Social Disparities and Environmental Exposures

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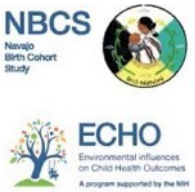
Center for Native Environmental Health Equity Research (Native EH Equity)
Navajo Birth Cohort Study/Environmental influences on Child Health Outcomes (NBCS/ECHO)

2000

2010



2016

2014

2016

National Institute of Environmental Health Sciences
Your Environment. Your Health.

P42 ES025589 – UNM METALS Center
P50 ES026102 -- Native EH Equity Research Phase 1
RO1 ES014565 – DiNEH Project

National Institute of Health Office of the Director
UG3, UH3 OD023344 – NBCS/ECHO

National Institute of Minority Health and Health Disparities
P50 MD015706 -- Native EH Equity Research Phase 2

USEPA 83615701 – Native EH Equity Research Phase 1

CDC U01 TS000135 – Original Navajo Birth Cohort Study

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There are no conflicts of interest to disclose

Work presented here reflects the presenter's synthesis of research approved, reviewed and monitored by

University of New Mexico Human Research Protection Office

And tribal Human Research Review Boards, Committees, or Tribal Councils as appropriate for compliance with tribal research policies

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BIOLOGY

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LAGUNA PUEBLO
APSÁALOOKE (CROW)
CHEYENNE RIVER SIOUX TRIBE

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Brief bio

- Toxicologist, Professor
- Director of multiple center-level grants to examine health in context of mine-waste exposures in Indigenous communities on Colorado Plateau and Northern plains/mountains
- More than 30 years working in partnership with Indigenous communities

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Query 1: Work to understand exposures (radiation or other) in Native communities and interactions with traditional lifestyles, culture, and health

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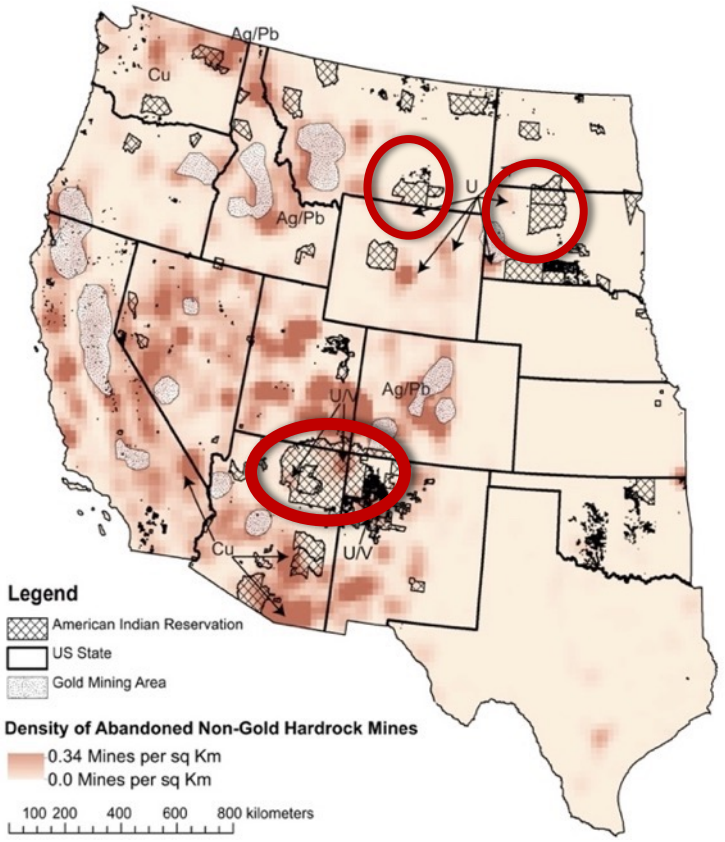
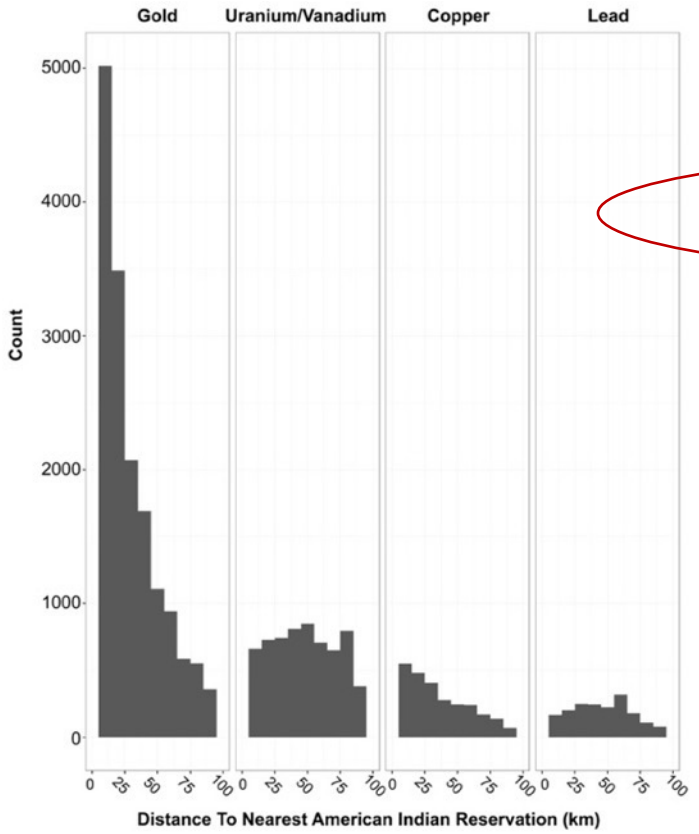
Not Just Uranium: Substantial Exposures to Metal Mixtures throughout Indian Country -- Many linked to Cold War Weapons Development

Lewis, Hoover, & MacKenzie (2017) Current Environmental Health Reports





15 Western States in US

- Home to >50% US indigenous population
- 161,000 abandoned hard rock mines
- 5,000 – 10,000 abandoned uranium mines
- **>600,000 Indigenous peoples w/in 10km of abandoned mine waste**
- Waste has contaminated 40% of Western US surface waters (USEPA)

Potential for sensitivity to toxicity unknown

- Heavy reliance on local resources
- Understudied genetic, epigenetic, metabolic, distribution differences
- Marginal infrastructure impacts overall health, access to care, schools, supplies

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Abandoned Mines and Tribal Lands

Navajo community with 4 emergency remedial actions to remove soil – pile in background remains in place

