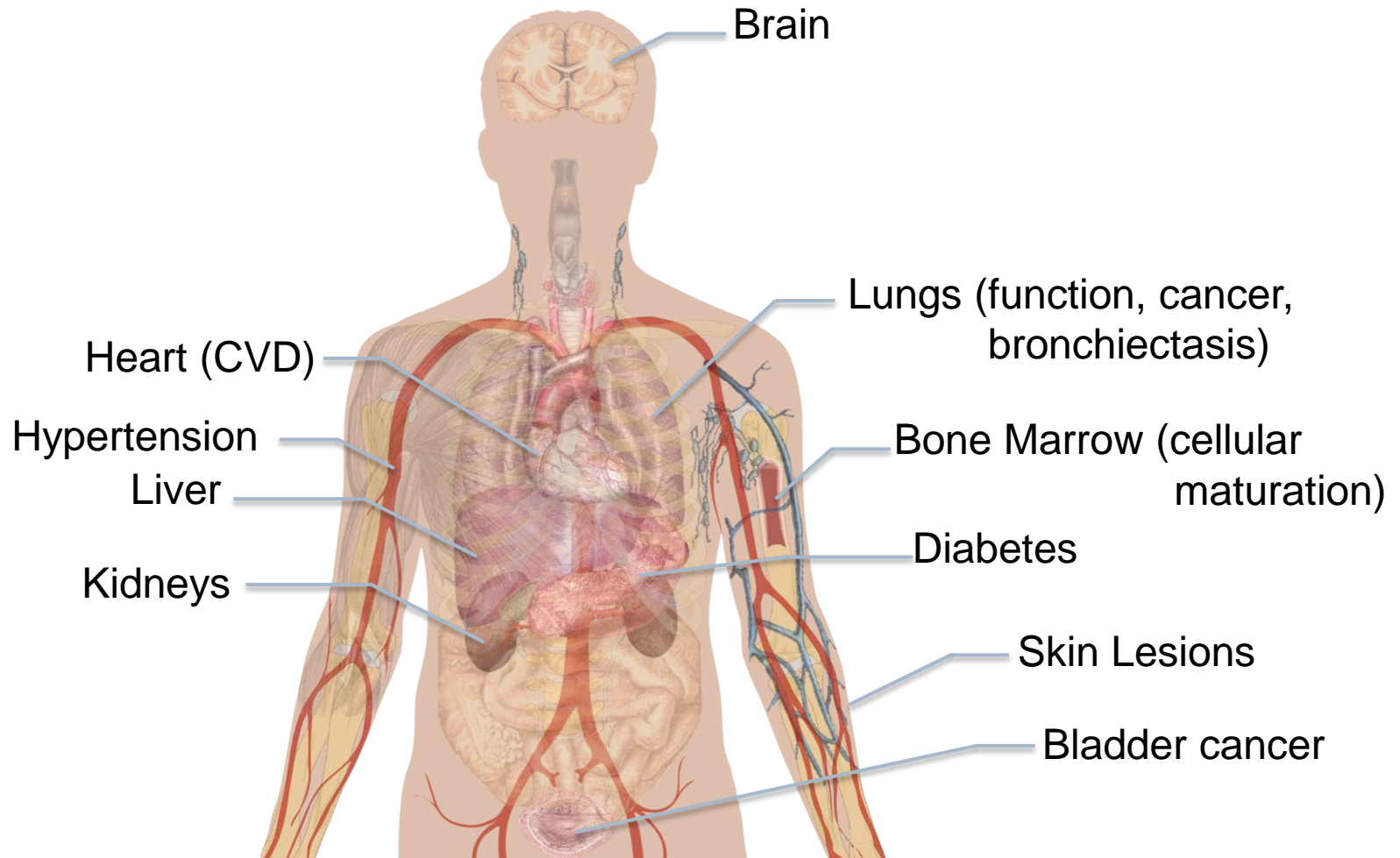
Arsenic accumulates in rice grain



FDA standard for rice is pending

- Inorganic arsenic**
- Water, food (rice, juice, other grains), air
 - Excreted through the urine in 3 phases
 - Half life 3 to 38 days
 - Highly toxic and carcinogenic, affects many organs and systems
 - Seafood: source of organic arsenicals that are non-toxic

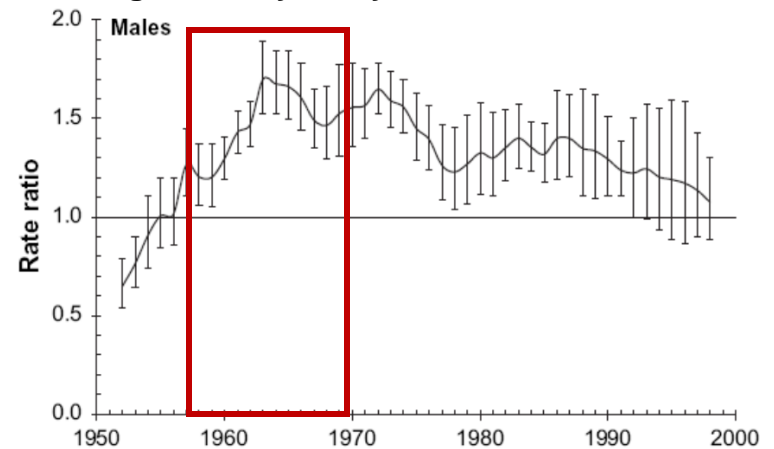
Arsenic is pleiotropic



Arsenic and CVD – epidemiological evidence

1930s 1980s	Case series / Ecological studies <ul style="list-style-type: none"> • German vintners (As in pesticides, PAD) • Taiwan & Chile (water As, PAD & other CVD) 				
1990s	Cohort studies in Taiwan <ul style="list-style-type: none"> • Ecological water As assessment • CVD mortality (all, CHD, stroke) 				
2007	Ecological study in Chile <ul style="list-style-type: none"> • Natural experiment before & after water As • Myocardial infarction mortality 				
2011 2013	HEALS cohort in Bangladesh <ul style="list-style-type: none"> • Water and urine As • CVD incidence & mortality (all, CHD, stroke) 				
As levels:	<table border="1"> <tr> <td>> 500 µg/L</td> <td>100 µg/L</td> <td>10-100 µg/L</td> <td>< 10 µg/L</td> </tr> </table>	> 500 µg/L	100 µg/L	10-100 µg/L	< 10 µg/L
> 500 µg/L	100 µg/L	10-100 µg/L	< 10 µg/L		

Ecological study of myocardial infarction in Chile



Yuan Y et al. Am J Epidemiol 2007

BMJ

HEALS cohort

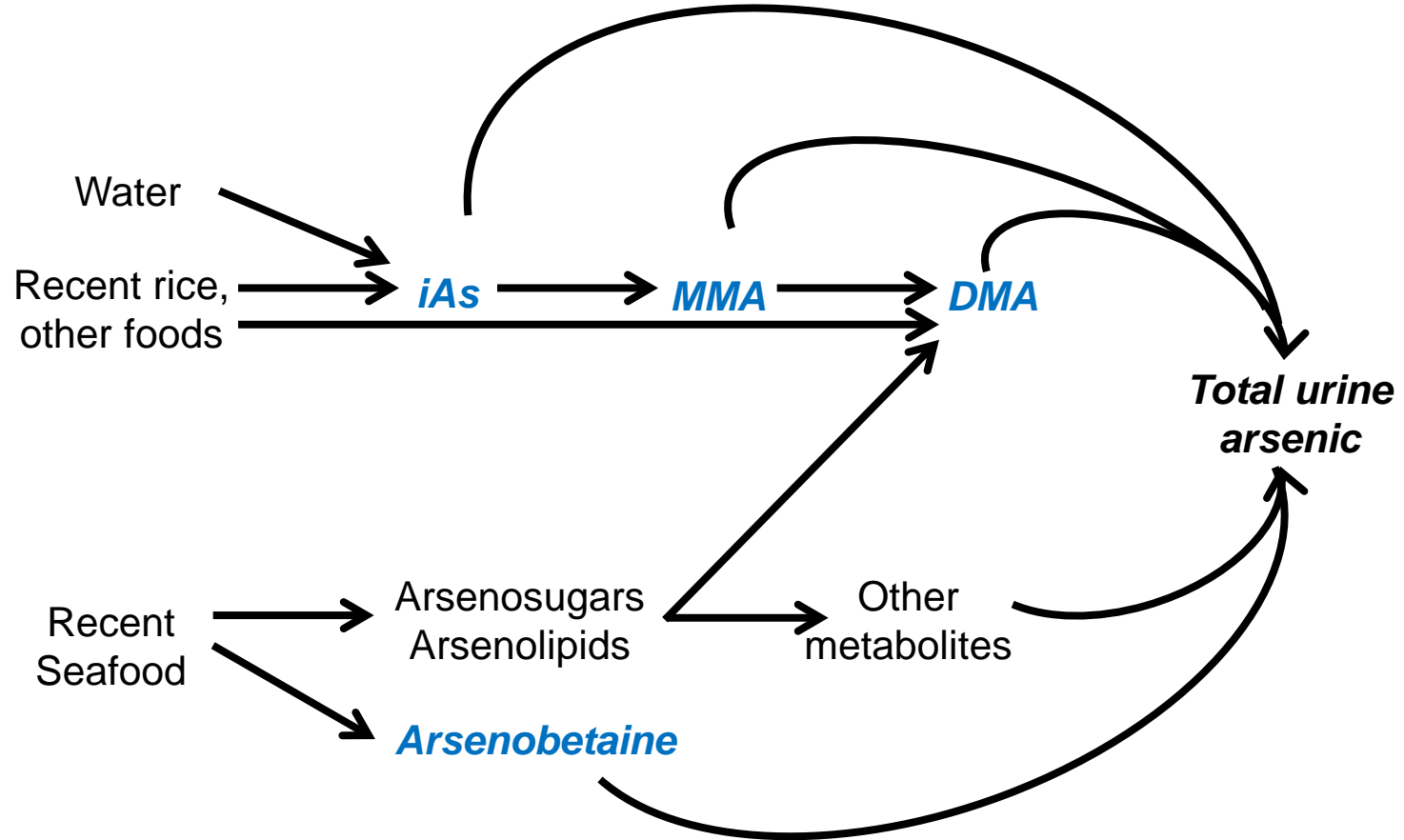
RESEARCH

Arsenic exposure from drinking water and mortality from cardiovascular disease in Bangladesh: prospective cohort study

Yu Chen, associate professor of epidemiology,¹ Joseph H Graziano, professor of environmental health sciences,² Faruque Parvez, associate research scientist,² Mengling Liu, associate professor of biostatistics,¹ Vesna Slavkovich, associate research scientist,² Tara Kalra, project coordinator/data analyst,³ Maria Argos, project coordinator/data analyst,³ Tariqul Islam, project director,⁴ Alauddin Ahmed, field coordinator,⁴ Muhammad Rakibuz-Zaman, study physician/laboratory manager,⁴ Rabiul Hasan, assistant field coordinator,⁴ Golam Sarwar, informatics manager,⁴ Diane Levy, senior staff associate,² Alexander van Geen, Lamont research professor in Lamont-Doherty Earth Observatory,⁵ Habibul Ahsan, professor of epidemiology³

