Environmental Health Inequalities in Indigenous Communities: Interventions and Opportunities

Ana Navas-Acien, MD, MPH, PhD
Environmental Health Sciences
Columbia University
an2737@columbia.edu
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
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 principles that motivate our work and partnership

- Value traditional knowledge
  - Water is life (Mní wičhóni)
  - 7th generation principle
  - Relationality – things are connected in a circular rather than linear process

- Collective leadership

- Sovereignty and data ownership
Strong Heart Study

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

N = 7,600 adults
13 tribes and communities

http://strongheart.ouhsc.edu/
Urinary arsenic levels in the Strong Heart Study communities

Arsenic concentrations in at least 25% of samples exceed:
- 50 ug/l
- Insufficient data

Map of the United States showing arsenic concentrations in different states.

- Arizona: 
  - Visit 1 (1989-91): ICC = 0.78
  - Visit 2 (1993-95)
  - Visit 3 (1998-99)

- Oklahoma:
  - Visit 1 (1989-91)
  - Visit 2 (1993-95)
  - Visit 3 (1998-99)
  - ICC = 0.66

- Dakotas:
  - Visit 1 (1989-91)
  - Visit 2 (1993-95)
  - Visit 3 (1998-99)
  - ICC = 0.75

ICC = Intraclass correlation coefficient
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*†
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%
88%
retention rate

Ongoing Surveillance: Morbidity & Mortality

Visit 3 pilot 1998-99
Visit 4 2001-03
Visit 5 2006-09
Visit 6 2014-16
Visit 7 2022-23

Strong Heart Family Study
3,050 participants ≥14 y

Continuous funding critical to maintain sustainable research projects
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
A Metal That Might Break Your Heart

Circ Cardiovasc Imaging. 2019;12:e009185. DOI: 10.1161/CIRCIMAGING.119.009185

See Article by Pichler et al

In the past decades, exposure to environmental metal contaminants (eg, arsenic, lead, cadmium, and mercury) through groundwater, food, soil, and ambient air has become a global public health concern. In this regard, arsenic—one of the most abundant environmental metals worldwide—affects >200 million people in >70 countries solely by drinking water route. While a high level of chronic inor-
Possible mechanisms for arsenic-related disease

- Arsenic can induce changes in gene expression not caused by changes in the DNA sequence
- Gene expression can be studied through epigenetics marks
- Blood DNA methylation is the most commonly studied epigenetic mark in epidemiological studies
- We are currently investigating epigenetics as a mechanism for heart disease related to arsenic
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Like highlighting, epigenetic markers tell a cell which parts of DNA are important.

Credit: Anne Bozack, PhD, MPH
Mediation Analysis – CVD incidence

- EWAS screening of blood DNAm associated with incident CVD using Cox adaptive elastic-net for high-dimensional data

- Mediation of arsenic-related CVD via DNAm using Aalen additive hazard models (Lange et al 2011)
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DMPs associated with As and As-mediated CVD and supportive mouse liver DNAm data from Koren Mann’s lab

<table>
<thead>
<tr>
<th>Tagged gene</th>
<th>Function</th>
<th>As</th>
<th>As-med. CVD</th>
<th>Exp. data</th>
</tr>
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<tbody>
<tr>
<td>SLC7A11</td>
<td>GSH biosynthesis</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>SLC7A5</td>
<td>GSH biosynthesis</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>PKN3</td>
<td>DNA repair and apoptosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>CSNK1D</td>
<td>DNA repair and apoptosis</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>ATG16L2</td>
<td>Autophagy pathway (diabetes)</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>APBB2</td>
<td>Beta cell function (diabetes)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>TYMP</td>
<td>Angiogenesis, endothelial cell growth</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>COL1A1</td>
<td>Type 1 collagen</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>TXNIP</td>
<td>Thioredoxin interacting protein</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>MAPK8</td>
<td>Mitogen-activated protein kinase 8</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

DMP: differentially methylated position; Exp.: experimental (liver DNAm).
*Other models different from K. Mann’s lab.
Data ownership and data sharing

- Who owns the data?

