

October 3, 2022

Ms. Rebecca Izzo-Manymules, Chair
Navajo Nation Human Research Review Board
P.O. Box 1390
Window Rock, AZ 86515

Re: NNR 04-145 — DiNEH Project, Project Year 2021-2022, Annual Report covering the period July 21, 2021 to July 20, 2022

Dear Rebecca Izzo-Manymules,

The Diné Network for Environmental Health (DiNEH) Project submits this letter and the attached annual report covering the 2021-2022 Project Year (July 21, 2021 to July 20, 2022). The report is formatted according to the Board's guidelines.

We submitted our annual Request for Continuation (RfC) via letter to the Board dated May 31, 2022. A copy of the RfC follows this cover letter. We have received approval of our RfC from the UNM Human Research Protection Office, and a copy is also attached.

Over the past year, our research priorities were focused in part on responding to policymaker requests for up-to-date research on COVID-19 case trends. Presentations to key tribal stakeholders, including the Navajo Nation Council's Health, Education and Human Resources Committee, and at the community level always referred to key findings of the DiNEH Project. We completed and submitted to the Board a manuscript on antinuclear antibodies testing as a method for examining the possible effects of exposure on immune system function, and continued working with collaborators studying biomarkers of kidney damage in relation to environmental exposures.

Principal partners in the Project remain the UNM Community Environmental Health Program (UNM-CEHP) and Southwest Research and Information Center (SRIC). From 2004 to 2011, the Project was based in and collaborated with 20 chapters of the Eastern Navajo Agency. Since 2012, the DiNEH Project has had no funding but has remained active to permit analyses of biological specimens to understand mechanisms of toxicity of environmental exposures, to prepare research papers for publication (subject to Board approval), and to present results to Navajo Nation-based organizations and officials, including representatives of the 20 Chapters in the study.

Please do not hesitate to contact us if you have questions or need additional information.

Respectfully Submitted,



Johnnye Lewis, Ph.D., D.A.B.T.



Eszter Erdei PhD, MPH



Chris Shuey, MPH

May 31, 2022

Michael Winney, IRB Coordinator
Navajo Nation Human Research Review Board
c/o Navajo Department of Health
P.O. Box 1390
Window Rock, AZ 86515

Re: **Request for Continuation** – NNR 04-145, Diné Network for Environmental Health Project

Dear Mr. Winney,

Please accept this letter as UNM's notification of our request to continue the DiNEH Project's Navajo Uranium Assessment and Kidney Health Project (NNR 04-145) for another year, from July 21, 2022 through July 20, 2023.

As indicated in our most recent quarterly reports, the Project team will be submitting our antinuclear antibody manuscript soon with the expectation of having the paper published by the end of the year. In the meantime, we are drafting a paper documenting our analyses of kidney biomarker injuries from environmental exposures. Depending on COVID-19 rules, we anticipate reactivating contact with the Project's community partners in the Eastern Agency. Community report-backs have been requested in light of new discussions of federal plans to remediate abandoned uranium mines in the region. Over the past two years, our interactions with community members and policy makers have been confined to telephone calls, videoconferencing, data analyses and manuscript preparation.

Keeping the Project active allows our team to do two things. First, we will continue to carry out statistical analyses, including modeling, of kidney biomarkers derived from the Project's biomonitoring program. This involves continuing our work with Dr. Donald Molony, a nephrologist at the University of Texas Houston Medical Center. In this context, our team has been actively engaging in discussions with other academic and community colleagues on how to follow up with the DiNEH Project cohort in ways that address their current health concerns. We believe that serving the impacted communities directly is our foremost duty.

Please do not hesitate to call Dr. Erdei at 505-272-8912 or Mr. Shuey at 505-262-1862 if you have questions or need additional information.

Respectfully Submitted,



Johnnye Lewis, Ph.D.
Principal Investigator



Esther Erdei, Ph.D.
Co-investigator



Chris Shuey, MPH
Co-investigator

DiNEH Network for Environmental Health (DiNEH) Project

Annual Report

**Johnnye Lewis, Ph.D., Principal Investigator
and Esther Erdei, Ph.D., M.P.H. and Chris Shuey, M.P.H., co-investigators
Report Covers: July 21, 2021 – July 20, 2022**

Introduction

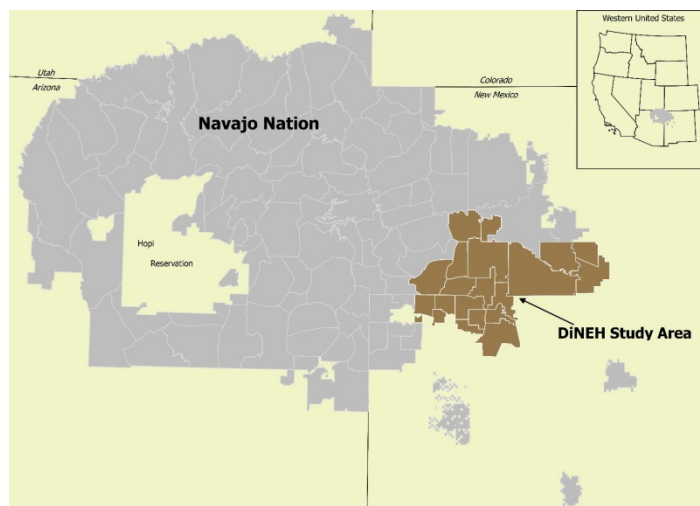
The Diné Network for Environmental Health (DiNEH) Project submits this Annual Report to the Navajo Nation Human Research Review Board (NNHRRB), covering the period of July 21, 2021 to July 20, 2022 (2021-2022 Project Year). Our **Request for Continuation** (RfC) was submitted in a letter dated May 31, 2022, a copy of which is attached to the cover letter to this report. A RfC was approved by the UNM Human Research Protections Office (HRPO) on December 3, 2021, and it too is attached to this report. Our next UNM HRPO continuation approval will be in December 2022.