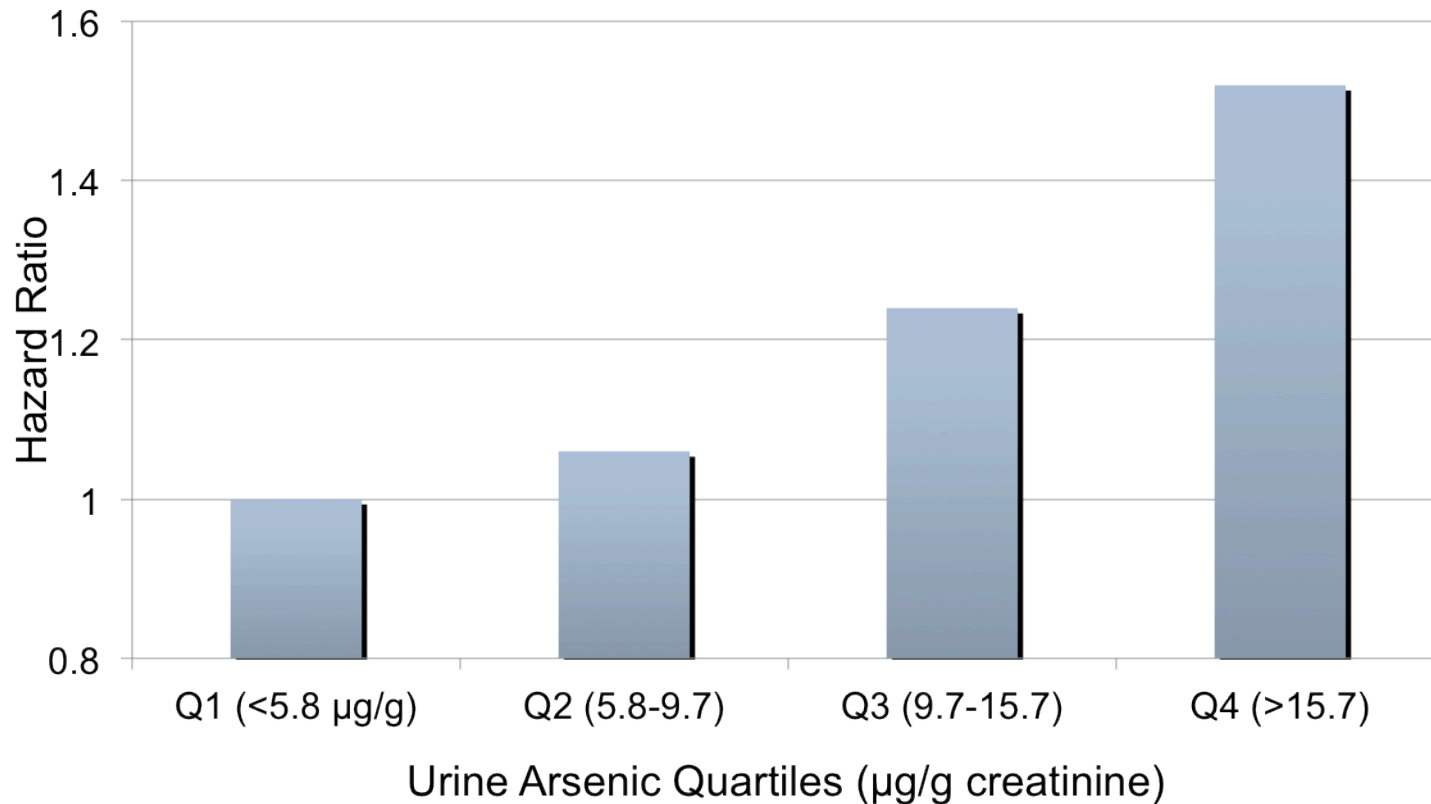
BMJ 2011;342:d2431

Arsenic exposure and metabolism



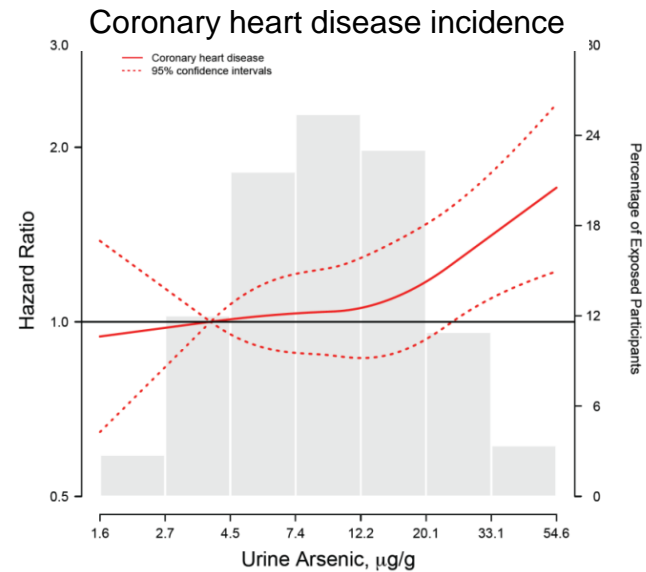
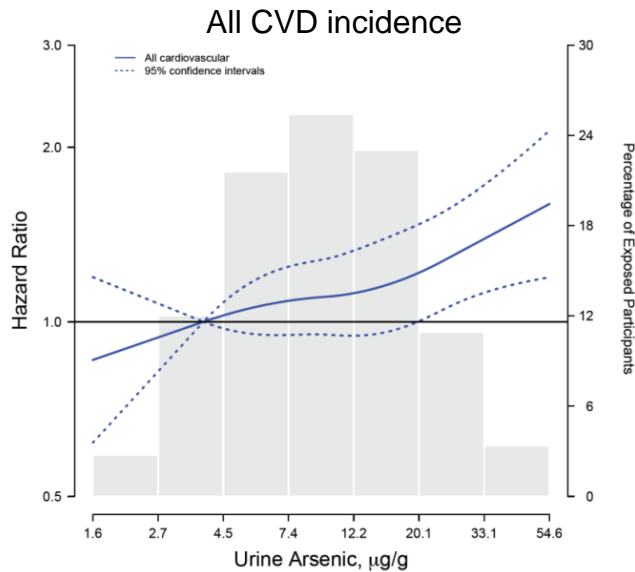
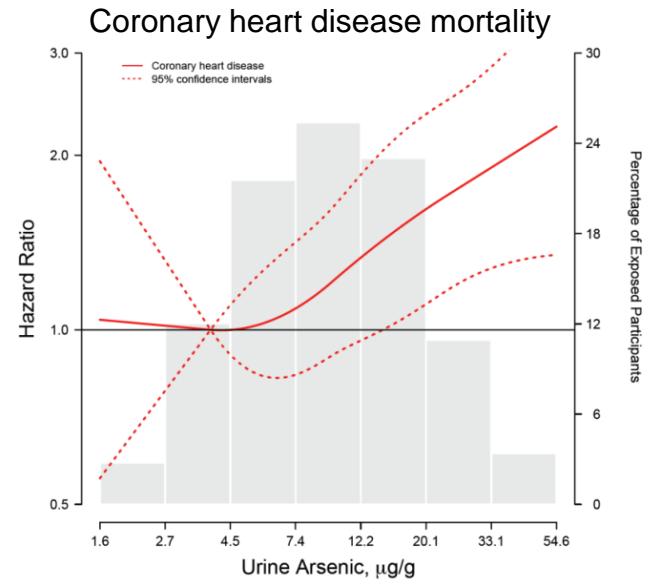
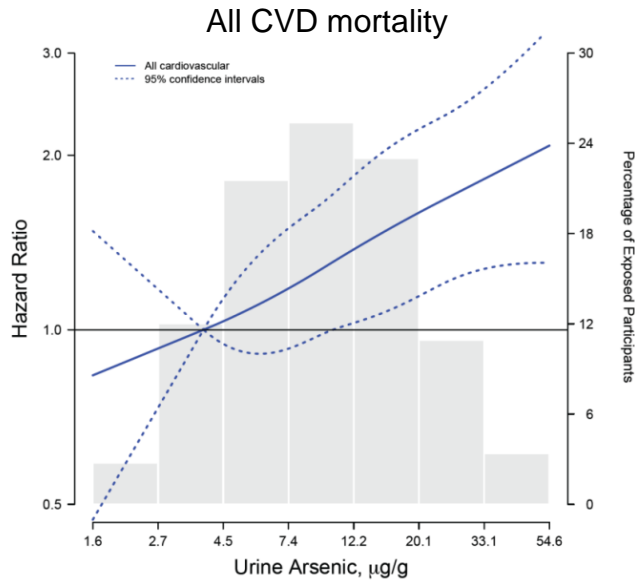
Other sources of arsenic (occupational settings and air pollution) are not shown. Urine As species commonly measured in epidemiologic studies are marked in **blue**.

Risk of cardiovascular mortality over 20 years by urine arsenic quartiles



Adjusted for sex, education, alcohol, smoking, and body mass index, total cholesterol, HDL-cholesterol, hypertension medication, systolic blood pressure, diabetes and estimated glomerular filtration rate

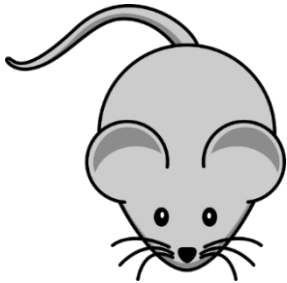
Arsenic and incident CVD



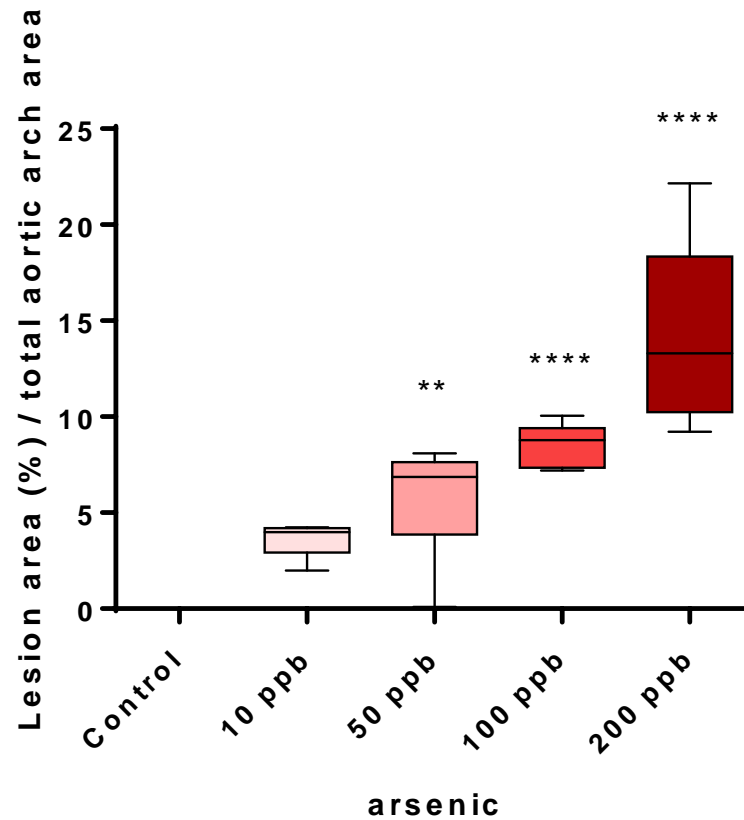
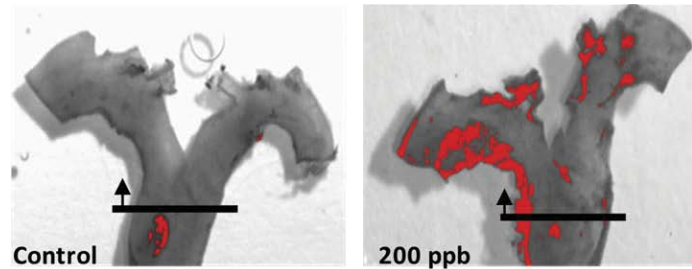
Moon et al. *Annals Intern Medicine* 2013

Lines represent hazard ratios (95% CI) based on restricted cubic splines and adjusted for age, sex, education, alcohol, smoking, body mass index, total cholesterol, HDL-cholesterol, hypertension medication, SBP, diabetes eGFR, and stratified by region

ApoE^{-/-} Model of Arsenic-induced Atherosclerosis



Tap water arsenic
for 13 weeks



N=6/group

Association between Lifetime Exposure to Inorganic Arsenic in Drinking Water and Coronary Heart Disease in Colorado Residents

Katherine A. James,¹ Tim Byers,¹ John E. Hokanson,¹ Jaymie R. Meliker,² Gary O. Zerbe,¹ and Julie A. Marshall¹