Navajo Nation

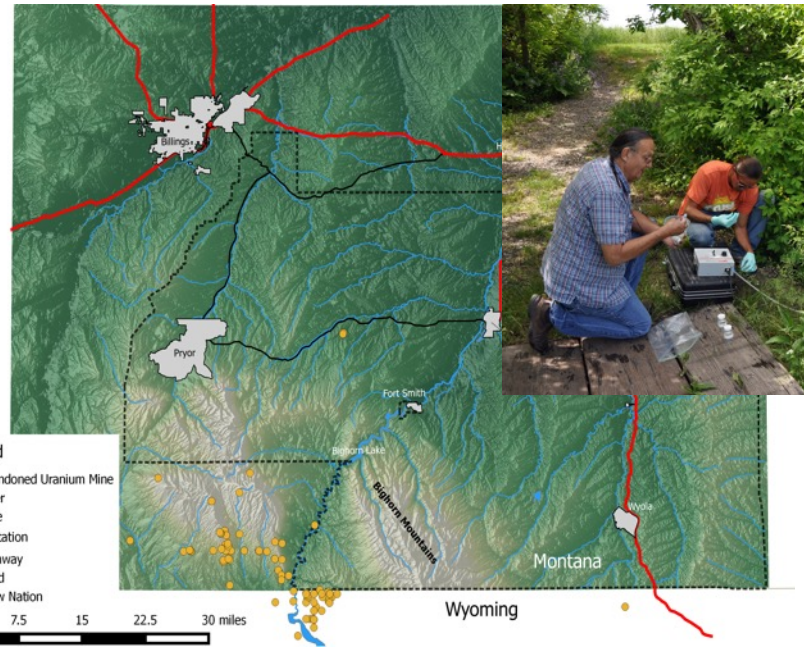
Child watches as 18 in of soil removed from his community

4th generation raised in shadow of waste

Cheyenne River Sioux Tribe

Homestake Gold Mine In Black Hills (>150 m upriver) → Whitewood Creek → Belle Fourche River → Cheyenne River (→ Missouri River ??)

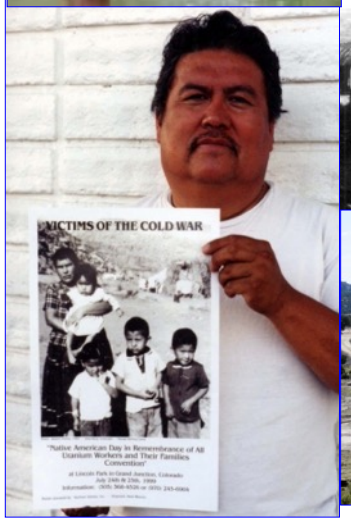
Arsenic deposited through flooding during active operation of the mine when "Whitewood Creek ran black"



Crow Nation -- >30 mi from abandoned U mines

POPULATION STUDY RESULTS:

ACTIVE-MINING ERA EXPOSURES (WORKERS AND FAMILY) INCREASED RISK OF KIDNEY DISEASE & OF MULTIPLE CO-MORBID CHRONIC DISEASES



N= >1300, average age 55
Continuum from no to hi exposure
Clinical validation subset = ~300

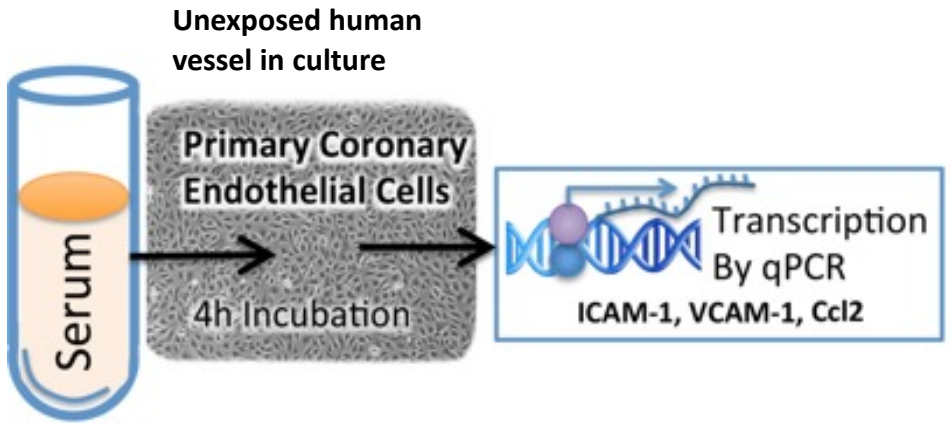
*Many workers had already died from lung cancer, cohort had more family members than workers

ONGOING ENVIRONMENTAL LEGACY EXPOSURES → INCREASED RISK FOR HYPERTENSION, AUTOIMMUNE DISEASE, 2 OR MORE CHRONIC DISEASES

Hund et al., 2015, Journal of Royal Statistical Society, Series A, Statistics in Society

Erdei. J Autoimmun. 2019. 99:15-23. doi: 10.1016/j.jaut.2019.01.006. PMID: 30878168; PubMed Central PMCID: PMC6489502.

Validating survey results with laboratory studies: hypertension

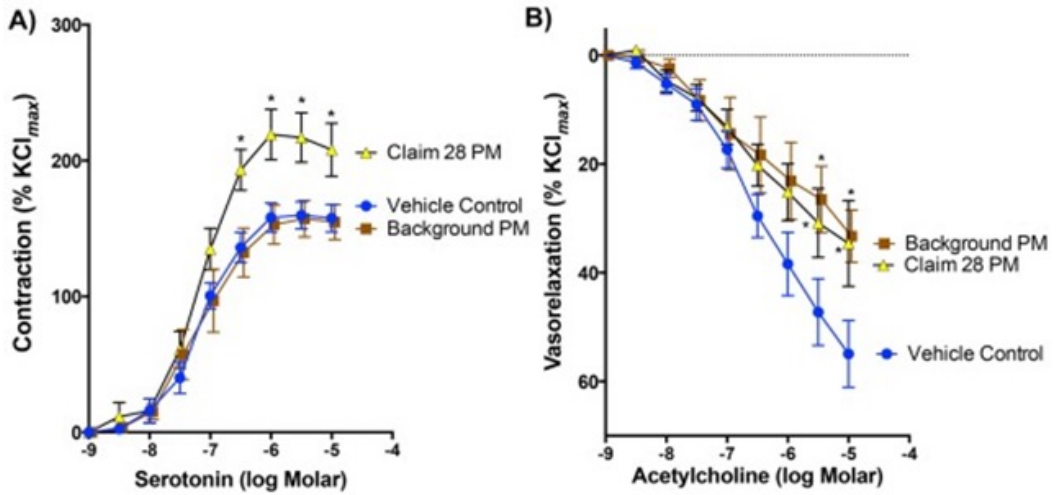


- Chronic inflammation known to play a role in stiffening of arteries
- Uranium exposure linked to increased CRP in population
- AUM proximity of serum donor *only* significant predictor of endothelial inflammatory markers
  - VCAM1 (0.006), ICAM1 (<0.0001), & Ccl2 (<0.0001)

Harmon et al., J Expo Sci Environ Epidemiol. 2017 (4):365-371. doi: 10.1038/jes.2016.79. PubMed PMID: 28120833; PubMed Central PMCID: PMC5781233.