While federal funding from the National Institute of Environmental Sciences (NIEHS) for the DiNEH Project ended 10 years ago, the work of the Project has continued through a conscious effort to keep the research team together and to maintain our long-standing relationships with Navajo communities impacted by uranium mining. The research team includes staff of the UNM Community Environmental Health Program (UNM-CEHP) and Southwest Research and Information Center (SRIC), two of the original organizations implementing the DiNEH Project between 2002 and 2010.

The period covered by this report includes the tail “end” of much of the COVID-19 pandemic era during which direct, in-person communication was curtailed in conformance with public health orders of the Navajo Nation Department of Health, the New Mexico Department of Health and Governor’s Office, and the UNM Health Sciences Center. Our UNM group developed and issued an internal policy in June 2020 that described requirements for allowing field staff to have contact with study participants. Provisions included full vaccinations (including “boosters”), always wearing masks and practicing physical distancing, and keeping all materials sanitized. In lieu of face-to-face contacts, we continued to use online, virtual meetings to maintain communications among staff members and, when appropriate, with participants. Our outreach and educational log provided in Table 1 below for the Project Year reflects these practices.

Background

The DiNEH Project’s Navajo Uranium Assessment and Kidney Health Project (NUAKHP) was conducted through a collaborative, community-based partnership among UNM-CEHP, SRIC and 20 chapters of the Eastern Navajo Agency between 2004 and 2012 (see map). Study partners from 2004 to 2008 also included the Eastern Navajo Health Board and the University of Texas Houston Medical Center (UTHMC), with ad hoc collaboration with the medical staff of the Crownpoint Comprehensive Health Care Facility. In 2010 and 2011, the DiNEH Project partnered with the Community Uranium Exposure-Journey to Healing (CUE-JTH) program of the Navajo Area Indian Health Service (NAIHS) to conduct community-based blood and urine



collections among 267 of the 1,304 participants in the study. Analysis of these biological samples for metals and biomarkers of biological impairment and disease, and their relationships to environmental exposures to uranium wastes, has been the focus of DiNEH Project over the past 10 years. UNM and SRIC staff, who have remained committed to the project since its inception in 2001, have also endeavored to communicate results of the research to communities and to Navajo Nation institutions and leaders to inform environmental health policy to help address the 80-year-old Navajo Uranium Legacy.

Personnel

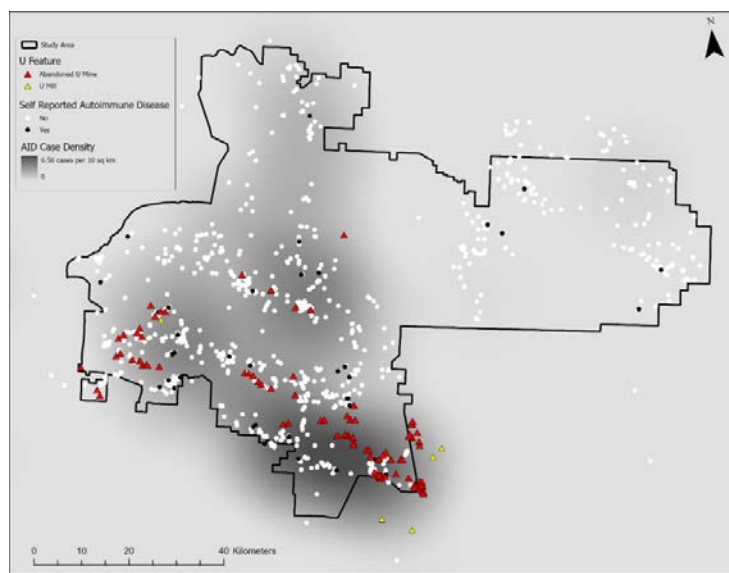
The DiNEH Project's core team of Esther Erdei (UNM; immunologist and epidemiologist), Chris Shuey (SRIC; environmental health specialist) and Curtis Miller (UNM; biostatistician) continued to be supported by Principal Investigator Johnnye Lewis (UNM; toxicologist), Laurie Hudson (pharmacologist) and Debra MacKenzie (immunologist). SRIC's field staff now working on the Navajo Birth Cohort Study-Environmental influences on Child Health Outcomes (NBCS-ECHO+) included two veterans of the DiNEH Project, Teddy Nez and Sandy Ramone, who bring continuity and expertise to NBCS-ECHO field studies. (Mr. Nez retired at the end of 2021.) Sarah Henio-Adeky, a Navajo language specialist who conducted hundreds of surveys with DiNEH Project participants between 2005 and 2011, rejoined SRIC's staff in January 2018 as the Eastern Agency community liaison to the UNM METALS Superfund Research Program (SRP). Her work educating community members about our ongoing zinc supplementation clinical trial ("Thinking Zinc") brings her in contact with DiNEH Project chapters and members, allowing for continued discussion of project research findings and policy initiatives. During the Project Year, the staff also enlisted the help of Houston based nephrologist, Don Molony, Ph.D., who was an early consultant to the Project (2006-2011) and, over the past three years, has been advising the team on interpreting biomarkers of kidney damage among DiNEH participants. SRIC is also integrating its newest Diné staff member, Kirena Tsosie, into aspects of the DiNEH Project that focused on water quality and access to water resources.

We should note that costs associated with personnel, research activities and community outreach were absorbed through the DiNEH Project staff's ongoing work in other funded programs. Mr. Shuey's contributions to these studies are covered by SRIC's General Fund (non-federal grants) as the result of decisions made by SRIC's Board of Directors.

Summary of Activities During the Project Year, 2021-2022

A. Mapping of Geo-coded Locations of Phase I and Phase II DiNEH Project Participants

During the course of preparing the ANA manuscript discussed in the next section, we found a need to show graphically that Phase II study participants (N=267) – those who were involved in blood urine collections in 2010-2011 -- were from the same population of the all 1,304 participants in the study (see map at right). UNM CEHP geographer, Daniel Beene, prepared an index map of geo-masked participant locations that we are using in the ANA and kidney papers discussed below. The map (shown below) cannot be used by outsiders to "find" participants because their actual locations are offset by several miles, but the map serves as a valuable representation of the distribution of participants across the study area.