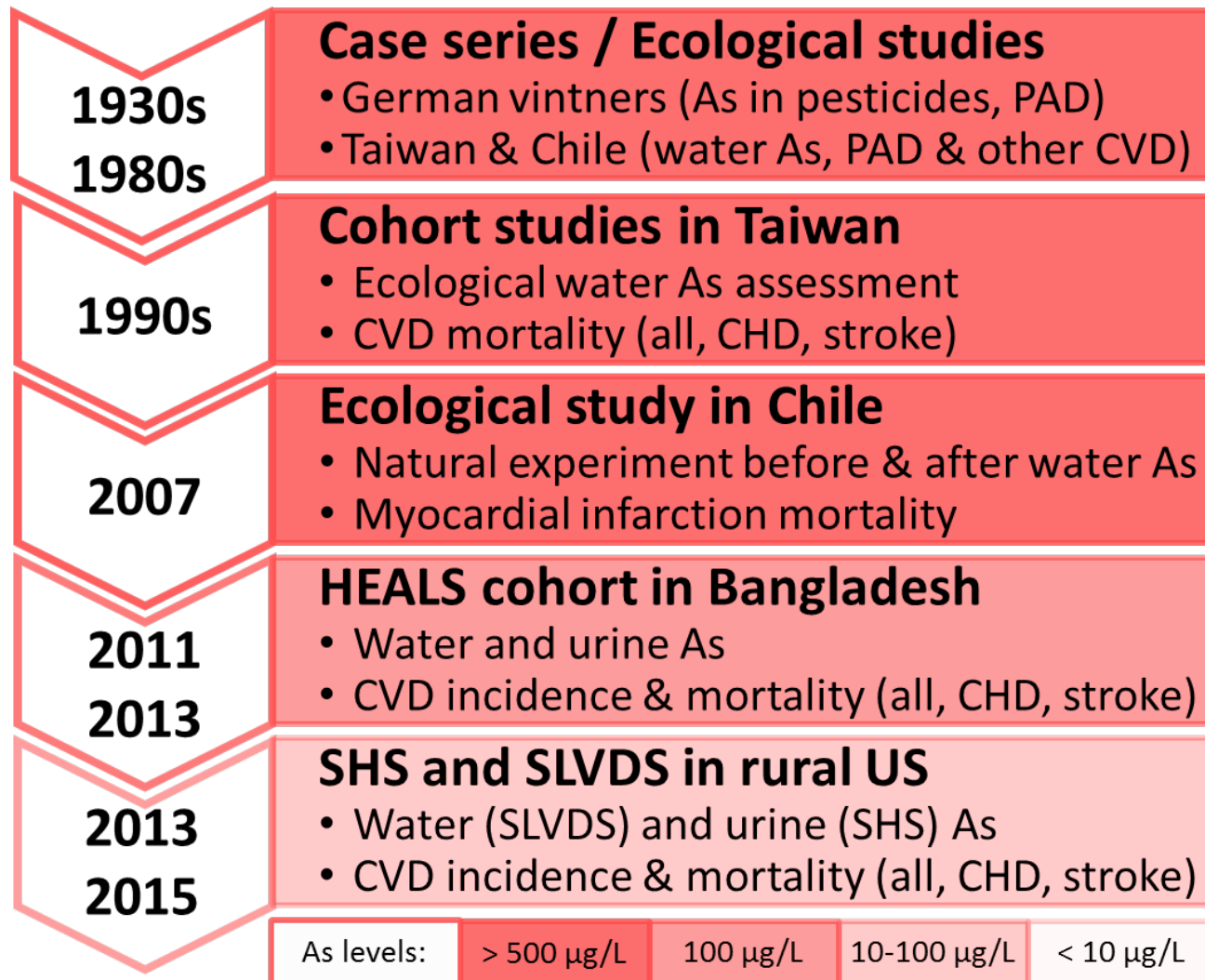
¹Colorado School of Public Health, University of Colorado Denver, Aurora, Colorado, USA; ²Department of Preventive Medicine, State University of New York, Stony Brook, New York, USA

Hazard ratio (95%CI) for incident coronary heart disease by water arsenic levels in the San Luis Valley Diabetes Study

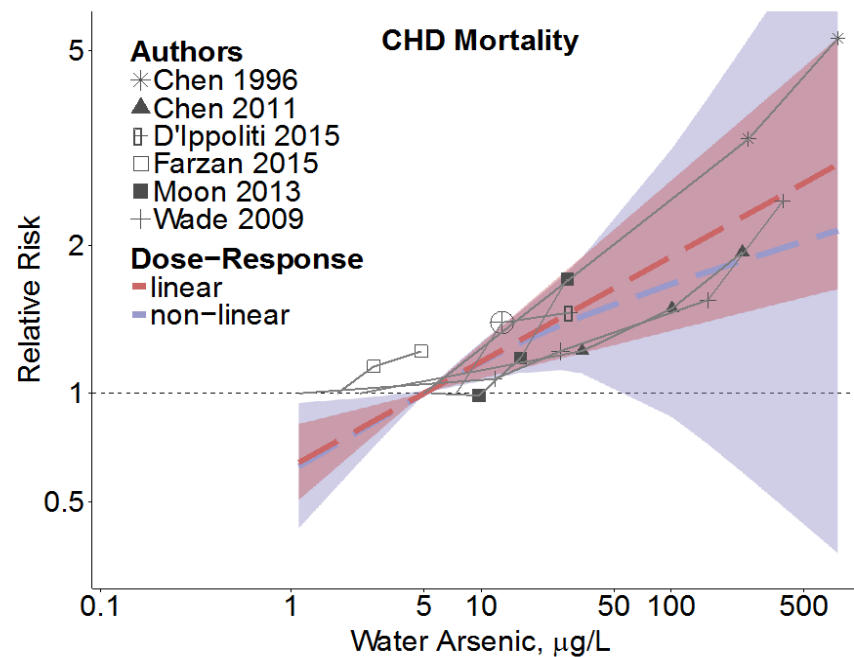
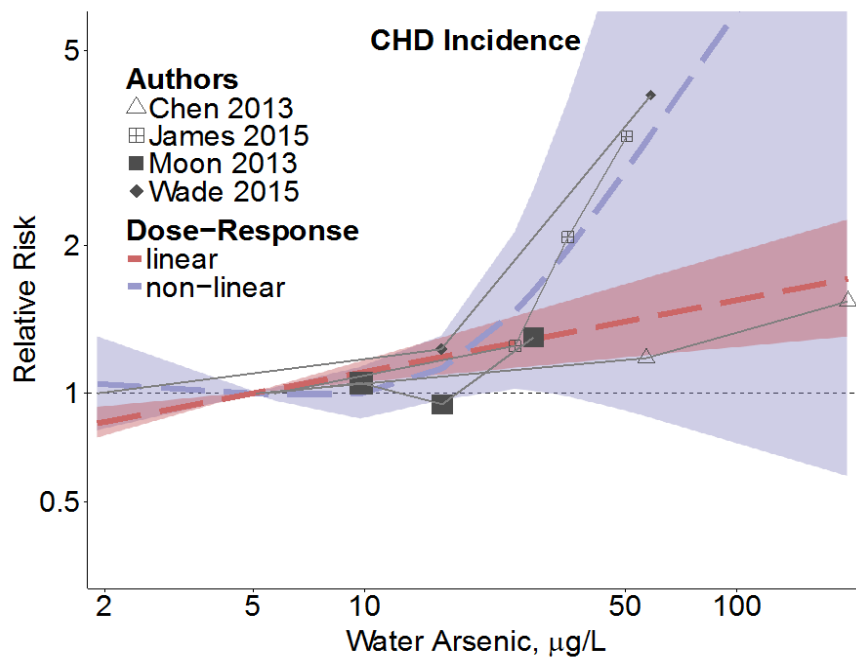
Variable	Univariate model HR (95% CI)	Full model HR (95% CI)
Arsenic exposure		
1–20 µg/L	1.0	1.0
20–30 µg/L	1.24 (0.70, 2.31)	1.25 (0.60, 2.61)
30–45 µg/L	2.14 (1.22, 3.98)	2.08 (1.11, 3.92)
45–88 µg/L	3.12 (1.11, 9.02)	3.34 (1.15, 9.30)

Adjusted for age, sex, ethnicity, income, family history CHD, diabetes, BMI, physical activity, LDL-cholesterol, triglycerides, HDL-cholesterol, folate, selenium

Summary of the epidemiological evidence



Dose-response meta-analysis



- Compared to 5 $\mu\text{g/L}$, the pooled relative risks (95% CI) for 10 $\mu\text{g/L}$ water arsenic based on a log-linear model were:
 - 1.11 (1.05, 1.17) (N=4) for CHD incidence
 - 1.16 (1.07, 1.26) (N=6) for CHD mortality,
- No evidence of non-linearity, although these tests had low statistical power
- Meta-analysis limited by the small number of studies and availability of published data

Need to combine studies - sharing

- A single study is unlikely to cover the full range of the relevant exposures, different genetic backgrounds, different characteristics – combining studies allows to compare across studies: look for consistencies and differences
- By combining epidemiologic studies of arsenic and CVD
 - 1) We extend the range of arsenic exposure levels
 - 2) Increase statistical power to evaluate dose-response, gene-environment interactions, nutrition-environment interactions, mediation analyses
- Consortium efforts are needed in environmental health
- Address and respect communities conditions for data sharing

Data ownership and data sharing

- Who owns the data?
- Who allows data sharing and in which terms?
- Who profits from research?

Recommendations

- Build relationships
- Use a participatory approach
- Accept research codes that tribes have developed to regulate the collection and circulation of information about their members
 - Tribes and Indian Health Service IRBs
 - Data ownership
 - Review of publications and lay summaries
 - Communication of study findings (individuals, community)
 - Anonymity of individuals and tribes
 - Value traditional knowledge

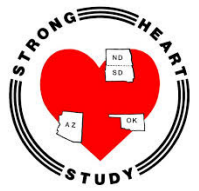


Indigenous peoples must benefit from science

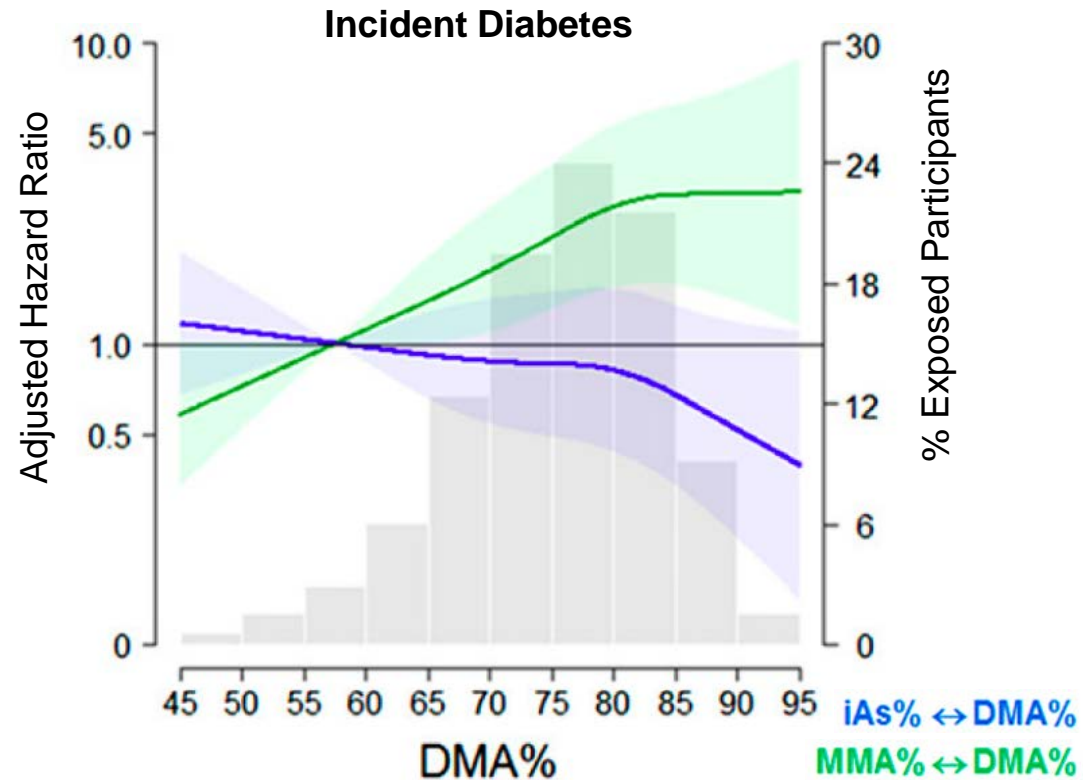
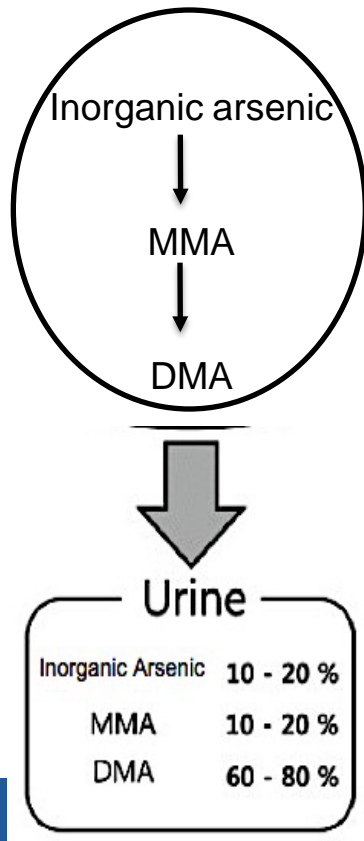
To drive sustainable development, Dyna Rochmyaningsih argues, science must empower rural communities — not just serve industry and governments.