Rodent model exposure to mine dust

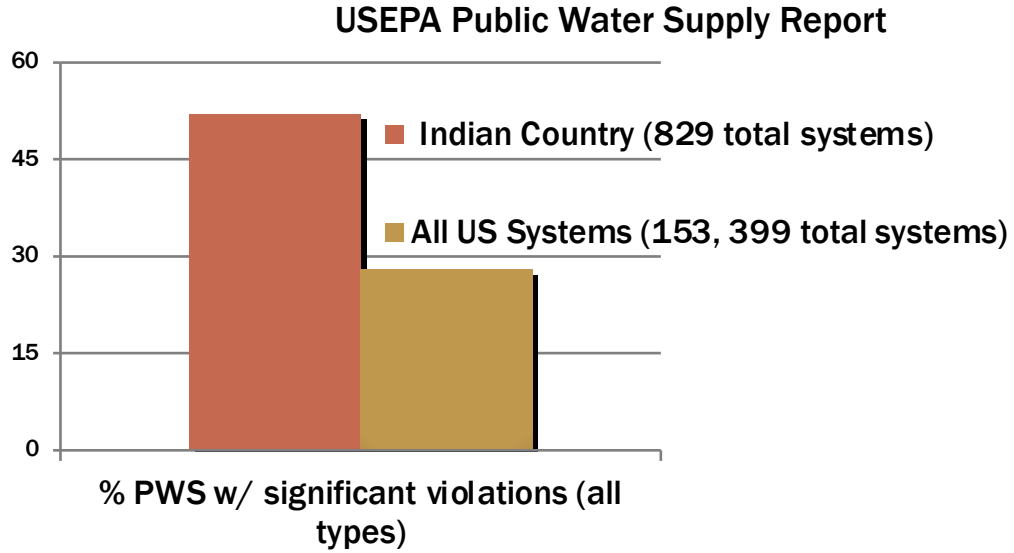
- Increased contraction to stimulus
- Decreased relaxation
- Reproduced with V or U exposure

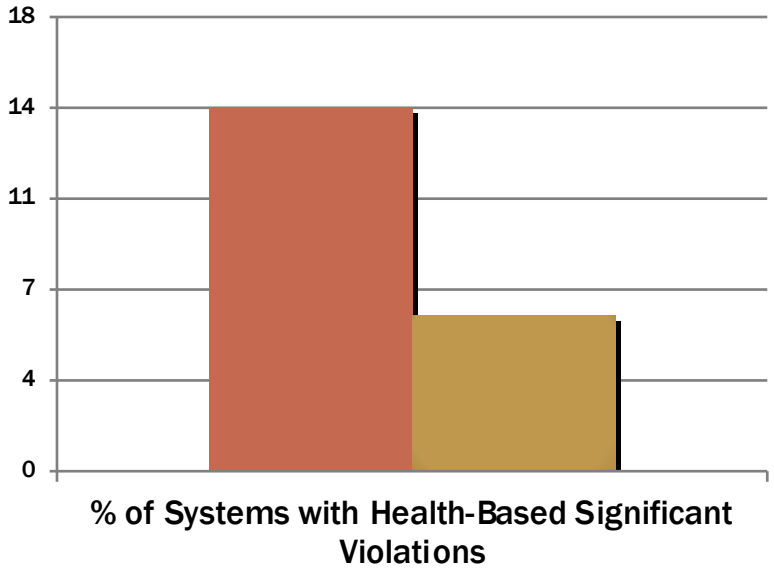


Zychowski et al., Toxicol Sci. 2018;164(1):101-114. doi: 10.1093/toxsci/kfy064. PubMed PMID: 29660078; PubMed Central PMCID: PMC6016706

Tribal Populations - Exposure:Toxicity Relationships Largely Unknown — Infrastructure Gaps Potentially Increase Vulnerability

- Infrastructure disparities increase exposures with ~30% of Navajo homes not connected to public water supply
- No real data to support relevance of standards to indigenous populations
- In addition to lack of water, lack of passable roads and long distances reduce likelihood of screening and access to care