B. Completion of manuscript titled, *Metal Mixture Exposures and Antinuclear Autoantibody Screening in Navajo Communities Exposed to Uranium Mine Wastes*

Just after the close of the reporting year, Dr. Erdei and Mr. Shuey completed refinements to the “ANA paper” cited above, and received final review by Dr. Lewis. The manuscript will be submitted to the *Journal of Exposure Science and Environmental Epidemiology* (JESEE) following final editorial preparation. The manuscript was submitted to the Board in November 2021. Refinements made in 2022 clarified the origin of concern about autoimmune disease in the study population and accuracy of the multiplexing laboratory to detect ANA and specific antigens. Major findings of the paper have not changed:

- Participants in the biomonitoring portion of the study (N=263) had significantly higher self-reported exposures than people who participated solely in Phase I of the study (N=1,074). Those exposures were:
 - proximity to waste sites
 - having worked in a mine
 - having lived in a mining camp
 - washed clothing of workers
 - playing on mine wastes as a child
 - used mine materials in home construction
 - came in contact with mine water
 - sheltered livestock on mining sites

This finding suggests that participants’ knowledge of their past and ongoing exposures to uranium motivated them to participate in the volunteer blood and urine collection events held at 14 community sites in 2010 and 2011.

- The overall prevalence of a positive ANA test was 27.2% (65 of 239) — almost two times higher than the national average ANA prevalence rate of 13.8% reported in the 2012 NHANES survey.
- No significant differences were detected in ANA positivity across gender or age groups, nor in serum antigen levels (anti-DNA and anti-U1-RNP) between females and males
- Odds ratios of having a clinically defined ANA response were significant for three exposure covariates:
 - proximity to waste sites (OR=3.07; 95th CI=1.15-8.22; $p=0.025$);
 - consumption of mercury in drinking water (OR=2.34; 95% CI=1.25-4.398; $p=0.008$; and
 - age (OR=1.07; 95% CI=1.011-1.124; $p=0.018$)

That ANA positivity is strongly predicted by increasing proximity to uranium waste sites is consistent with our previous finding (Erdei et al., *Autoimmunity*, January 2019) that proximity was also a significant predictor of four specific serum autoantibodies (AuAbs) detected in participants’ serum samples. These AuAbs are often used as biomarkers of drug-induced autoimmunity or autoimmunity of unknown origins, but they require expensive, specialized laboratory detection methods, whereas the ANA screening test is cheaper, quicker and commonly used.

- Odds ratios of having a clinically defined positive anti-dsDNA serum response were significant for two exposure covariates:
 - Arsenic consumption in drinking water (OR=1.79; $p=0.012$)
 - Radium consumption in drinking water (OR=1.04; $p=0.001$)

- Linear regression models showed nickel consumption in drinking water significantly predicted increased serum anti-U1-RNP production.
- The multiplexing immunofluorescence ANA test, which is widely used as a screening method for early immune system impairment at hospitals throughout the Navajo Nation, also appears to be an effective predictor of environmental exposures, giving Navajo-based clinicians another screening tool for possible uranium waste exposures.

The public health implications of this finding are captured in the paper's conclusion:

The unexpected increase in ANA positivity (27.2%) among Eastern Navajo community members exposed to complex metal mixtures in uranium mine wastes indicates an unmet clinical need for immune impairment surveillance in the region. Incorporating autoimmunity assessments in routine primary care screening services for people living in mining waste-exposed communities should be considered to improve clinical practice. Since minority groups have been shown to have increased rates of autoimmune diseases, screening early for autoimmune markers has both clinical importance and community health benefits.

With respect to drinking water exposures, in our previous AuAbs paper, we reported that uranium exposure through drinking water sources was a strong predictor of AuAbs positivity – at average concentrations of less than 10% of the federal and tribal drinking water standard. In the more recent ANA study, we found that mercury was a significant predictor of a positive ANA test; that arsenic and radium were significant predictors of a positive anti-dsDNA serum response; and that nickel was a significant predictor of a positive anti-U1-RNP response. In the cases of Hg, As and Ni, the average concentrations in water sources used by the Phase II participants were well below their respective drinking water standards. Mercury and arsenic are known to have toxic properties in minute concentrations; therefore, it is possible that their drinking water standards may not be protective of potential immune impairment.

The significant positive anti-dsDNA response to radium consumption may be the result of actual exposures. At least seven of the Phase II participants drank from water sources containing radium in high concentrations. Nine water sources tested by the DiNEH Project and used by Phase II participants had radium concentrations ranging from ½ to more than the MCL (i.e., 5 picoCuries per liter). We note that radium occurs naturally in groundwater, especially in geological formations that are rich in uranium. While naturally occurring, it is well-documented human carcinogen.

The implications of these findings were highlighted in the ANA paper:

..[T]he protectiveness of national primary drinking water standards applicable to public water systems for immune system alternations should be further examined. The health impacts of long-term exposure even at low concentrations of multiple metals need to be considered. While the vast majority of water supplies on the Navajo Nation meets or exceeds national standards, unregulated and regulated water supplies remain at risk in areas where natural conditions and mixed-metal mining wastes have contributed to localized contamination of land and water.

C. Kidney Biomarker Research and Analyses

In 2021-2022, our team made great progress toward one of the original aims of the DiNEH Project – to investigate the possible role of uranium and other environmental metals in the high rates of chronic kidney disease (CKD) observed in the Crownpoint Service Unit over the past 20-25 years. Our inquiry is based on analyses of biomarkers of kidney damage in urine and blood from the 267 people who participated in the biomonitoring phase of the study. The assays were done at Dr. Lewis' laboratory in the UNM College of Pharmacy and Dr. Donald Molony's laboratory at the University of Texas Houston Medical Center several

years ago. Dr. Molony is a nephrologist who was part of the original DiNEH study team, and a recognized expert in using renal biomarkers to assess kidney damage from metals exposures.