MITIGATION
MUST BE THE
RESPONSIBILITY OF
EVERYONE
ON THE PLANET,
NOT JUST
SCIENTISTS,
BUSINESSMEN AND
POLICYMAKERS.

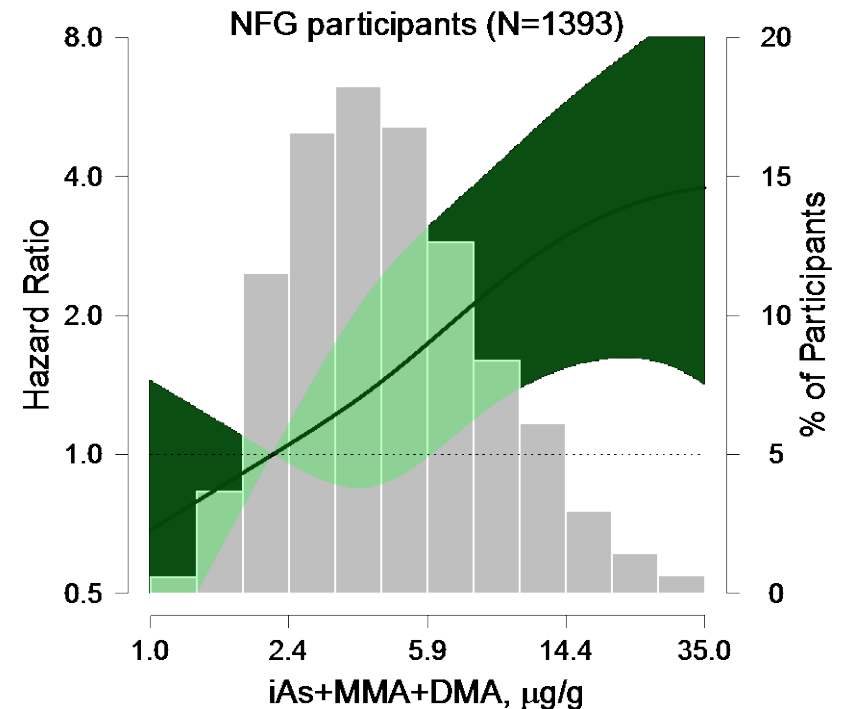
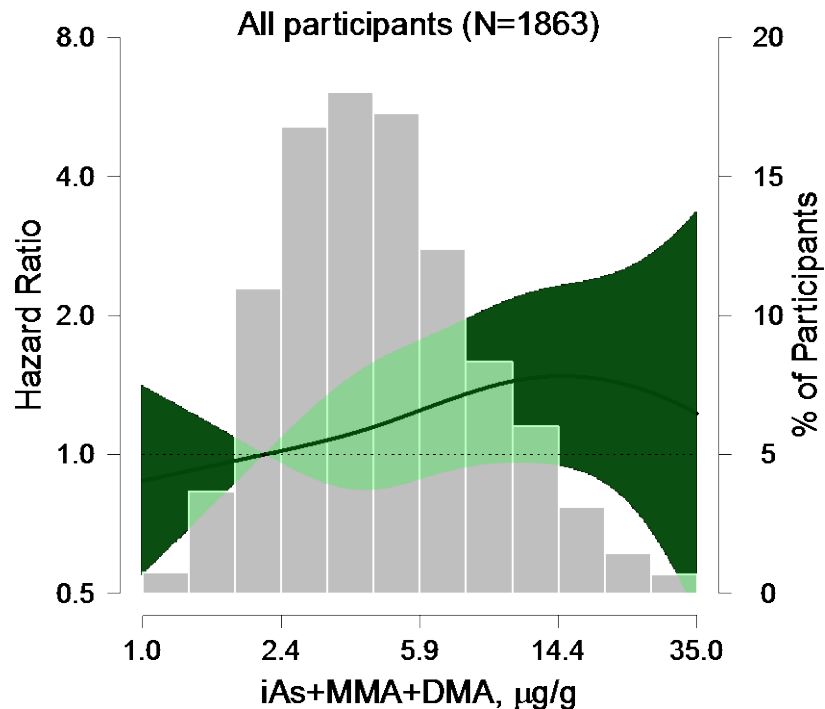
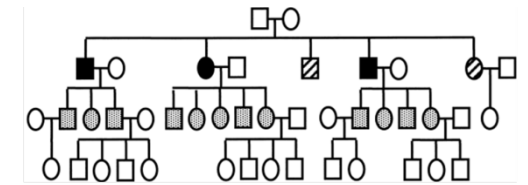
Arsenic and diabetes



- Arsenic exposure was associated with prevalent diabetes and with diabetes control (Gribble et al. AJE 2012)
- Arsenic metabolism associated with incident diabetes and with markers of insulin resistance (Kuo et al. Diabetes Care 2015)

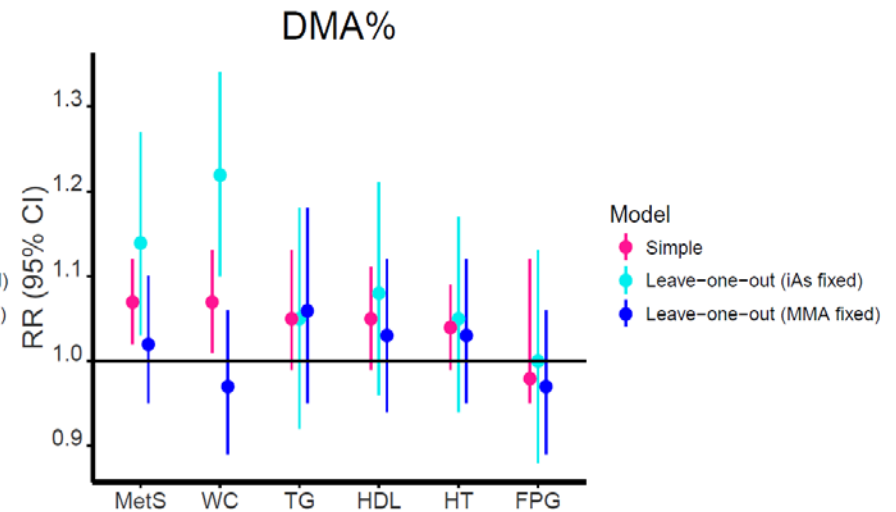
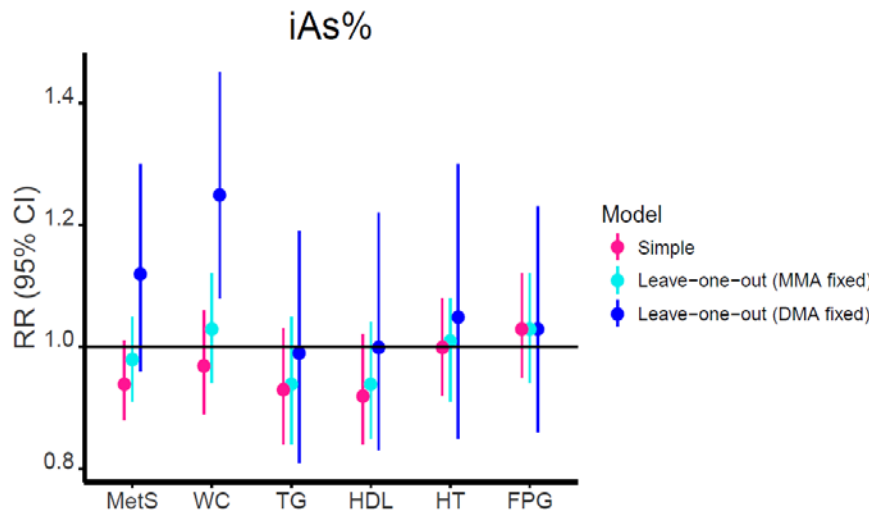
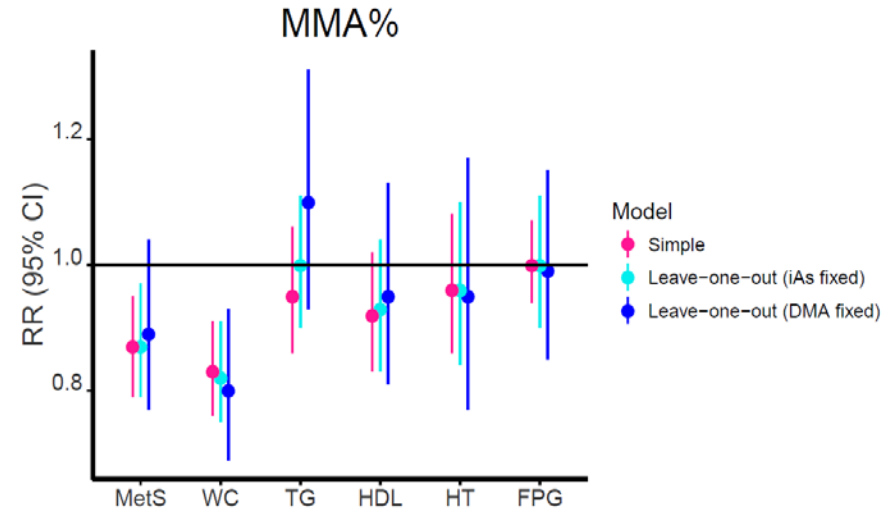
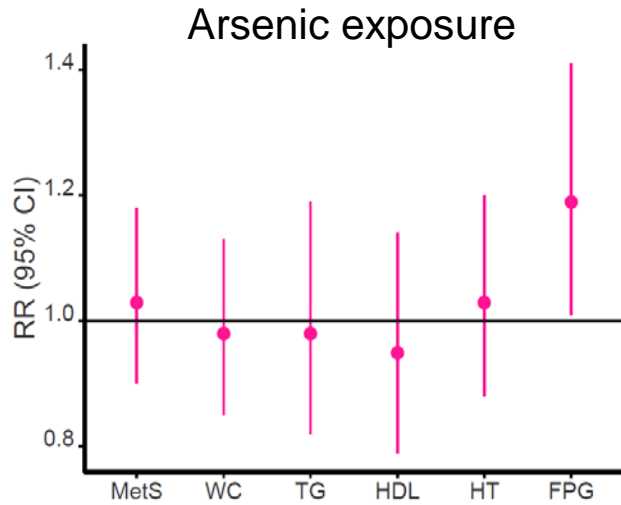


Arsenic and incident diabetes in the Strong Heart Family Study



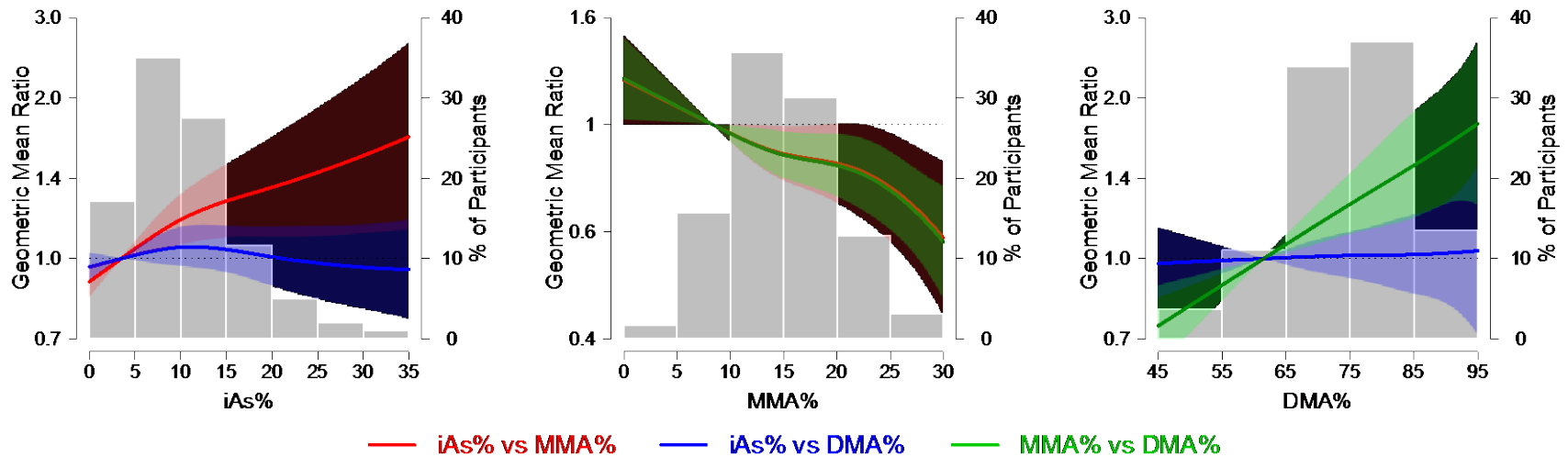
Hazard Ratio for incident diabetes by arsenic exposure in all participants and in participants with normal fasting glucose (NFG), stratified by center and adjusted for age, sex, education, smoking, body mass index, waist circumference, kidney function, estimated dietary vitamin B2, vitamin B6 and folate and *AS3MT* genotype.