Perceptions of exposures in Native communities

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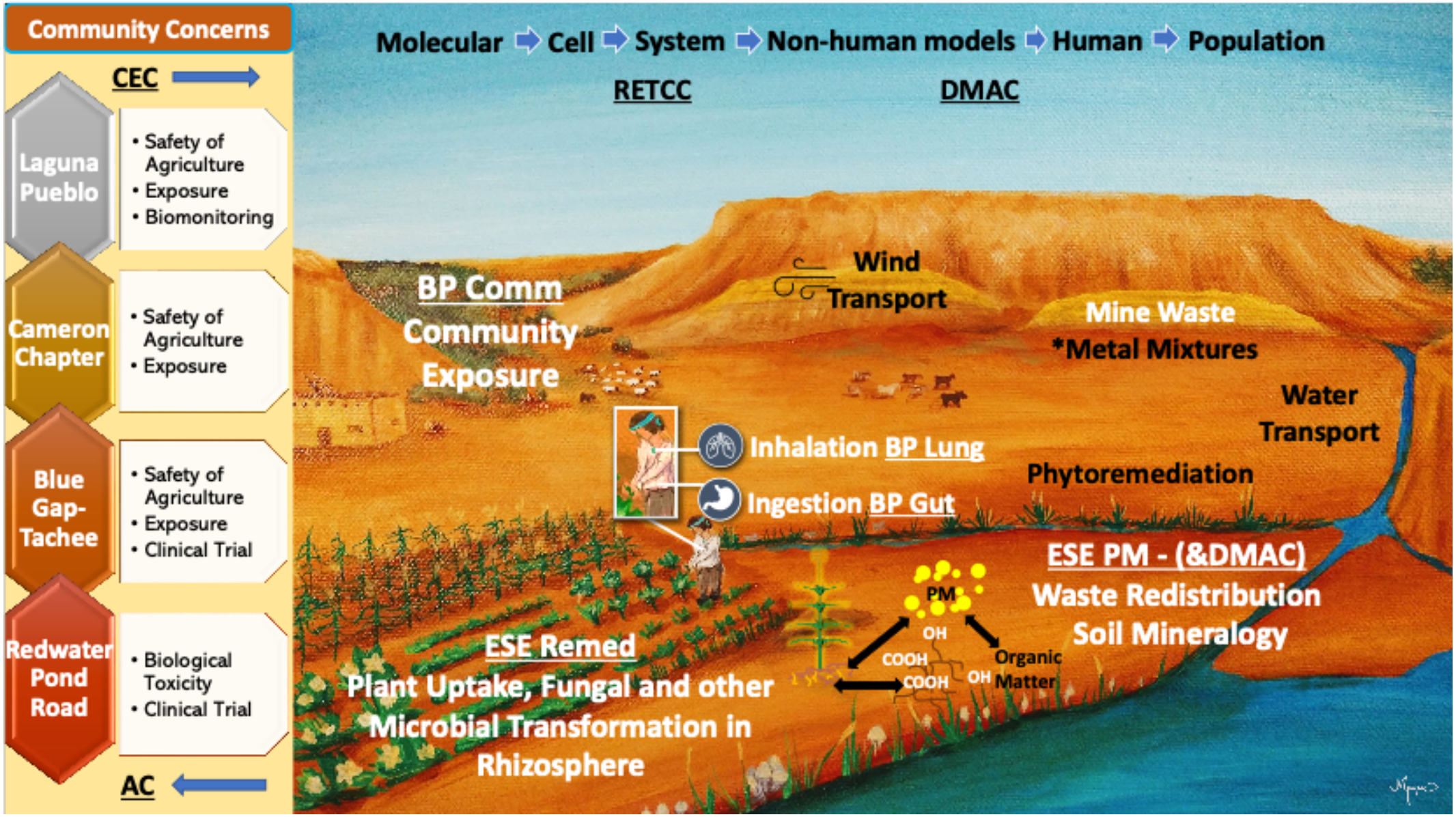
METALS Superfund Research Center



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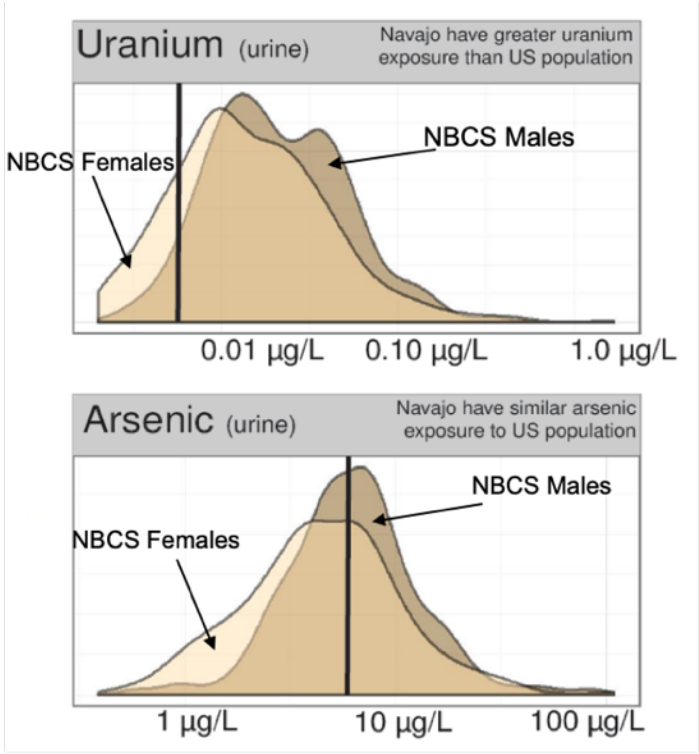
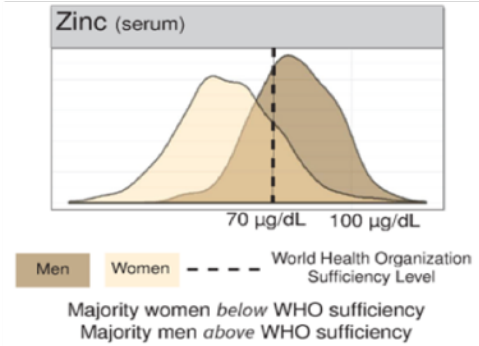
Exposures continue more than 35 yrs post final mine closure: NBCS parents median age 26

- 26% moms, 36% dads exceed 95%ile of NHANES U in urine
- Some babies born with U exceeding 95th %ile
- % babies >95th%ile
  - birth (0.5%)
  - 2-6 mo (14%)
  - 12 mo (19%)
- Breastfeeding decreases during same period, indicating direct exposure



Note: Arsenic primarily more toxic inorganic forms than NHANES due to dietary differences