In the past year, Dr. Miller conducted iterative statistical analyses of urinary biomarkers to assess relationships with proximity to uranium waste sites, exposures to metals in drinking water, and excretion of urinary metals. Given the large number of renal biomarkers measured in the biomonitoring program, he has used a Principal Component Analysis method to reduce correlations and the number of potential covariates, while still considering the modifying influences of other risk factors, including age, gender, presence of type 2 diabetes and hemoglobin A1c levels. Preliminarily, Dr. Miller has concluded that the models show relationships between certain combinations of environmental metals and CKD environmental exposure. Three different combinations of renal biomarkers also are associated with CKD.

These analyses were being examined closely by the DiNEH team in regular Zoom conversations. Based on the statistical analyses and discussions, Dr. Erdei has developed the first draft of a paper describing the occurrence of CKD in DiNEH study participants, outlining the influence of confounders (e.g., diabetes, high blood pressure, age, BMI) in the final statistical model, and summarizing the statistical findings.

Concurrently, Dr. Molony and colleagues developed the final draft of a critical literature review of research findings related to the nephrotoxicity of uranium by itself and in concert with other trace metals. Their review of human population studies published in the last 10 years show a strong healthy-worker bias in evaluation of the associations with urinary uranium biomonitoring. These recent findings, which stand in stark contrast to studies documenting uranium's role in kidney disease published between 1985 and 2004, appear to have influenced the current federal approach that does not consider uranium as a high priority for research on long-term exposures and their consequences for kidney health among exposed communities.

D. Changes in Cytokine and Immune Cell Productions.

Our cytokine research was interrupted by the COVID pandemic for most of 2020 through 2022. Recent work analyzing these markers is summarized here: All Phase II serum samples (N=263) were analyzed by Dr. Erdei for 13 human cytokines¹ and a subset of whole blood samples were also studied for lymphocyte subpopulation changes (N=69) associated with proximity to abandoned uranium mining waste sites. The research team conducted correlation analyses between metal exposure measures and these immune outcomes, respectively. The most recent modeling by Dr. Miller showed that BMI (body-mass index) was a significant predictor of three inflammatory cytokines. Dr. Erdei met regularly with Dr. Miller to streamline the Bayesian statistical modeling. All univariate analysis yielded meaningful results among various cytokines, especially inflammation producing cytokines, but complex modeling efforts are needed to gather more insights to their associations with biomonitoring information and water contamination measures of metal mixtures in DiNEH communities.

E. Compiling and Sharing DiNEH Water Quality Data with NNEPA

During the 2021-22 Project Year, the DiNEH staff accomplished two long-standing objectives: (1) Make Navajo water quality data available to community members, agency partners and policy makers through a secure, searchable online database, and (2) obtain NNHRRB approval to share data generated exclusively by DiNEH Project with the Navajo Nation Environmental Protection Agency (NNEPA).

The first objective was accomplished with the development of the Navajo WaterGIS interactive website (<https://unmcop.unm.edu/metals/#section3>) by UNM geographer Daniel Beene. It houses water quality data from more than 2,000 water sources, including more than 100 in the DiNEH study area alone. The database

¹ Cytokines are small proteins, such as interferon and various interleukins, which are secreted by certain cells of the immune system. Cytokines are crucial in controlling the growth and activity of other immune system cells and blood cells; they affect the growth of all blood cells that help the body's immune and inflammation response.

was developed over parts of a decade by Mr. Shuey, former UNM geographer Dr. Joe Hoover (now at University of Arizona), and Mr. Beene, a UNM doctoral candidate. Our effort to compile and map water quality information in understandable formats began in 2010. Our group published a summary of the initial compilation of data from nearly 500 water sources in a paper by Dr. Hoover and others (including Mr. Shuey) that was approved by NNHRRB (Hoover et al., 2017). The report found that arsenic (15.1%) and uranium (12.5%) were the more frequent water contaminants to exceed their federal and drinking safe drinking water standards.

The second objective was achieved in June 2022 with the Board's approval of Dr. Lewis's written request to share DiNEH Project-derived water quality data with NNEPA staff. This initiative started in October 2021 when the DiNEH staff received several written requests from NNEPA staff and consultants for DiNEH water quality data to support an assessment of natural resources damages around abandoned mine sites. Mr. Shuey informed Jeremy Bekis with the NNEPA Superfund Program of the Board's approval on June 21, 2022.

F. Community Outreach and Education, 2021-2022

A consolidated community outreach and education log for the project year is shown in Table 1 below. The DiNEH staff used or referred to relevant findings and results of the DiNEH Project in every one of the listed events. Of particular importance is our consistent finding that proximity to waste sites increases risks of cardiovascular disease (hypertension, in particular) and autoimmunity during the legacy period and kidney disease during the mining era. These findings of associations between exposures and chronic disease are particularly relevant to the Red Water Pond Road Community (RWPRC), whose members participated in the DiNEH project blood and urine collections in 2007 and 2010-11 and who have been living with uranium mining and waste sites for 50+ years. As shown in the Table 1, RWPRC members also highlighted their participation in the DiNEH Project to bolster their concerns about the potential health effects of living with uranium wastes in advocating that the U.S. Nuclear Regulatory Commission (USNRC) to find a different, remote site for permanent disposal of the Northeast Churchrock Mine wastes. (Photo below: RWPRC member Edith Hood addresses the NRC Commissioners on April 22, 2022.)



Staff of the Thinking Zinc clinical trial cites the DiNEH Project as evidence that our group can conduct a community-based clinical intervention using blood and urine collection events at chapter houses and senior centers – a venue rarely used in other clinical trials held in urban centers. The Nahata' Dziil Commission Governance in Sanders, AZ remains concerned about lingering uranium contamination of public water supply wells and livestock wells located in the Puerco River Valley, some 80 miles downstream from the Church Rock Mining District.

In addition to these activities, and pursuant to our research approval by NNHRRB, both Dr. Erdei and Mr. Shuey gave presentations at the 2021 Navajo Research Conference. Dr. Erdei presented results of our AuAbs and ANA research and Mr. Shuey presented findings of our field radiation investigations supported in part by the Navajo Birth Cohort Study.