Arsenic exposure and metabolism and the metabolic syndrome (MetS)



Relative risk (RR) for MetS, waist circumference (WC), triglycerides (TG), HDL-cholesterol, hypertension (HT) and fasting plasma glucose (FPG) per interquartile range (IQR) of arsenic exposure (iAs+MMA+DMA levels) and arsenic metabolism (iAs%, MMA%, DMA%). Models adjusted for age, sex, center, education, smoking, alcohol, body mass index, kidney function, urine creatinine, Σ As (for As metabolism)

Insulin resistance (HOMA-IR) by arsenic metabolism biomarkers in the SHFS (n=1548)



Model was adjusted age, sex, center, education, BMI, smoking, waist circumference, glomerular filtration rate, fasting glucose levels at baseline, estimated dietary vitamin B2, vitamin B6 and folate and *AS3MT* genotype.

Role of genetics

- Inorganic arsenic is methylated into MMA, then DMA and excreted in urine
- Heritability estimates proportion of total variability attributed to genetics
 - 53% iAs, 50% MMA, 63% DMA (Tellez-Plaza et al *EHP* 2013)
- Genomewide association study in Bangladesh (HEALS), and candidate gene studies highlight *AS3MT* variants
- *AS3MT* (10q24) encodes enzyme arsenic (III) methyltransferase
 - Possible role in methylating iAs to MMA and DMA

Illumina MetaboChip

- Approximately 200,000 SNPs
- Common variants from previous GWAS studies of diabetes, obesity and cardiometabolic diseases and less common variants not on GWAS chips
- We also fine mapped candidate genes

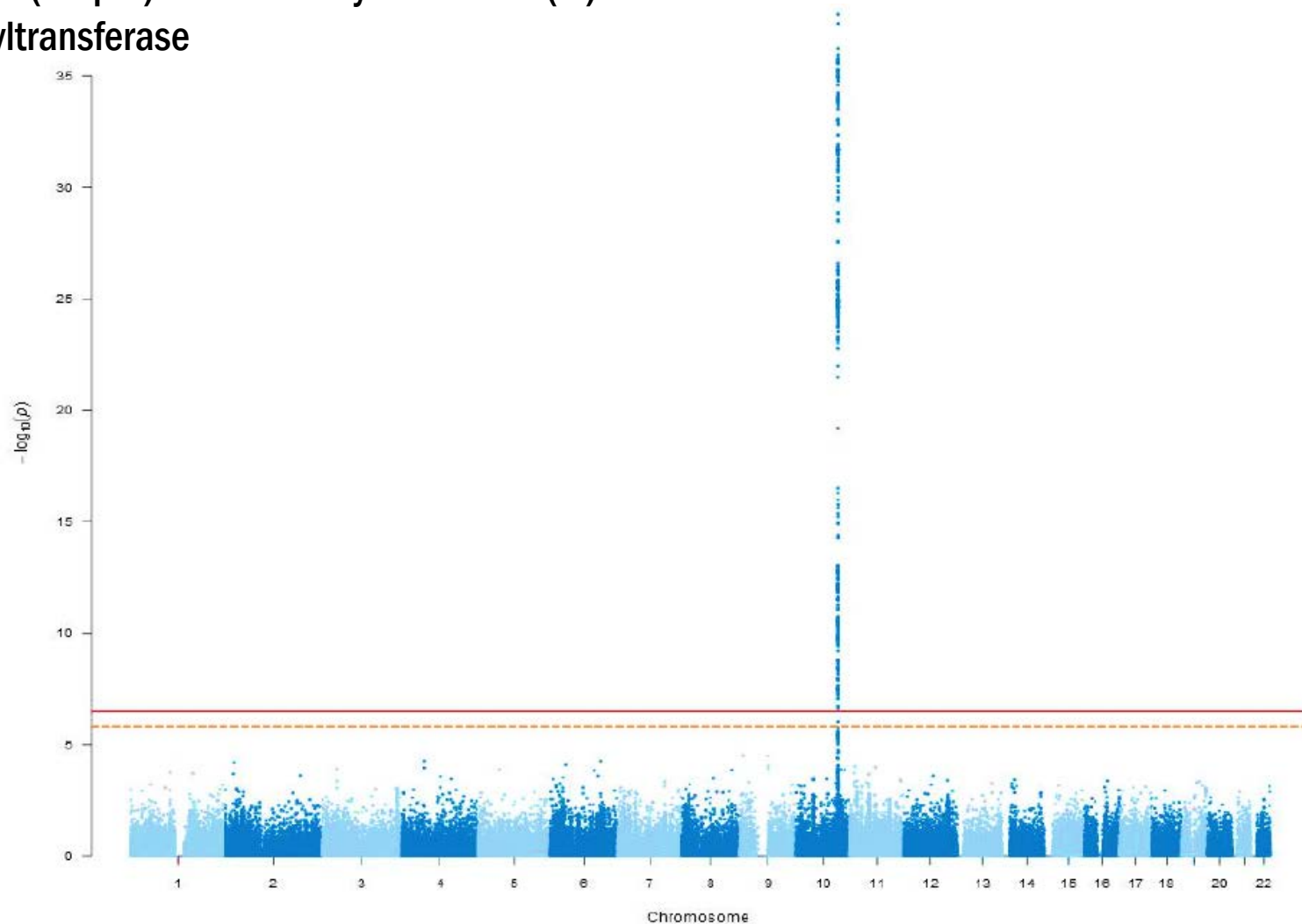


Panel	Total SNPs	Correction Bonferroni	Effective SNPs	Correction LD
MetaboChip	120,975	4.1330e-7	64374.845	7.7670e-7
Candidate (arsenic)	670	7.4626e-5	549.389	9.3359e-5

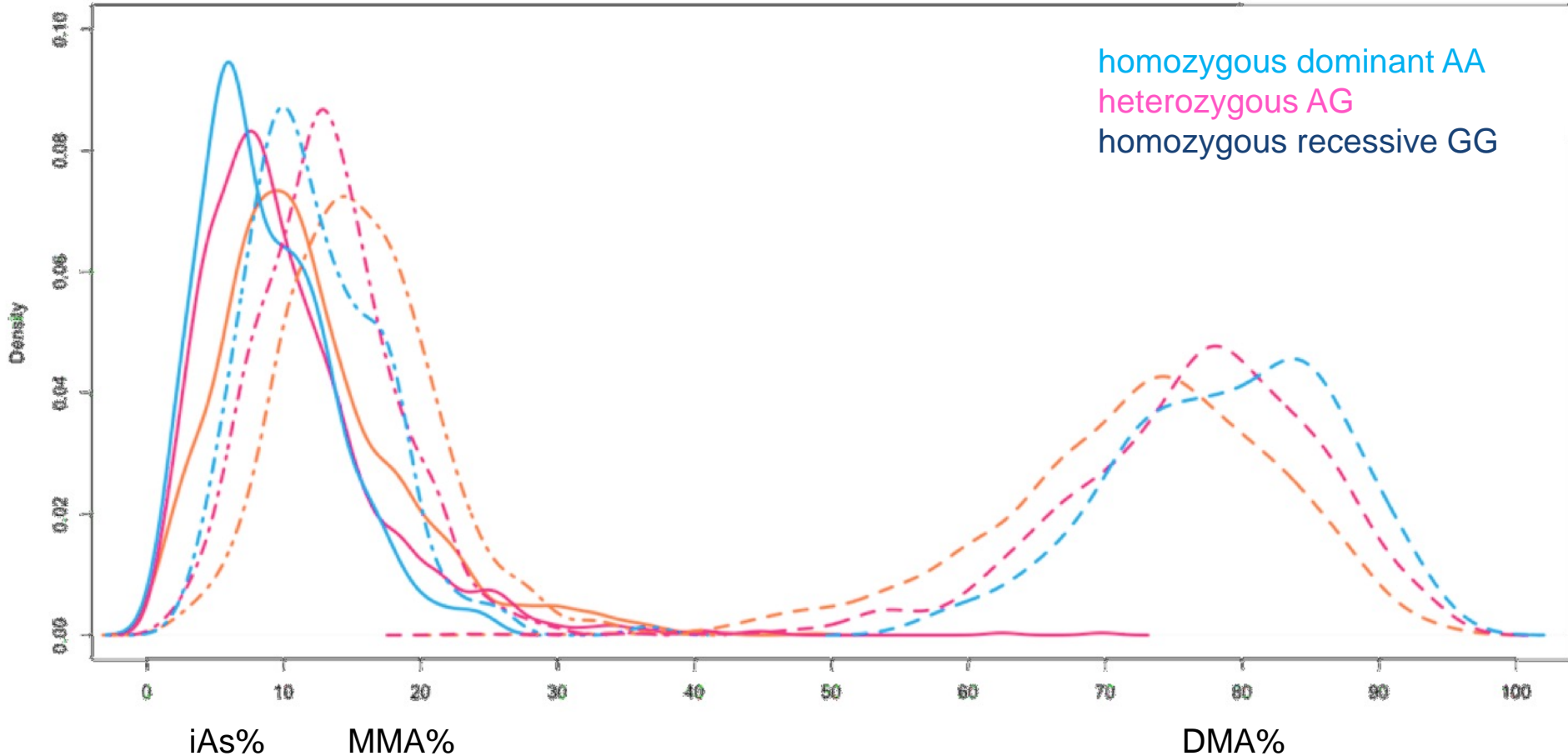
LD: linkage disequilibrium

Manhattan plot for arsenic metabolism biomarkers (DMA%) in Strong Heart Family Study (n=2,428)