Vertical line: NHANES 50th %ile US population



Significant zinc deficiency

Majority women *below* WHO sufficiency
Majority men *above* WHO sufficiency

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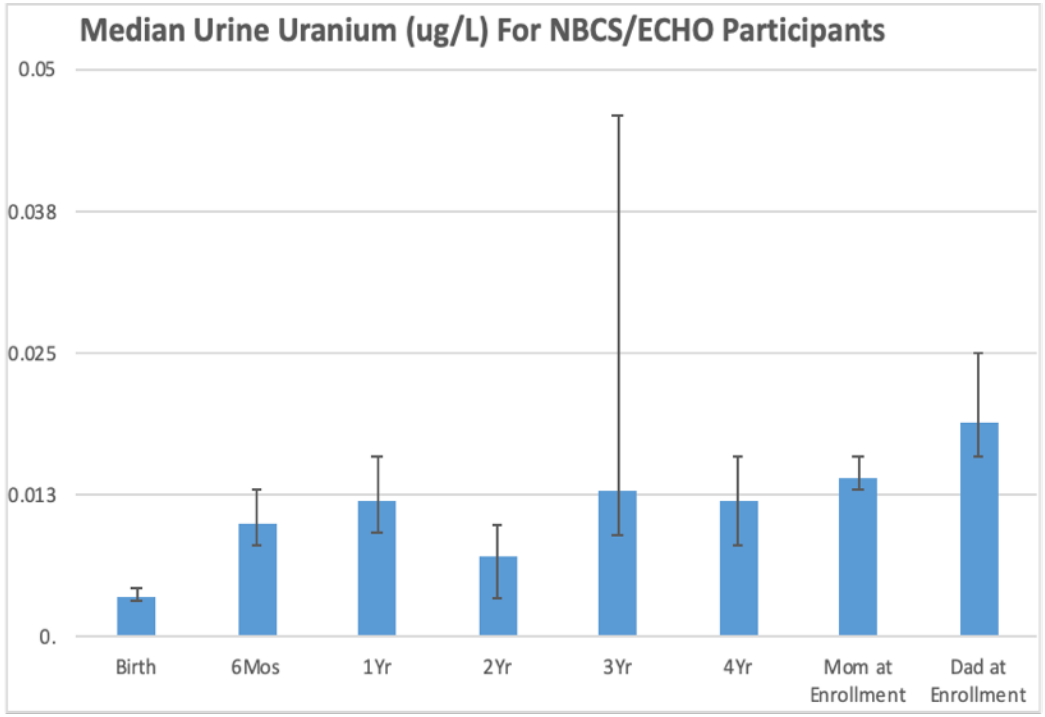
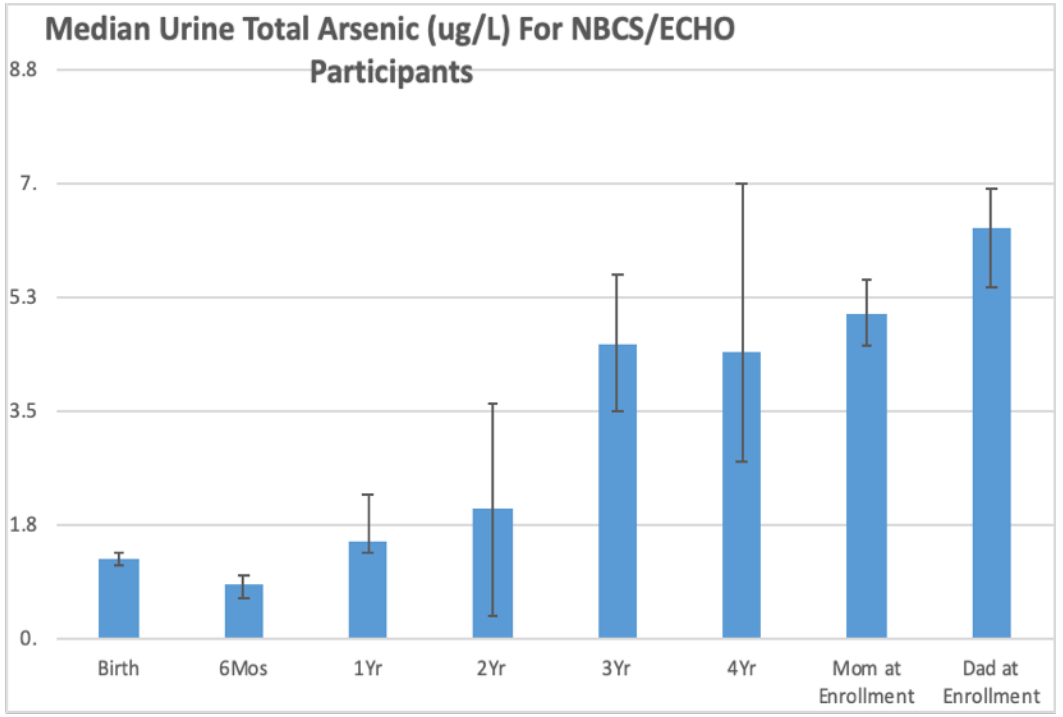
NBCS/ECHO:
Exposures continue through childhood
By age 4, children approaching adult urine metals





- Median concentration for urine uranium in the US ***adult*** population from NHANES (2015-16) = (0.005 µg/L)
- NBCS children birth to age 4 = 0.0035 – 0.013 µg/L

- Median concentration for total arsenic in urine in the US ***adult*** population from NHANES (2015-16) = (5.41 µg/L)
- NBCS children birth to age 4 = 1.2 – 4.5 µg/L

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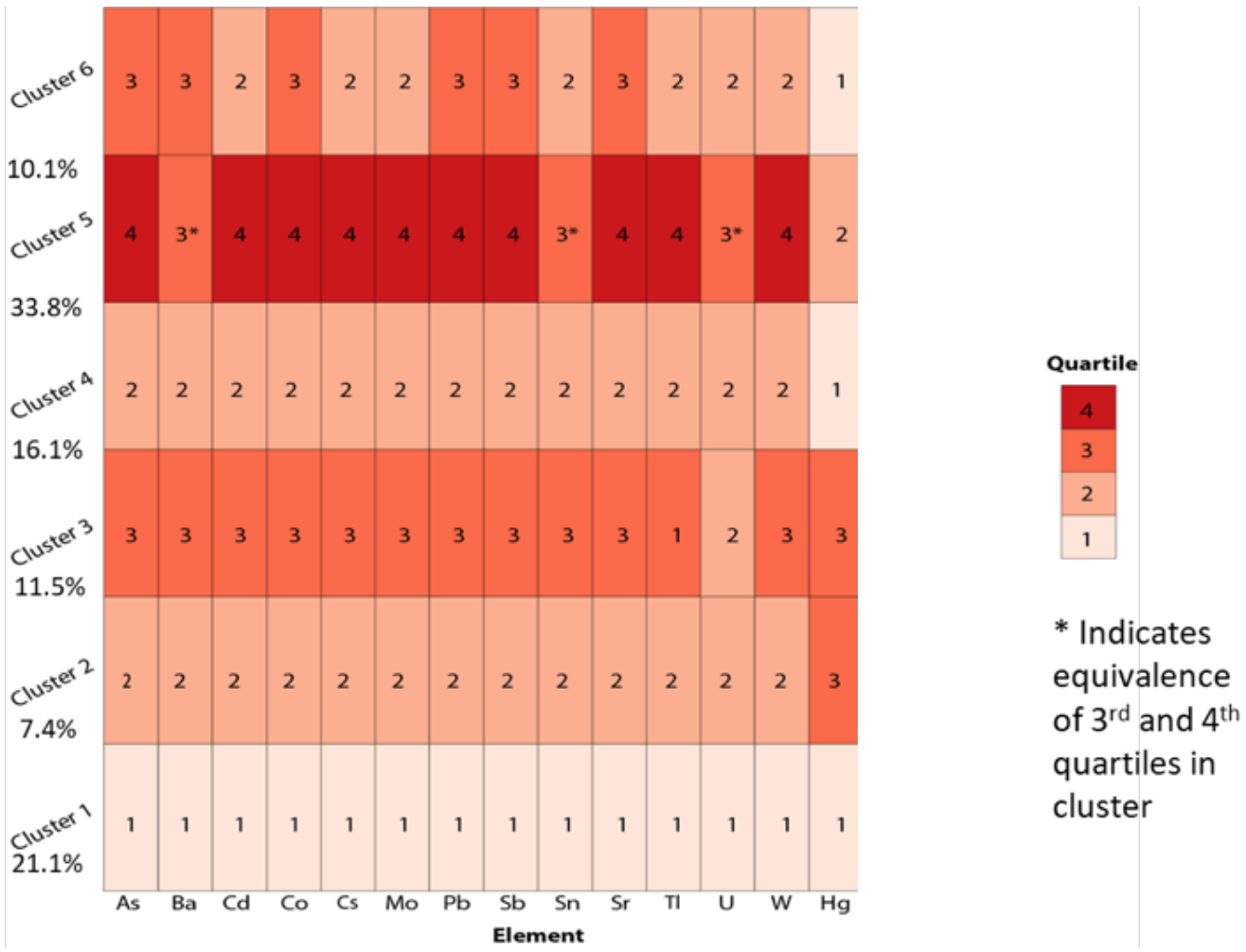
Exposures and outcomes reflect patterns of mixtures
Mixtures increase preterm birth ~3 fold