The UNM team consisting of staff of the DiNEH Project, Navajo Birth Cohort Study, Thinking Zinc and the UNM METALS Superfund Research Center, gave a 1-1/2 hour panel discussion on findings and results of our various population studies to the annual meeting of the New Mexico Public Health Association (NMPHA) in May 2022. Mr. Shuey and Dr. Erdei summarized DiNEH Project findings based on information previously vetted by NNHRRB. Those slides are attached as **Appendix A**. The presentation highlights DiNEH Project

Table 1. DiNEH Project Community Outreach and Education Log, Project Year 2021-2022

Abbreviations:

Date	Activities/Events	Staff	Location	Audience/Stakeholders
7/29/21	Community on water quality in both public water supplies and unregulated wells along the Puerco River in Navajo communities in eastern Arizona.	Shuey, Nez	Nahata' Dziil Commission Governance, Sanders, AZ	~20 NDCG officials and reps of federal and NN agencies, universities, NGOs
9/10-15/21	Outreach for Thinking Zinc community collection event in Blue Gap-Tachee and surrounding chapters; includes info on DiNEH Project results	Shuey, Henio-Adeky; J Naize	ABQ, Pinehill and BG/TC offices, homes; used phones, text, email, in-person visits	~45 people participating in the study, including 37 in the Eastern Agency
10/9/21	Thinking Zinc community collection event at which DiNEH project materials, including published papers presentations, were available as handouts	Erdei, Henio-Adeky, Shuey	Blue Gap-Tachee (AZ) Senior Center	15 participants + ~12 community members
10/20/21	Presentation on radiation monitoring data, metals in home dusts, indoor radon and water quality data from both the DiNEH Project and Navajo Birth Cohort Study.	Shuey	NNHRRB biannual research conference, held virtually	~150 attendees at the online conference
10/20/21	Presentation summarizing data generated in the DiNEH project on antinuclear antibodies (ANA) testing and metal mixture exposures from uranium mines.	Erdei	NNHRRB biannual research conference, held virtually	~150 attendees at the online conference
11/10/21	Discussion with Churchrock Chapter president about results of Thinking Zinc and DiNEH Project	Shuey, Hudson, MacKenzie,	Zoom call between ABQ and Church Rock	1 participant in both studies
4/22/22	During an unprecedented visit by the three sitting members of the U.S. Nuclear Regulatory Commission (NRC) to the RWPRCA Shade House, member expressed community concerns about the Federal Government's refusal to remove the wastes from the community to a central disposal facility. Mr. Shuey was invited to speak about the results of health studies, including the DiNEH Project's findings related to increased health risks for living in close proximity to mine wastes.	Shuey; members of Red Water Pond Road Community Association (RWPRCA)	RWPRCA "Shade House" on Red Water Pond Road, ~11.5 miles NE of Gallup in Coyote Canyon Chapter	~100 attendees, including NN President J Nez, NNEPA Director V Shirley, and 3 sitting members of the NRC
4/28/22	RWPRCA members presented their citizen-science poster titled "Living with Uranium Wastes for 50 Years and Four Generations" at the UNM Health Sciences Center annual Research Day on main campus. The poster was first presented at the 2018 10 th International Conference on Metals Toxicity and	Shuey; members of Red Water Pond Road Community Association (RWPRCA)	UNM Student Union ballroom, main campus	~200 attendees, including officials from federal, state and tribal agencies, UNM faculty and staff, and community organizations

	Carcinogenesis and later revised for presentation at the Harvard University Belfer Center's Managing the Atom conference in December 2020.			
4/29/22	April 29 -- Tour of the Jackpile Mine on Pueblo of Laguna (POL) for NIH and NIEHS program officers overseeing UNM research activities. RWPRCA members saw Jackpile Mine for the first time ever seen the massive open pit mine 45 miles west of Albuquerque. DiNEH Project findings were mentioned in briefing for Laguna officials at the tribal headquarters and then later at the site of the mine.	Shuey; members of Red Water Pond Road Community Association (RWPRCA)	Pueblo of Laguna Tribal Administration building, stop points on tour of Jackpile Mine and adjacent Village of Paguate	~30 attendees, including NIEHS and NIH officials, POL officials and environmental staff, and community members
5/19/22	Panel presentation by UNM researchers on results of DiNEH Project, Navajo Birth Cohort Study, Thinking Zinc, and the METALS Superfund Research Center	Shuey, Cerrato, El Hayek, Erdei, MacKenzie, Henio-Adeky	New Mexico Public Health Association annual meeting (online)	~200 attendees
7/16/22	RWPRCA's annual commemoration of the 1979 Church Rock Uranium Mill Tailings Spill. Various speakers highlighted DiNEH Project findings and summarized available literature on uranium workers' health status in support of reauthorization of the Radiation Exposure Compensation Act (RECA).	Shuey; Henio-Adeky; members of RWPRCA	RWPRCA "Shade House" on Red Water Pond Road, ~11.5 miles NE of Gallup in Coyote Canyon Chapter	~100 attendees, including Navajo Nation officials and community groups from throughout the Four Corners Area

contributions to continuum of environmental health research conducted over the past 22 years. More than 200 people attended the NMPHA annual meeting by Zoom.

G. Outreach to and Collaboration with Policy Makers and Navajo Nation Agencies.

Table 2 below lists outreach and collaborations with Navajo Nation agencies and policy makers. Kirena Tsosie and Chris Shuey continued to participate in the Navajo Nation COVID-19 Water Access Coordination Group (WACG) in the 2021-2022 Project Year. WACG is an ad hoc collaboration of the Indian Health Service, Navajo Nation Division of Community Development, Navajo Nation Department of Water Resources, federal agencies, other universities and NGOs whose mission was to build and promote use of 59 new Transitional Water Points (TWP) at Chapter Houses in Navajo communities having both high rates of COVID-19 infections and large numbers of homes that do not have piped-in safe drinking water for human consumption and handwashing. We sat in on twice-monthly virtual meetings of WACG in 2021 and once-a-month sessions in 2022. Out of this collaboration, the DiNEH (SRIC) staff was invited to meet with staff of Dig Deep and the Johns Hopkins University water projects (which are Board-approved) to share our past work to assess water quality in unregulated water sources in the Eastern Agency. WACG also produced a new website, navajosafewater.org, which allows users to find the locations of new and permanent water points.