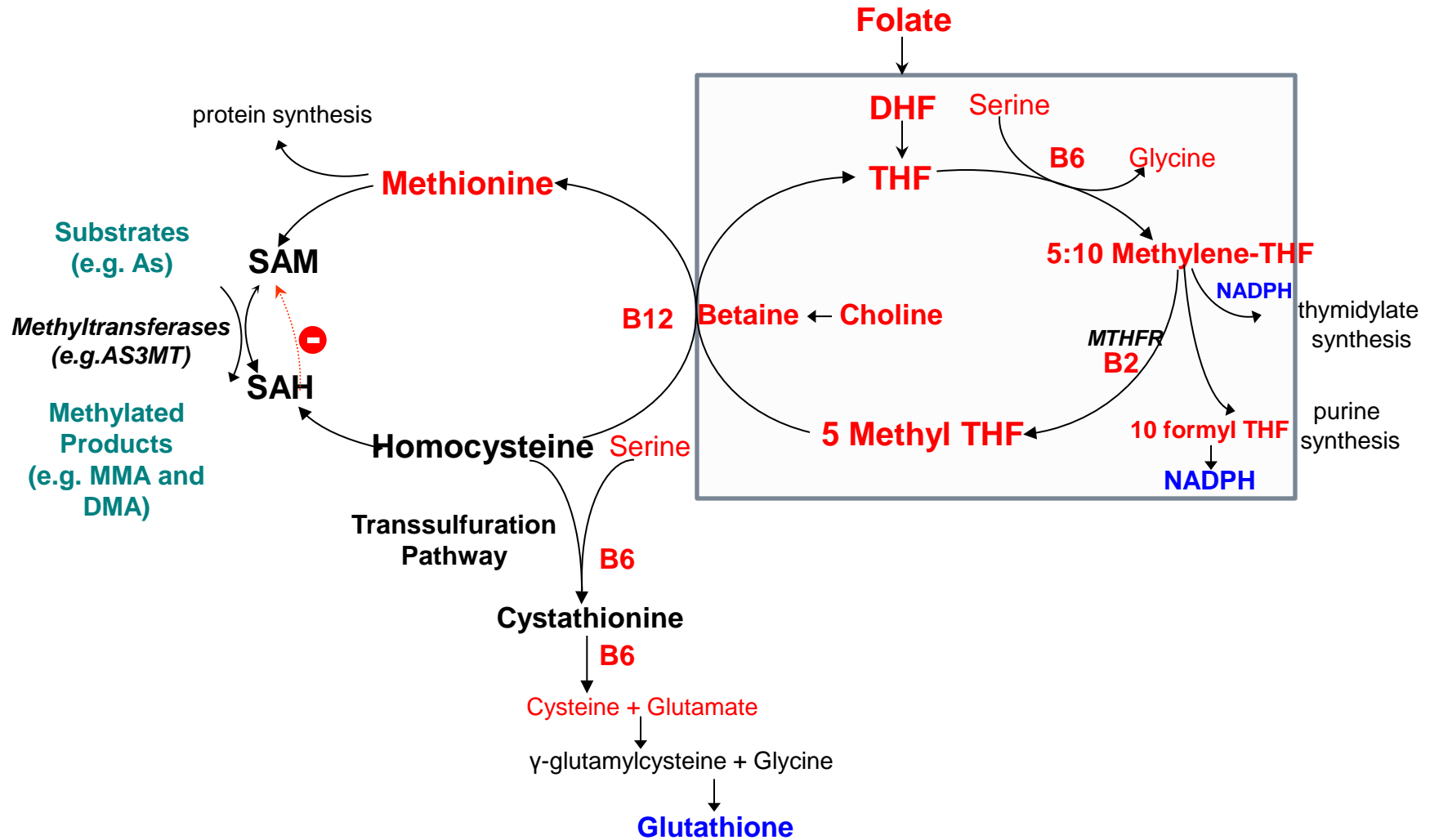
AS3MT(10q24) encodes enzyme arsenic (III) methyltransferase



Arsenic species % by rs12768205 (index SNP)

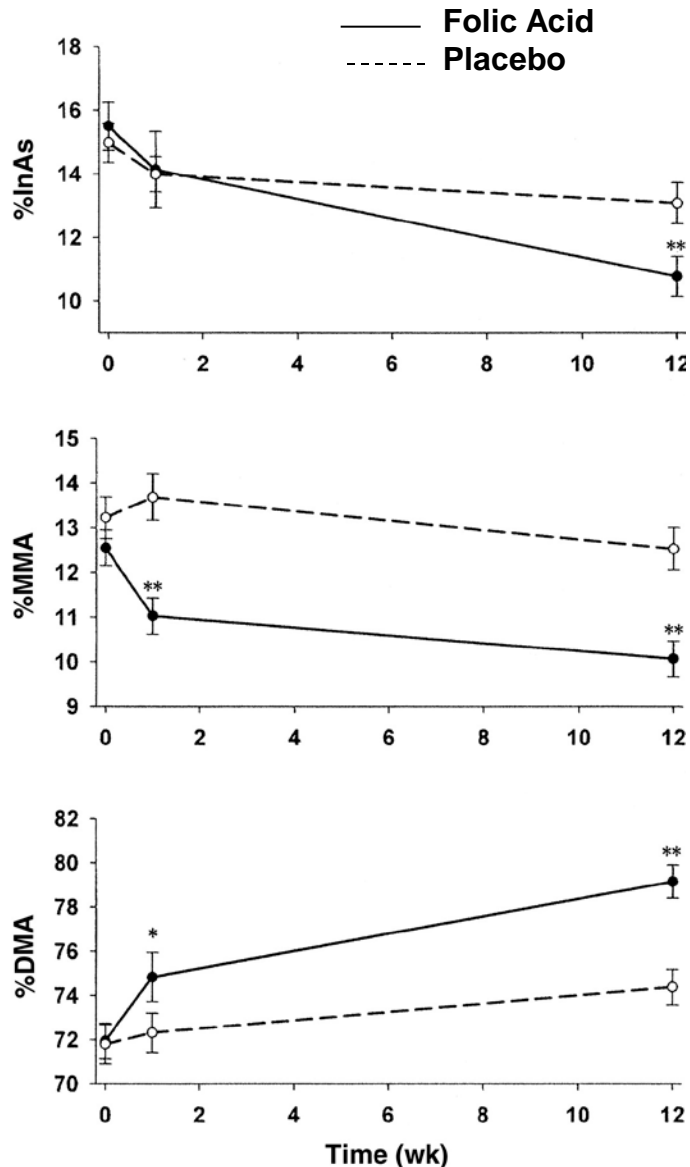


One carbon metabolism and methylation

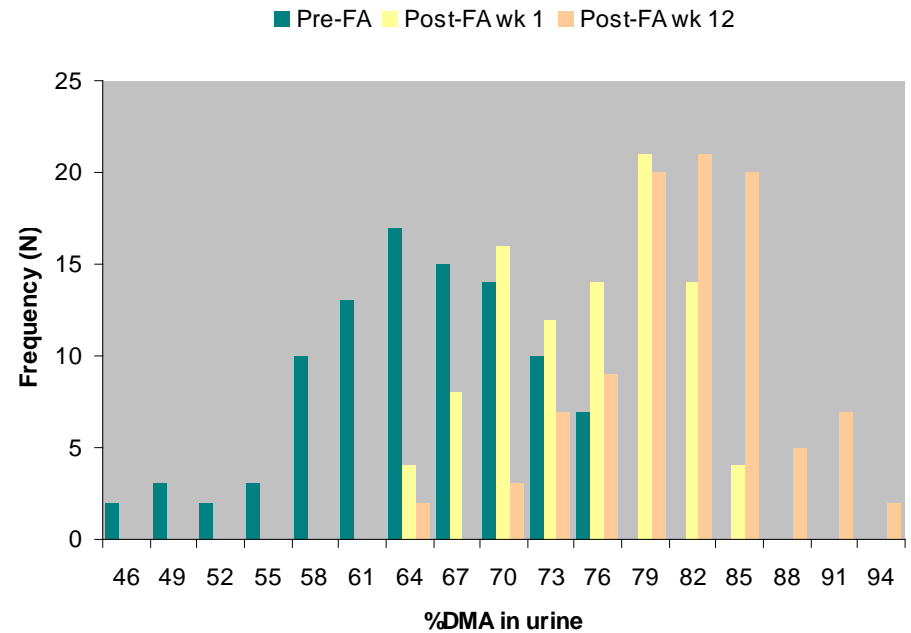


Nutrients/nutrient intermediates are marked in **red**, antioxidants in **blue**. Some enzymes are shown in *italic*. The box includes reactions that also occur in the mitochondria.

Effects of Folic Acid Supplementation on Arsenic Metabolites in Urine

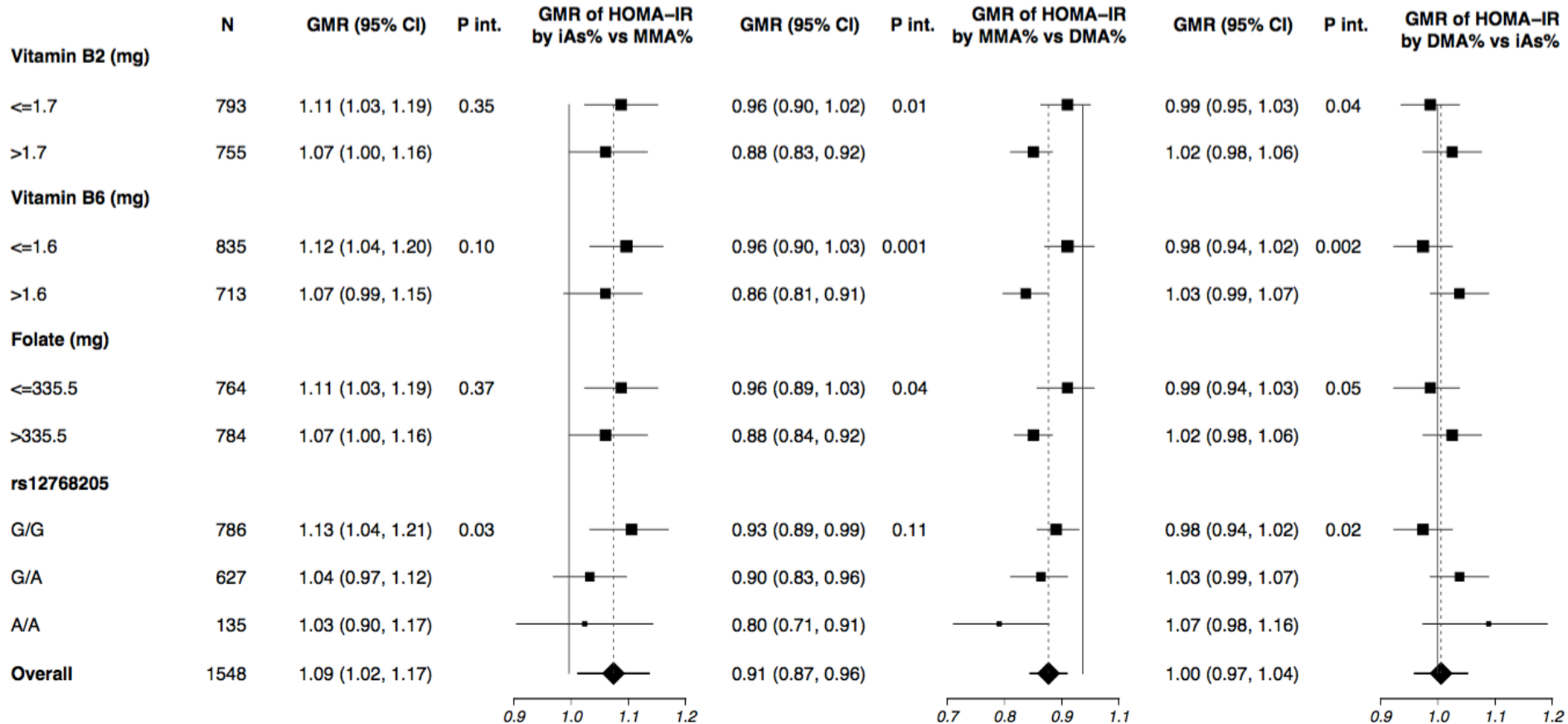


*P < 0.01; **P < 0.0001

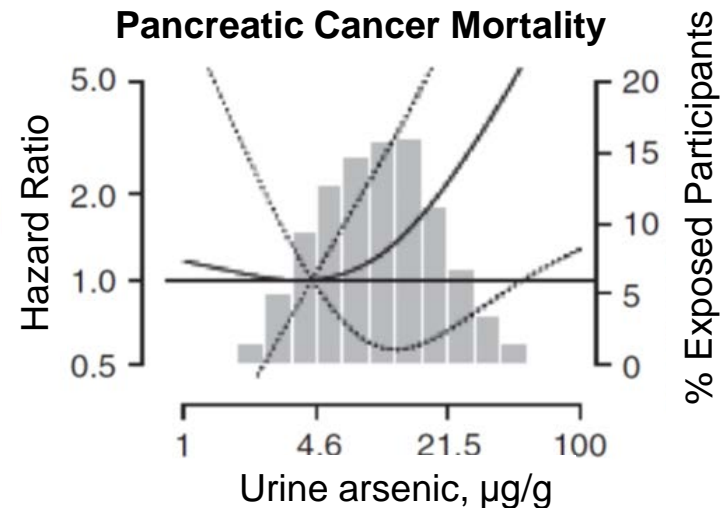
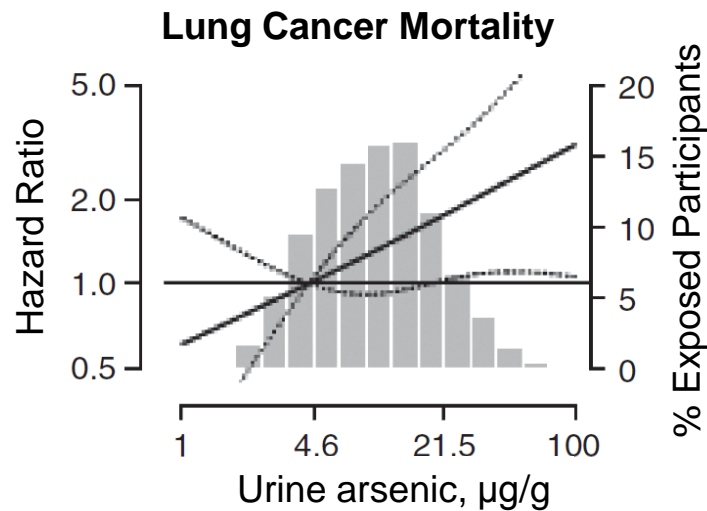
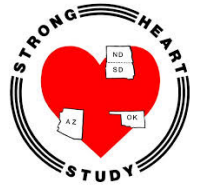