- **~45% with highest exposures to multiple metals in mixture have 3-fold greater risk of preterm birth (Clusters 5 & 6 relative to Cluster 1)**

- More than 20% of moms have low to no exposures to any metals



Total N=417

Hoover et al., submitted, in review November 2021

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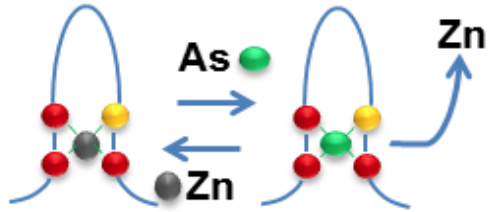
Maternal exposure to metals increases oxidative stress, DNA damage

Navajo Birth Cohort Study Participants (132)

Urine: As, U, F_2-Isoprostanes
U:NBCS>NHANES
As: NBCS~NHANES

Serum: Zn
NBCS<NHANES



>40 bench research publications by UNM METALS researchers

- As, Cs (but not U) **increased oxidative stress**
- Inhibition of zinc finger proteins
  - enzymes (PARP) that function in DNA repair
  - **Increase** in retention of **DNA damage**
- Population results consistent with lab studies on metals
- **Zinc modulates** effect of As and U

Cooper et al., Toxicol Appl Pharmacol. 2016;291:13-20. doi: 10.1016/j.taap.2015.11.017. PubMed Central PMCID: PMC4718819.

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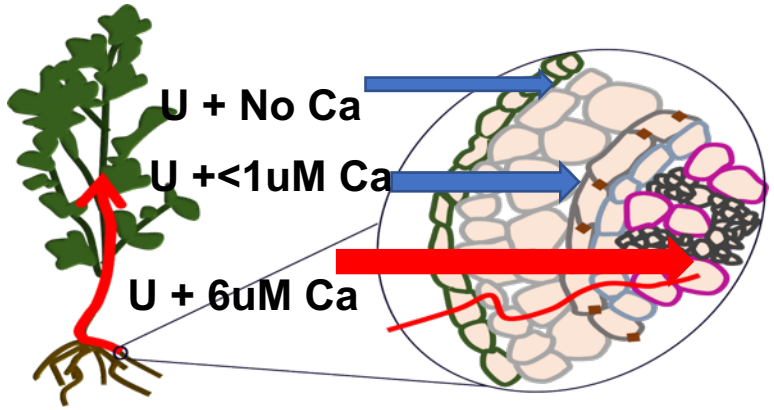
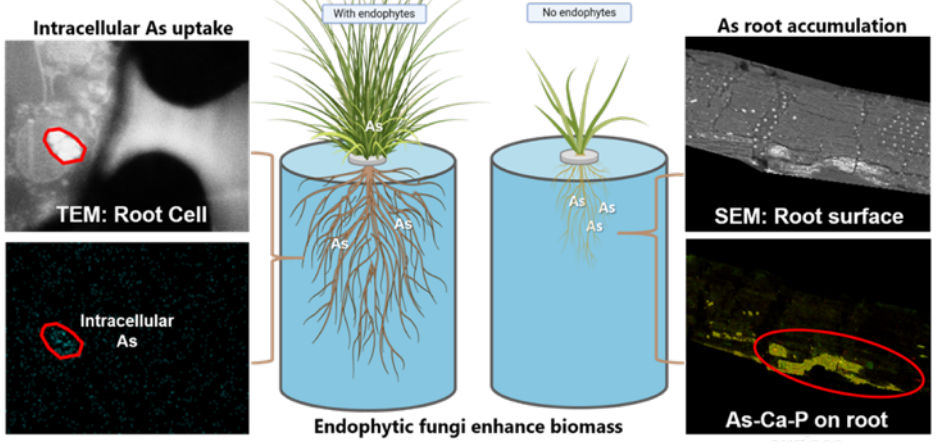
Environmental controls on exposures

Plant Uptake: Ca & fungi in rhizosphere control U and As uptake, root to shoot translocation