Table 2. DiNEH Project Outreach to Policy Makers, Project Year 2021-2022

Period	Institution/Organization/Agency	Project Staff	Audience/Actions
July 2021 through July 2022	Staff participation in Water Access Coordination Group (WACG), organized by Navajo Area IHS and Navajo Division of Community Development to increase access to and use of safe drinking water in rural areas of the Navajo Nation.	Shuey, Tsosie	~50 officials from tribal and federal agencies, universities, NGOs; development of navajosafewater.org
Oct. 21, 2021	Written testimony on health impacts of exposure to uranium mine wastes and uranium in drinking water in the Eastern Agency in support of Eastern Navajo Dine Against Uranium Mining’s petition for relief before the Inter-American Commission on human rights.	Shuey	Mr. Shuey’s declaration, which cited DiNEH project results, was 1 of 4 expert witness documents supporting the petition
October 2021 through July 2022	Staff development of water quality database for unregulated water sources on the NN; with Board approval, led to collaboration with Navajo EPA on accessing water quality data as part of its study of natural resources damages from abandoned mines; DiNEH water quality data specifically approved by NNHRRB at request of NNEPA Superfund Program	Shuey, Beene	NNEPA staff access to DiNEH water quality data approved by NNHRRB in June 2022
October 2021 through April 2022	At the request of the New Mexico Natural Resources Trustee, Maggie Hart-Stebbins, provided comments on funding of water projects in Navajo communities impacted by the Gold King Mine Release in August 2015 and 1979 Church Rock Tailings Spill.	K. Tsosie, C. Shuey	Four phone sessions with Ms. Hart Stebbins; provided written comments.
4/22/22	Oral testimony to USNRC on health impacts of moving the Northeast Church Rock Mine wastes to the UNC tailings pile.	Shuey	~100 attendees, including NN President J Nez, NNEPA Director V Shirley, and 3 sitting members of the NRC.
6/21/22	NNHRRB approved water-quality data sharing agreement with NNEPA, and Mr. Shuey informed NNEPA Superfund staff of the availability of DiNEH water quality data for water sources in the Eastern Agency.	Shuey	2 NNEPA staffers

Abbreviations for Tables 1 and 2:

- NGO – Non-governmental Organizations
- NMELC – New Mexico Environmental Law Center
- NNC19WACG – Navajo Nation COVID-19 Water Access Coordination Group (“WACG”)
- RWPRCA – Red Water Pond Road Community Association
- SRIC – Southwest Research and Information Center
- USNRC – U.S. Nuclear Regulatory Commission

H. Publications of the Project

Peer-reviewed papers describing results of the DiNEH Project since 2008 are listed here in chronological order. All were approved by the Board.

Erdei E, Shuey C, Miller C, Hoover J, Cajero M, Lewis J. Metal Mixture Exposures and Antinuclear Autoantibody Screening in Navajo Communities Exposed to Uranium Mine Wastes. *J Exposure Sci Environ Epidemiol* (submitted, in review), 2022.

Erdei E, Shuey C, Pacheco B, Cajero M, Lewis J, Rubin R. Elevated autoimmunity in residents living near abandoned uranium mine sites on the Navajo Nation. *J Autoimmunity* 2019; <https://doi.org/10.1016/j.jaut.2019.01.006>.

Harmon ME, Lewis J, Miller C, Hoover J, Ali AS, Shuey C, et al. Arsenic association with circulating oxidized low-density lipoprotein in a Native American community. *J Toxicol Environ Health Part A*. 2018; DOI: 10.1080/15287394.2018.1443860.

Hoover JH, Coker E, Barney Y, Shuey C, Lewis J. Spatial clustering of metal and metalloid mixtures in unregulated water sources on the Navajo Nation – Arizona, New Mexico, and Utah, USA. *Sci Total Envir*, 633 (2018) 1667–1678; August 15, 2018. (<https://www.sciencedirect.com/science/article/pii/S0048969718306880?via%3Dihub>)

Harmon ME, Lewis J, Miller C, Hoover J, Ali AS, Shuey C, et al. Residential proximity to abandoned uranium mines and serum inflammatory potential in chronically exposed Navajo communities. *J Exposure Sci Environ Epidemiol*. 2017; DOI: 10.1038/jes.2016.79.

Harmon, ME, Campen, MJ, Miller, C, Shuey, C, Cajero, M, Lucas, S, et al. Associations of Circulating Oxidized LDL and Conventional Biomarkers of Cardiovascular Disease in a Cross-Sectional Study of the Navajo Population. *PLoS One*. 2016; 11(3):e0143102.

Hoover J, Gonzales M, Shuey C, Barney Y, Lewis J. Elevated Arsenic and Uranium Concentrations in Unregulated Water Sources on the Navajo Nation, USA. *Expo Health*. 2017; DOI 10.1007/s12403-016-0226-6.

Hund L, Bedrick EJ, Miller C, Huerta G, Nez T, Ramone S, et al. A Bayesian framework for estimating disease risk due to exposure to uranium mine and mill waste on the Navajo Nation. *J R Statist Soc A*. 2015; <https://doi.org/10.1111/rssa.12099>.

deLemos JL, Brugge D, Cajero M, Downs M, Durant JL, Geroge CM, Henio-Adeky S, Nez T, Manning T, Rock T, Seschillie B, Shuey C, Lewis JL. Development of risk maps to minimize uranium exposures in the Navajo Churchrock mining district. *Environmental Health* (2009), 8:29. doi:10.1186/1476-069X-8-29.

deLemos JL, Bostick BC, Quicksall AN, Landis JD, George CC, Slagowski NL, Rock T, Brugge D, Lewis J, Durant JL. Rapid Dissolution of Soluble Uranyl Phases in Arid, Mine-Impacted Catchments near Church Rock, NM. *Environ. Sci. Technol*. 2008, 42, 3951–3957. doi: 10.1021/es071738k.