- Who allows data sharing and in which terms?
Examples of community harm

• Havasupai Tribe
  - Genetic data originally collected for diabetes research used for research on schizophrenia, inbreeding, population migration on the basis of “broad consent form”

• Barrow alcohol study
  - NYT article with offensive title released at the same time as a conference presentation
  - Community bond went from A to C+
Tribal communities are resisting unrestricted data sharing
E.P.A. to Limit Science Used to Write Public Health Rules

Contaminated waste water flowing from the Lee Mountain mine near Rimini, Mont., into a retention pond last year. Matthew Brown/Associated Press

By Lisa Friedman

Nov. 11, 2019

Data Transparency Rule
Data ownership and data sharing

- Who owns the data?
- Who allows data sharing and in which terms?
- Who profits from research?
Genomics data: the broken promise is to Indigenous people

In lamenting the “broken promise that undermines human genome research”, this journal implies that researchers have a right to access information across databases (see Nature 590, 198–201; 2021). In our view, this problematically frames ‘equity’ and ‘progress’ for scientists and dismisses the rights of those who contributed the DNA. As Indigenous geneticists, we remind researchers of the broken promise to extend medical benefits to communities whose genomic data are publicly available.

The genomes of Indigenous people are sought for their unique variation: new genotype–phenotype associations in isolated, small populations are used to advance precision medicine. We take issue with the fact that the Human Genome Diversity Project publicly shares with industries that profit from the ‘big data’ economy genomic information gleaned from central-south American Indigenous individuals (K. Fox N. Engl. J. Med. 383, 411–413; 2020). Meanwhile, wide disparities persist in the health of Indigenous people, owing to intractable power inequities, including in research, that precision medicine is unlikely to address (K. S. Tsosie et al. Nature Rev. Genet. 20, 497–498; 2019).

We contend that the FAIR Principles (see go.nature.com/2nqzcxo) for data sharing grant too much decision-making authority to researchers outside of tribal governances. To understand the duty to steward data, look instead to the CARE Principles (collective benefit, authority to control, responsibility and ethics; see go.nature.com/3ysenhk). Data are not a gift. At best, they are ‘on loan’, and hence revocable if misused. Data are a responsibility not an entitlement.

Krystal S. Tsosie, Keolu Fox, Joseph M. Yracheta
Native BioData Consortium, Eagle Butte, South Dakota, USA.
kkrystal@nativebio.org

The Summer Internship for Indigenous Peoples (SING) Consortium hosts workshops to engage students and tribal members in genomics.
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.
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
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

Making those meetings possible is Marcia O’Leary, RN
Manager of Missouri Breaks Research, the local organization that conducts the Strong Heart Study in North and South Dakota
Strong Heart Water Study for private wells

Cluster Randomized Controlled Trial

Tribal Level Intervention
Policy planning and sustainability

Community Level Intervention
Community promoter training program
Water arsenic testing program

Household and Individual Level Interventions

Standard Program
150 Households
300 Participants (2 per home)
• Arsenic removal device
• Written maintenance instructions (1 visit)

Intensive Health Promotion Program
150 Households
300 Participants (2 per home)
• Arsenic removal device
• Health promotion program including maintenance instructions (5 visits)

Funded by National Institute Environmental Health Sciences (R01ES025135)
The Ecological Model for Strong Heart Water Study

**Tribal Nations**
- **Environmental Factors**
  - Arsenic mitigation policies for private well users
- **Target Behaviors**
  - Developing sustainable arsenic mitigation policies

**Community**
- **Environmental Factors**
  - Access to water arsenic testing
- **Target Behaviors**
  - Building local capacity to implement arsenic mitigation programs

**Family/Household**
- **Environmental Factors**
  - Access to arsenic mitigation options for private well users
- **Target Behaviors**
  - Maintaining arsenic removal devices

**Individual**
- **Environmental Factors**
  - Resources on the health implications of arsenic
- **Target Behaviors**
  - Using 100% arsenic-safe water for drinking and cooking
  - Building knowledge on arsenic health implications
More than 50 filters have been installed and participants are being followed for arsenic biomarkers and health outcomes.
Urgent need for high quality air pollution assessment in North Dakota

Where Oil and Politics Mix

After an unusual land deal, a giant spill and a tanker-train explosion, anxiety began to ripple across the North Dakota prairie.

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 (completed)
• R01ES025216: Arsenic, epigenetics and CVD SHS (ongoing)
• R01ES025135: Participatory interventions to reduce arsenic (ongoing)
• P42ES010349: Columbia University Superfund Research Program (ongoing)
Strong Heart Study Team
Students and trainees move the science forward – drive and creativity