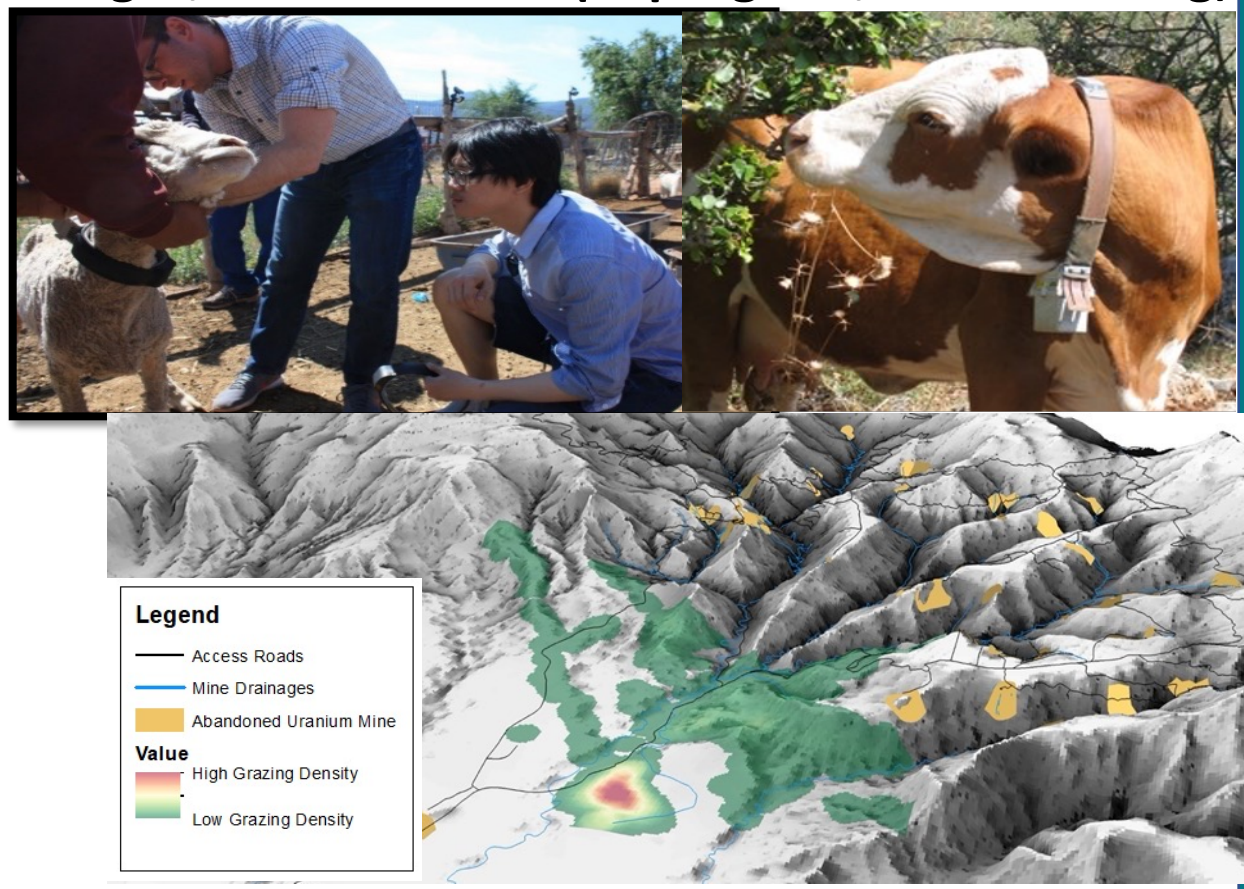
El Hayek et al., Environ Sci Technol. 2018; 20;52(22):13089-13098. doi: 10.1021/acs.est.8b02724. PubMed Central PMCID: PMC6341987.

Fungi enhance growth, also transport into plants



DeVore et al., ACS Earth Space Chem. 2021 17;5(6):1278-1287. doi: 10.1021/acsearthspacechem.0c00302. PMCID: PMC8302048.

Livestock vary in time grazing in waste-impacted drainages, water sources (in progress, 4 mo tracking)



U toxicity & bioavailabilitiy increased in carbon-rich particulates

El Hayek et al., Environ Sci Technol. 2021; 55(14):9949-9957. doi:10.1021/acs.est.1c01205 PubMed PMID: 34235927; PMCID: PMC8413144.

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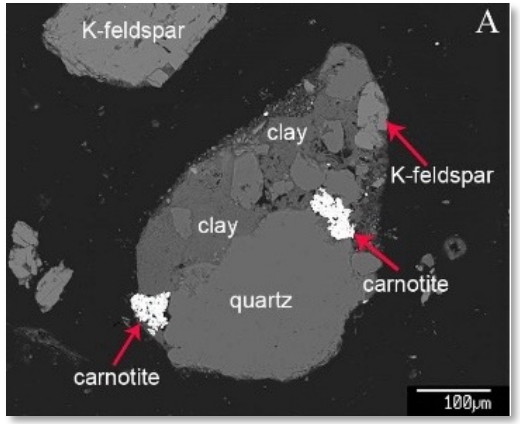
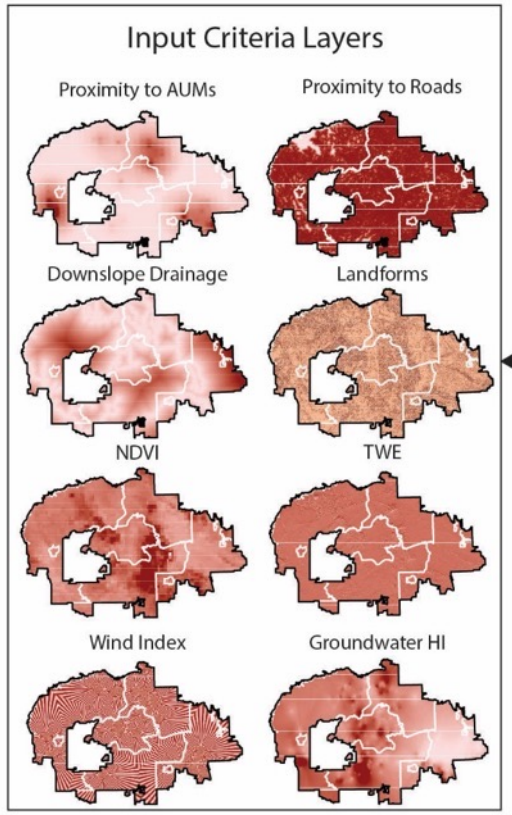
Redistribution with time (35-80 yrs)

- Waste weathered to nanoparticulates of varying mineralogy (30-80 yrs)
- Readily lofted in air, inhaled, solubilized

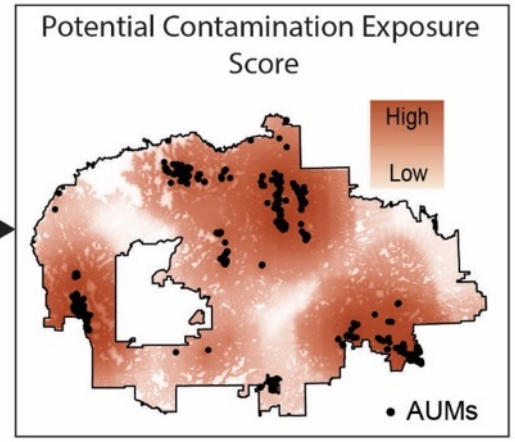
Dust storm New Mexico 2014



Clusters of soluble carnotite nanoparticles (U/V) on respirable clay particle



GIS Modeling & Analysis (GIS-MCDA)



Limited local met data being addressed with additional stations, improving prediction – fit now ~.7 (NURE, research samples)

Lin, et al., 2020. Environmental Science and Pollution Research, 27, 30542-30557.