I. Benefits to the Navajo Nation and Future Plans

Even though we have not had funding specific to the DiNEH Project since 2012, staff members of the UNM Community Environmental Health Program and Southwest Research and Information Center have worked diligently to keep this project going over the past decade. Of critical importance is providing reports to participating Eastern Agency chapters and individual participants in the study. Furthermore, the DiNEH Project is the only study done on the Navajo Nation that found that environmental exposures to uranium mine wastes increase risks of kidney disease during the mining period and cardiovascular impairment and autoimmunity in the legacy period. Not only have these findings been used to inform federal and tribal remediation policies (see Tables 1 and 2 above), but also to provide clinicians with insight into how environmental exposures may be exacerbating chronic diseases and other existing health disparities in the Navajo population.

That we were not able to meet face-to-face with community members and chapter officials during the pandemic heightens our sense of obligation to report results and inform policy at the local, regional and national levels. As we approach 2023, we are eager to resume in-person meetings as soon as Navajo chapters are back to operating at full capacity. (Many chapters still limit the number in-person contacts, choosing to conduct virtual meetings.) In addition, we are intent on reaching out to hospital and healthcare personnel serving the Navajo people to continue to explain the relevancy of our findings for clinical diagnoses and prevention of downstream health effects.

With continued approval of the DiNEH Project from NNHRRB, we are planning to apply for grants that would allow our Team to bring in-depth training in environmental health and policy, exposure assessment education and community engagement of the participating communities. Additional funding would permit our current NBCS field staff to begin contacting participating chapters to provide updates and report-backs, and to gauge the interest of community members in further participation in DiNEH studies. Our team would be happy to submit a more detailed plan to the Board to provide further justification for continuing this critical research.

APPENDIX A

DiNEH Project-related slides shown in an omnibus presentation to the May 2022 annual meeting of the New Mexico Public Health Association

Overview of Community-partnered Research to Assess Health Effects of Environmental Exposures to Uranium in Tribal Communities

**New Mexico Public Health Association Annual Meeting
May 19-20, 2022**

Chris Shuey, MPH, Community Engagement Core Lead
Jose Cerrato, Ph.D., Mineralogy and Toxicity of Mine Wastes
Eliane El Hayek, Soil and Plant Uptake in Agricultural Areas Near Mines
Esther Erdei, Ph.D., DiNEH Project Methods and Findings
Debra MacKenzie, Ph.D., Navajo Birth Cohort Study-ECHO+
Sarah Henio-Adeky, BA, Navajo Translation of Thinking Zinc Clinical Trial

Funding: NIH/NIEHS P42 ES025589 (UNM METALS)

This material was developed in part under cited research awards to the University of New Mexico. It has not been formally reviewed by the funding agencies. The views expressed are solely those of the speakers and do not necessarily reflect those of the agencies. The funders do not endorse any products or commercial services mentioned in this presentation.



COLLEGE OF PHARMACY
METAL EXPOSURE AND TOXICITY ASSESSMENT
ON TRIBAL LANDS IN THE SOUTHWEST



Stanford
University

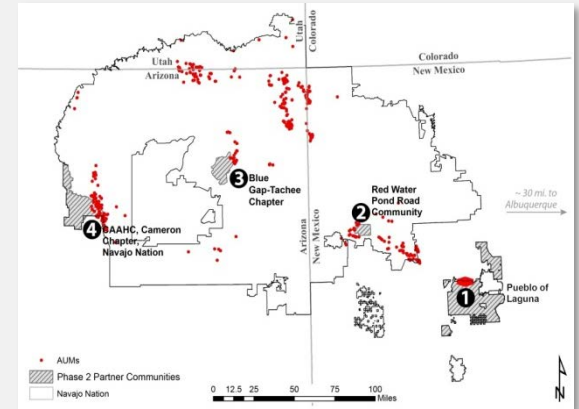
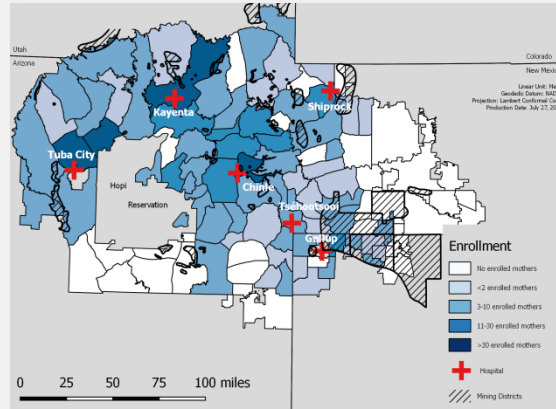
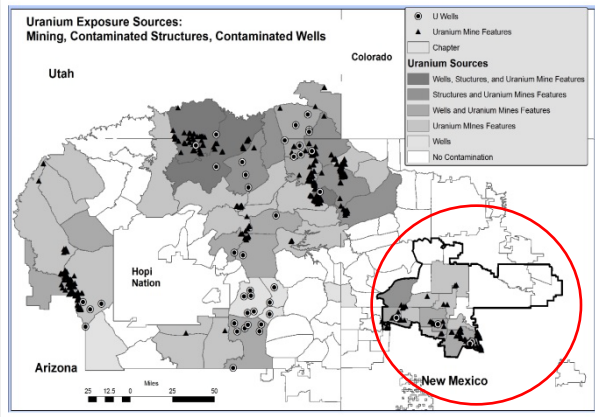


Major Community-Partnered Environmental Health Research Studies of the UNM Community Environmental Health Program (J. Lewis, director) and Southwest Research and Information Center (C. Shuey)