14% decline in blood arsenic concentrations

HOMA-IR by arsenic metabolism biomarkers interaction analyses



Arsenic and Cancer



- Cancer was not originally included in the consent forms in all study sites, maybe in some broad sentences about studying health and disease in general, not specifically
- Special community approval was needed to conduct this research
- Study participants are currently being reconsented for cancer and other outcomes

Comments from a community member

“The SHS has been here a long time,” LeBeau observes. “That relationship is established. I think that’s the way it should be. It fits well within the community.”

Among the stubborn stereotypes swirling around American Indians is that they won’t participate in or comply with scientific studies—a notion the SHS has been disproving for a quarter century.

“Understanding requires data,” LeBeau reasons. “Without that, you can’t change things. Maybe this won’t help me, but [it might help] my kids, my grandkids.”

LeBeau is woven into his community. Entwined with his people’s past. Unwilling to say the heck with the future.

“Our culture is here, our language, our elders, our ceremonies,” he says, alluding to men whose prayers emanate from sweat lodges, women who piece together star quilts and children whose elders are buried at Wounded Knee. “It’s happening here.”

Ryman LeBeau, Chair of the Environment and Natural Resource Committee

Research data relevant at multiple levels

- **Local level:** prevention and intervention
provide control data
- **Regional level:** increase resources, prevention strategies
- **Country and global level:** policy
 - EPA risk assessment
 - IARC: cancer evaluation
 - WHO: drinking water standards

Contribute to EPA arsenic risk assessment

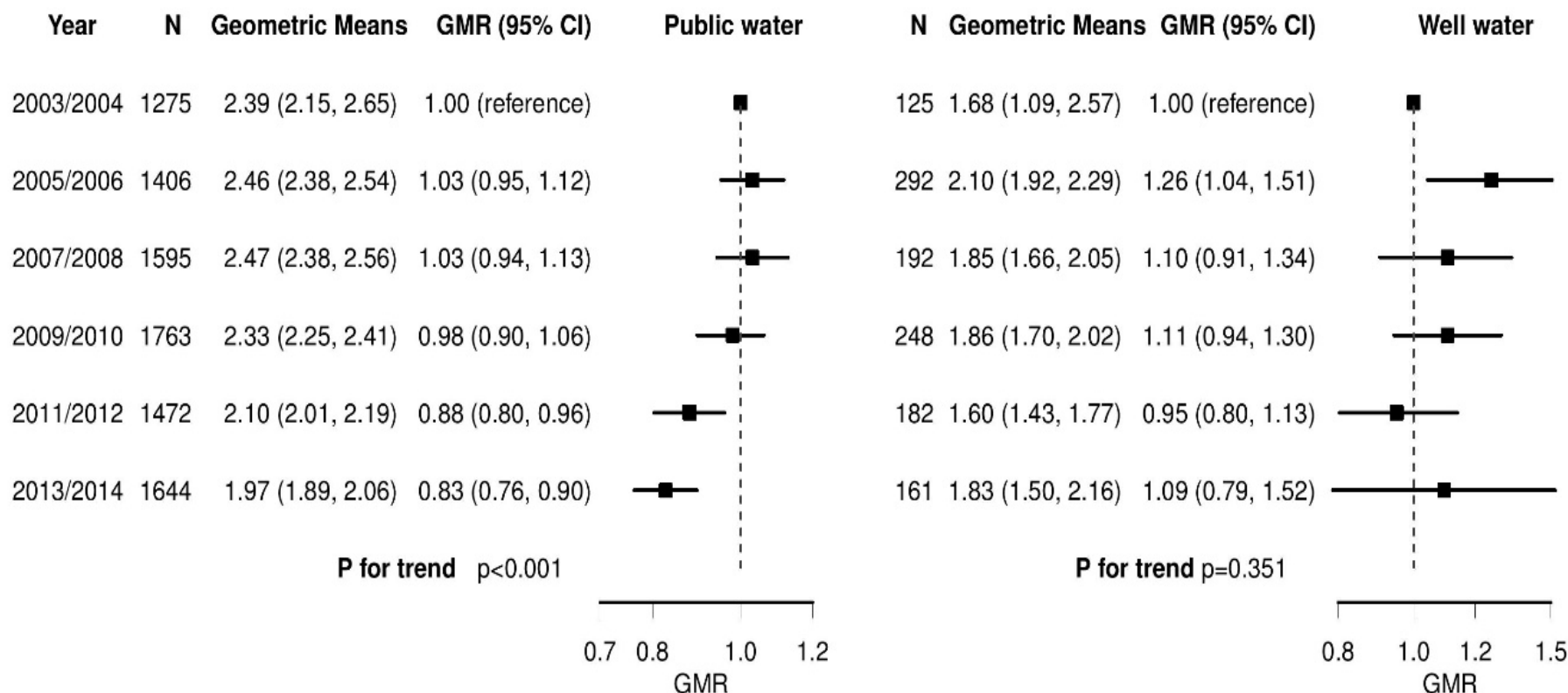
- EPA recently requested urine arsenic data from the Strong Heart Study to improve their pharmacokinetic modeling for the ongoing arsenic risk assessment
- We consulted with the Strong Heart Study steering committee, which includes community members
- Approval to provide the data and support the EPA was granted (provide aggregated data not raw data)
- EPA agreed that if a publication is prepared, it will be submitted to the tribes for approval



Impact of the EPA arsenic MCL



Urinary DMA corrected for dietary and tobacco sources of arsenic and adjusted for age, race/ethnicity, education and body mass index.



Findings support the critical role of federal drinking water regulations in reducing toxic exposures and protecting human health

Mni Wiconi water reaching Pine Ridge reservation

Gathering heralds arrival of lines that carry clean water

Mary Garrigan, Journal staff Aug 19, 2008



Workers for S.J. Louis, a construction company out of St. Paul, Minn., dig a trench Wednesday for pipe west of Wanblee. When finished, this pipeline will bring water from the Missouri River to Potato Creek, Kyle and Red Shirt. (Photo by Ryan Soderlin, Journal staff)

WANBLEE - Words of congratulations and gratitude for the arrival of Missouri River water to the Pine Ridge Indian Reservation flowed freely at a Mni Wiconi connection dedication here Wednesday. But the people who live in this small community on the reservation's northeastern edge will have to wait a few more months for the water itself to begin flowing into their homes.

About 250 people gathered in the Crazy Horse School gymnasium to mark a milestone for the rural water project, whose Lakota name translates to "Water is life."

After 15 years of construction and nearly half a billion dollars in federal funds, the 24-inch core pipeline and its clean, safe, high-quality drinking water from the Missouri River has finally crossed the reservation's border.

Planning a prevention intervention study in South and North Dakota



Meeting at Eagle Butte, SD



Meeting at Martin, SD

Planning a prevention intervention study in South and North Dakota



Meeting at Eagle Butte, SD



Meeting at Martin, SD

Making those meetings possible is Marcia O'Leary, RN
Manager of Missouri Breaks Research, the institution that runs the
Strong Heart Study