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Opportunities and challenges in relation to low dose radiation exposures

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Context: Sovereignty, broken treaties and the erosion of trust

- **Treaty Rights: Entered into by US Government**
  - Historically poorly adhered to by federal government – treaty lands given to resource extraction throughout country

- **Substantial environmental and economic injustice has resulted from lack of federal adherence to treaties and honor of sovereign rule .**
  - Congressional reversals of treaty obligations to allow for resource exploitation
  - Mining in Black Hills reversed treaty documented ownership of Sioux
  - Cold War Uranium mining throughout Navajo → >500 abandoned mines, left many others with significant waste
  - Death of generation of Native miners

- **Sovereign Nations: Right to self-governance existed prior to colonization/contact**
  - Sovereignty extends to data sovereignty and protection of privacy of individuals and tribe
  - History with researchers historically checkered – "helicopter science", use of biospecimens beyond consent
  - Many tribes now have own research policy, FWA accredited IRBs in addition to academic and IHS review

*Lewis J.L, Hoover, J., MacKenzie, D. "Mining and Environmental Health Disparities in Native American Communities." **Curr Environ Health Rep**. 2017 Jun;4(2):130-141. doi: 10.1007/s40572-017-0140-5. Invited Review.*

Conducting meaningful research requires rebuilding trust, inclusion of communities as well as tribal government

- Listening sessions not enough – genuine, and early, dialogue critical
  - Community members + agencies + councils/executive
- Willingness to learn from community and conduct research from holistic perspective
- Incorporating community members into the design and implementation
- Follow-through and regular feedback
- Respect for data ownership and data sovereignty
- Commitment for evidence based actions to reduce risk, provide benefit to community
  - RECA difficulties have further eroded trust

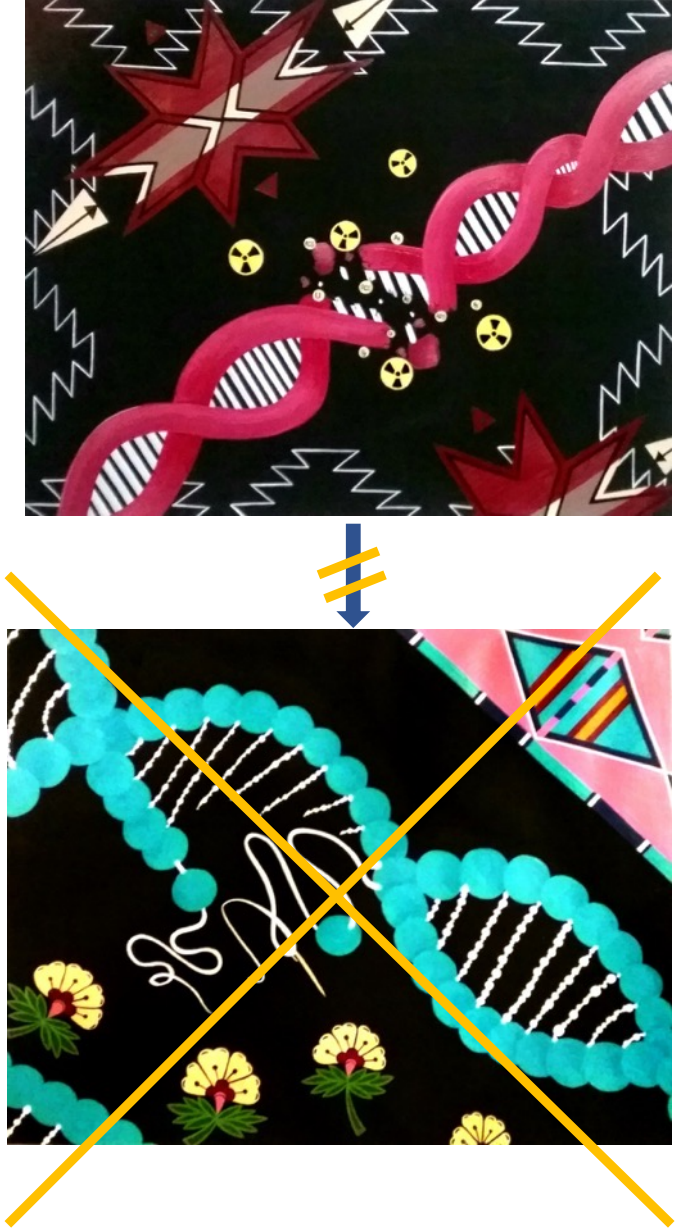
Views on Research priorities

- Perfect storm --> DNA damage induced by radiation not repaired due to metal mixtures, dietary zinc deficiency
  - Increased sensitivity to development of multiple chronic diseases
  - Perturbation of fundamental mechanisms (ox stress, chronic inflammation, DNA repair, increased preterm birth
  - Potential for development of multiple cancers
  - Communities perceive no separation between radiation and mine waste – all related

- Recognize potential for increased sensitivity
  - Increased reliance on local resources → increased exposures
  - Likelihood of multiple concomitant exposures
  - Lack of infrastructure
  - Multi-generational exposures and preexisting conditions

- Recognize potential for stress as contributor to disease
  - Losses to culture and traditional lifestyle
  - Loss of elders and impacts to family
  - Multigenerational exposures

- Potential for genomic variants – very little known



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History is long, trust is minimal
Listening, honesty & inclusion essential to success
Radiation and mining fundamentally linked in community

- Integration of community into planning and implementation
- Consider multiple endpoints given the potential for perturbation of multiple fundamental pathways to chronic disease
- Consider impacts beyond health – livestock, wildlife, ecosystem
  - These are all within the definition of "health"
- Consider impacts to future generations
  - Pregnancy
  - Child development

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METALS Researchers & Community Partners

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- ***Cameron***

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NBCS Navajo Birth Cohort Study

ECHO Environmental influences on Child Health Outcomes
A program supported by the NIH

The people of the Navajo Nation:

- > 1000 participating Navajo families
- Many supporting chapters
- HEHSC, Tribal and Agency Councils, Executive Branch, NNEPA, GIB
- NAIHS & PL-638 hospital laboratory staff, leadership, and health boards

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