Strong Heart Water Study for private wells



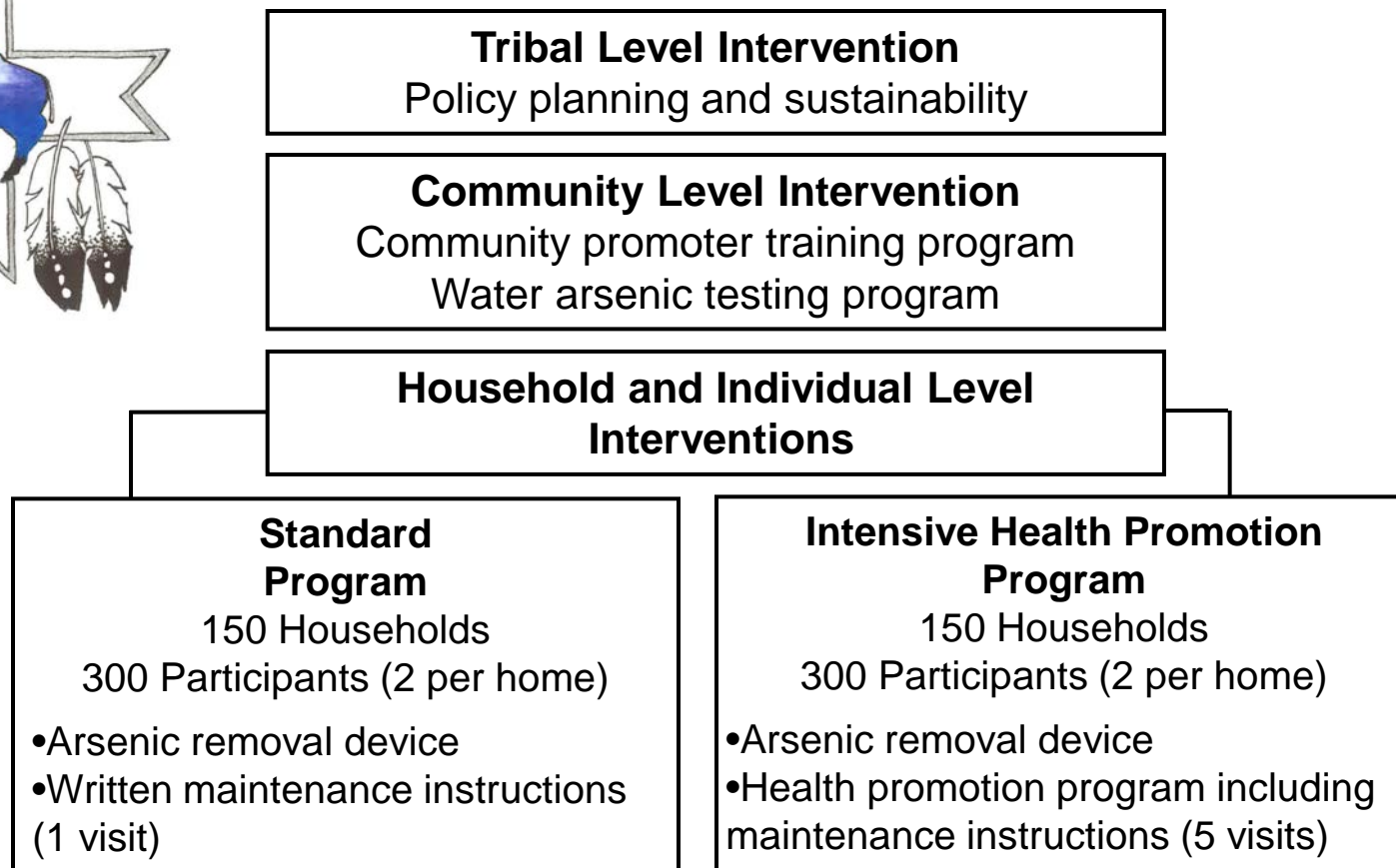
Christine George



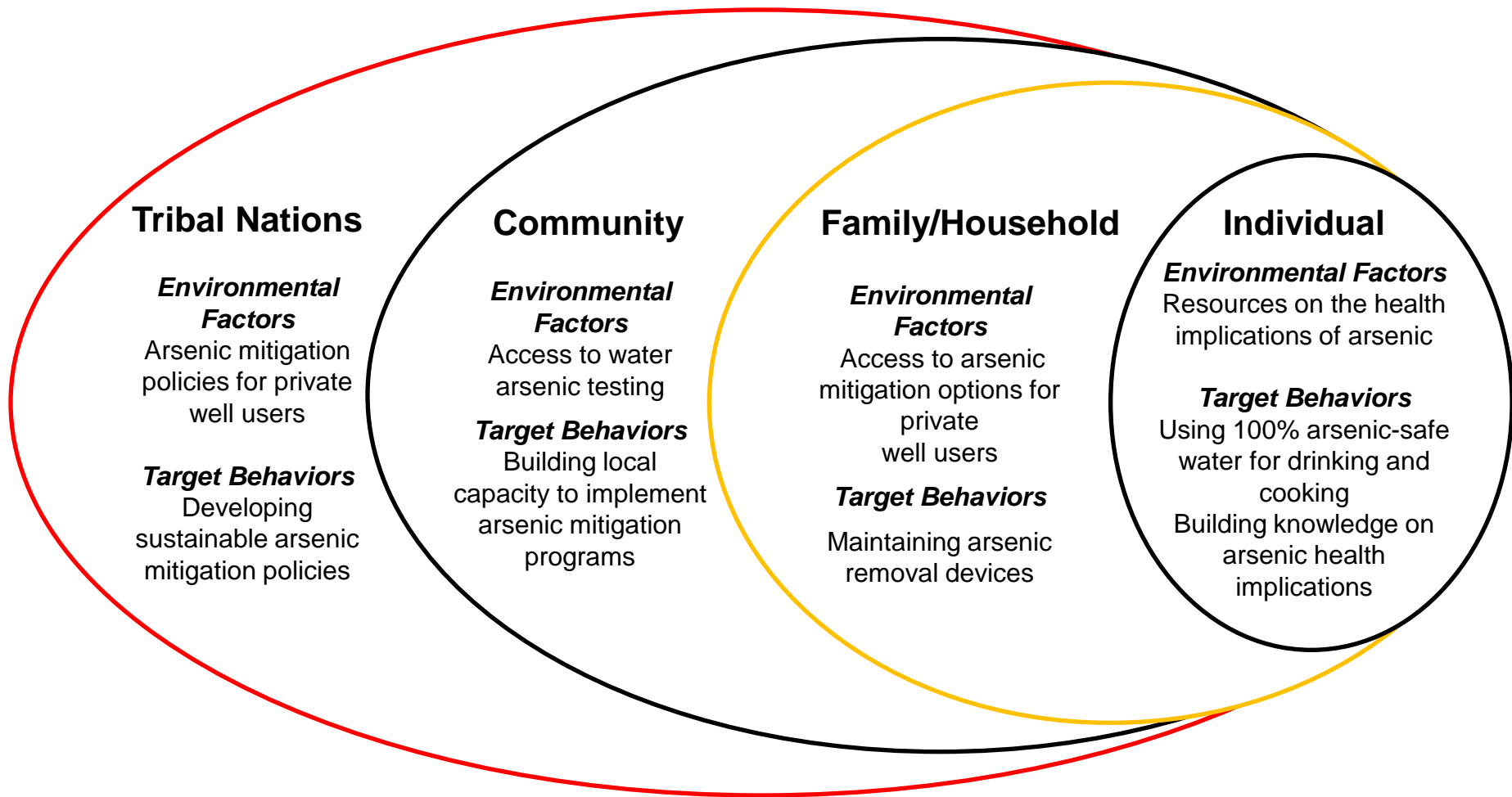
Joseph Yracheta



Cluster Randomized Controlled Trial



The Ecological Model for Strong Heart Water Study

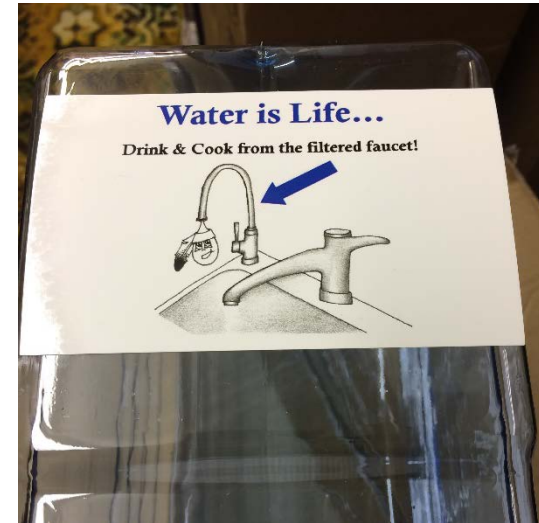




SHWS Intervention Pilot



- 6 filters installed during the pilot study in February and March 2017
- Pilot testing of the study materials



Intervention Evaluation

Baseline

1 Month Visit

6 Month Visit

**Long Term
1-3 Years Visit**

- Baseline**
- Urine arsenic
 - Water arsenic
 - Water Qx
 - ICAM-1, VCAM-1
 - HbA1c
 - Lung function
 - Blood pressure

- 1 month**
- Urine arsenic
 - Water arsenic
 - Water Qx
 - Water meter

- 6 months**
- Urine arsenic
 - Water arsenic
 - Water Qx
 - Water meter
 - ICAM-1, VCAM-1
 - HbA1c
 - Lung function
 - Blood pressure

- Long term
(1-3 years)**
- Urine arsenic
 - Water arsenic
 - Water Qx
 - Water meter

TACT₂

TRIAL TO ASSESS CHELATION THERAPY

The logo for TACT2 features the word "TACT" in a large, blue, serif font. The number "2" is a large, black, stylized swan, with its head and neck forming the top curve of the number. Below "TACT" is the text "TRIAL TO ASSESS CHELATION THERAPY" in a smaller, red, sans-serif font.

- Replicative trial of EDTA chelation and high-dose oral vitamins in 1200 post-MI diabetic patients
- Selecting the population that showed the greatest benefit
- Storing biospecimens for measuring metals and testing future mechanistic hypotheses

Lead, cadmium and cardiovascular disease

What we know:

- Increased blood pressure levels
- Increased CVD mortality (several studies including NHANES)
- Increased CVD incidence in several populations, although the number of studies is small:
 - Normative Aging Study (lead)
 - Strong Heart Study and other studies (cadmium)
- Increased subclinical cardiovascular disease (carotid atherosclerosis, peripheral artery disease)
- Experimental studies support these cardiovascular effects

Urgent need for high quality air pollution assessment in North Dakota



Deborah Sontag, NYT, 11/22/14

Jim Wilson, photographer

In the picture: Dr. Lyle Best and his dog



300 yards from a home



A Belch from the porch



Oil tank explosion on 3/7/2015

Communities and participants make research possible

- Engagement and participation
- Support of science
- Contributions to research questions
- Contribution to conduction of research
- Research can and must benefit communities
 - Benefits are sometime slow
 - Researchers need to be actively engaged

Funding

- R01HL090863: Arsenic, CVD and diabetes SHS (completed)
- R01ES021367: Arsenic, genetics, diabetes SHFS (NCE, renewal submitted)
- R01ES025216: Arsenic, epigenetics and CVD SHS (ongoing)
- R01ES025135: Participatory interventions to reduce arsenic (ongoing)

Strong Heart Study

Strong Heart Study co-investigators and community members

Barbara Howard, Jason Umans, Darren Calhoun, Cynthia West (*MedStar/Arizona*)

Lyle Best, Marcia O'Leary, Joseph Yracheta, Marie Gross, Stacey Jolly (*North/South Dakota*)

Elisa Lee, Everett Rhoades, Fawn Yeh, Ying Zhang, Tauqeer Ali, Julie Stoner (*Oklahoma*)

Shelley Cole, Karin Haack, Jean MacCluer (*Texas Biomed*)

Nora Franceschini, Saroja Vorungati, Kari North (*UNC*)

Richard Devereux, Mary Roman, Peter Okin (*Cornell U*)

Jinying Zhao (*U of Florida*)

Mentors

Eliseo Guallar

Ellen Silbergeld

Richey Sharrett

Hopkins co-investigators

Winnie Tang, Zhibin Wang,

Virginia Weaver, Kellogg

Schwab, Luke McDonald (*EHS*)

Linda Kao, Dani Fallin (*Epi*)

Dhananjay Vaidya (*GIM*)

Ciprian Crainiceanu, Karen Bandeen-Roche (*Biostats*)

Indian Health Service

David Harvey

Graz Laboratory

Kevin A. Francesconi,

Walter Goessler

Strong Heart Water Study

Community Consultants

- Reno Red Cloud
- Carlyle Ducheneaux
- Robert Thompson

Strong Heart Study Investigators

- Marcia O' Leary
- Joseph Yracheta
- Lyle Best
- Jason Umans
- Fawn Yeh
- Amanda Fretts

Indian Health Service

- CAPT David Harvey

Johns Hopkins University

- Christine George
- Allison Barlow
- Kellogg Schwab
- Luke MacDonald
- Lawrence Moulton
- Joel Gittelsohn

Columbia University

- Maria Grau

Students and trainees move the science forward – drive and creativity



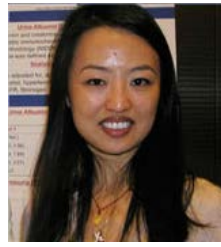
Maria Tellez-Plaza
Ass. Professor,
Spain



Miranda Jones, Ass. Professor,
Hopkins



Matt Gribble
Ass. Professor,
Emory



Laura Zheng
Post-doc,
Mt Sinai NY



Chin-Chi Kuo
Assoc. Professor,
Taiwan



Esther Garcia-Esquinas
Instructor,
Spain



Kat Moon
Post-doc,
Hopkins



Farrah Mateen
Ass. Professor,
Harvard



Poojitha Balakrishnan
Post-doc, CU



Pablo Olmedo
Ass. Professor,
Spain



Maria Grau,
Data Analyst,
CU



Miranda Spratlen,
PhD student
Hopkins



Martha Powers, PhD
student
Hopkins



Yuanjie Pang, PhD
student
Oxford



Anne Nigra,
PhD
student
CU



Tiffany Sanchez,
Post-doc
CU



Jungen Ji,
MPH
student
CU

Collective Competence

- Authority is rooted in collective competence
- Decision making is horizontal, precedent oriented and consensual
- Process is fluid, iterative, recorded orally, benchmarked by key events (not chronologically)
- Leadership is shared, diffused and ascribed
- Tribal communities are sociocentric

Spiro Manson, PhD

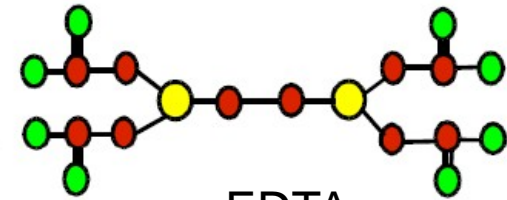
University Colorado Denver

NHLBI Forum, Aug 2, 2016

Metal chelation

Ethylene Diamine Tetra Acetate Anion (EDTA)

- Administered intravenously (slow infusion)
- Distributed across bone and soft tissues where it binds metal cations (“organic coating”)
- EDTA-metal complex is stable, non-toxic and excreted through the kidneys
- FDA approved uses:
 - Lead poisoning (CaNa_2EDTA)
 - Hypercalcemia (Na_2EDTA)
- Historically, controversial role in CVD prevention



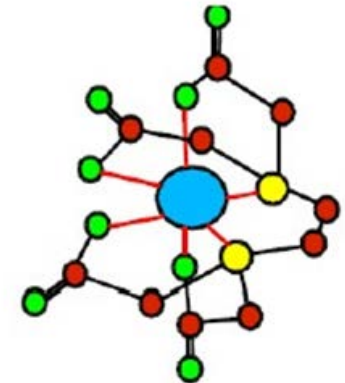
EDTA

+



Metal cation

=



EDTA-metal complex