<p>DiNEH Project (RO1) (2001 – 2012)</p>	<p>First research to examine community impacts on health in partnership with and at request of 20 chapters in and adjacent to Eastern Agency of Navajo Nation (NIEHS)</p>
<p>NBCS & NBCS/ECHO (2010 – ongoing)</p>	<p>Responsive to congressional mandate to community concerns from DiNEH Project: “What is exposure doing to the health of future generations?” (CDC, NIH-OD)</p>
<p>Center for Native Environmental Health Research Equity (2015 – ongoing)</p>	<p>Comparative community partnered study with Navajo, Sioux, and Apsaloóke to examine ecosystem and health effects in tribes from distinct language groups and cultures impacted by mine waste, combined effects of microplastics and organic emissions from waste combustion. (NIEHS, USEPA, NIMHD)</p>
<p>UNM METALS Superfund Research and Training Center (2017-2022, 2022-2027)</p>	<p>Multidisciplinary and transdisciplinary team science research partnership with Navajo and Pueblo communities to examine environmental and health risks from mine waste to communities and design interventions to reduce and reverse impacts (NIEHS)</p>

Community questions about exposures have driven UNM environmental health research



DiNEH Project, 2002-2012

- Does U in drinking water increase risk of kidney disease?
- Do multi-pathway exposures to metals in mine wastes increase risks of chronic disease?
- **Population:** 1,304 in 20 chapters; 267 in biomonitoring

Navajo Birth Cohort Study, 2010-present

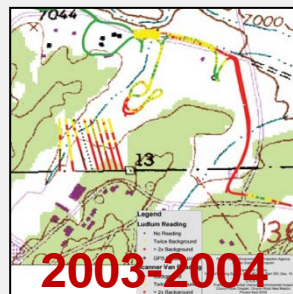
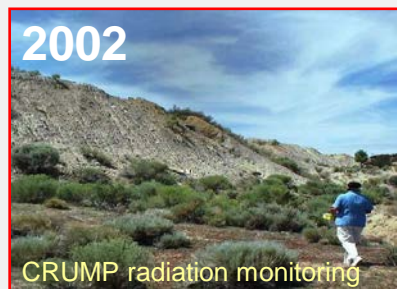
- Do exposures to U mine waste affect child health, development?
- Do exposures to metals in mine wastes increase chronic disease?
- **Population:** >1,000 families totaling ~1,800 mothers, fathers, children; ongoing

METALS SRP, 2014-present

- Do mixed-metal U mine wastes contribute to air, water and farmland contamination?
- Do exposures to U wastes result in immunologic, cardiovascular, pulmonary effects?
- **Populations:** Diné, Laguna across four communities

How have impacted tribal communities participated in EH research?

Red Water Pond Road residents played active role in CRUMP (2002-'07), DiNEH Project (2006-2007) and EPA removal actions (2007-'12)



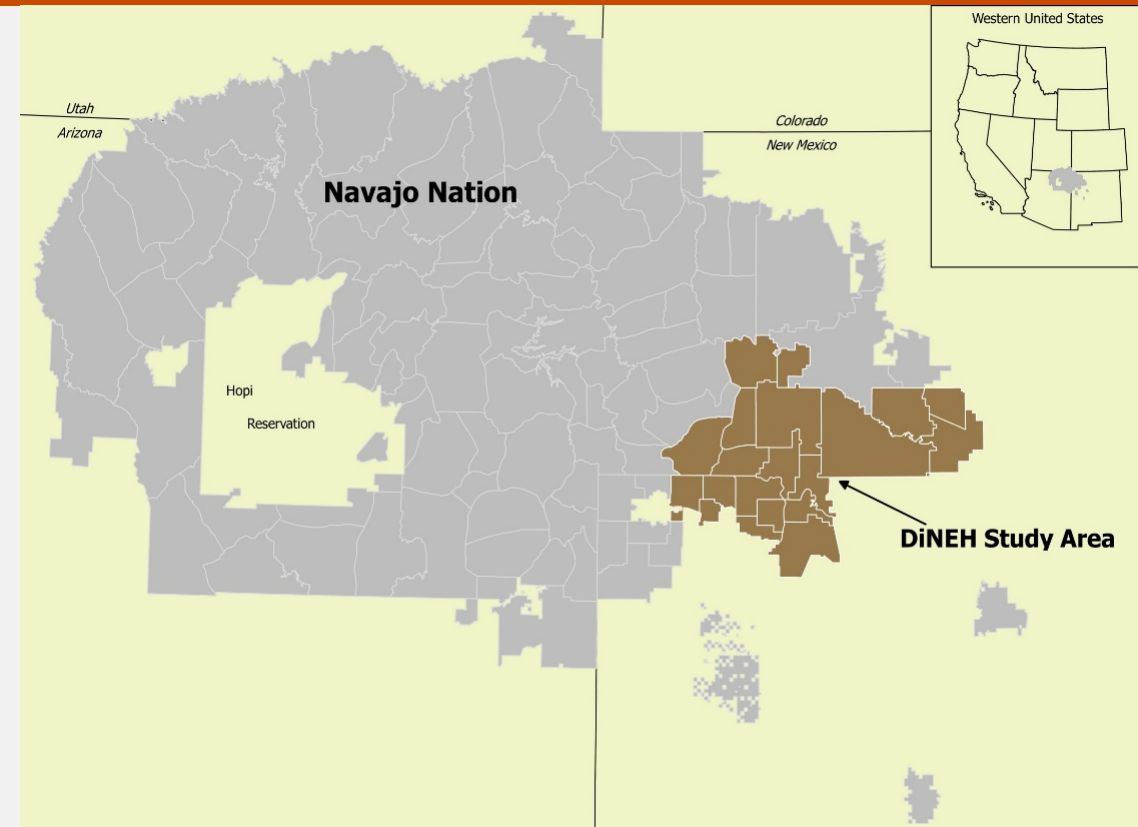
RWPRC residents helped measure gamma radiation rates and collect soil samples around homes next to the Northeast Church Rock Mine, leading to a USEPA-mandated RSE in 2006-2007 and three removal actions (below).



Three USEPA-ordered “interim removal actions” removed 18” to 25’ of radium- and uranium-contaminated soils (~136,000 cy) from around homes, mine-water arroyo. Residents were “relocated” to hotels in Gallup for 3 to 7 months each time. 8

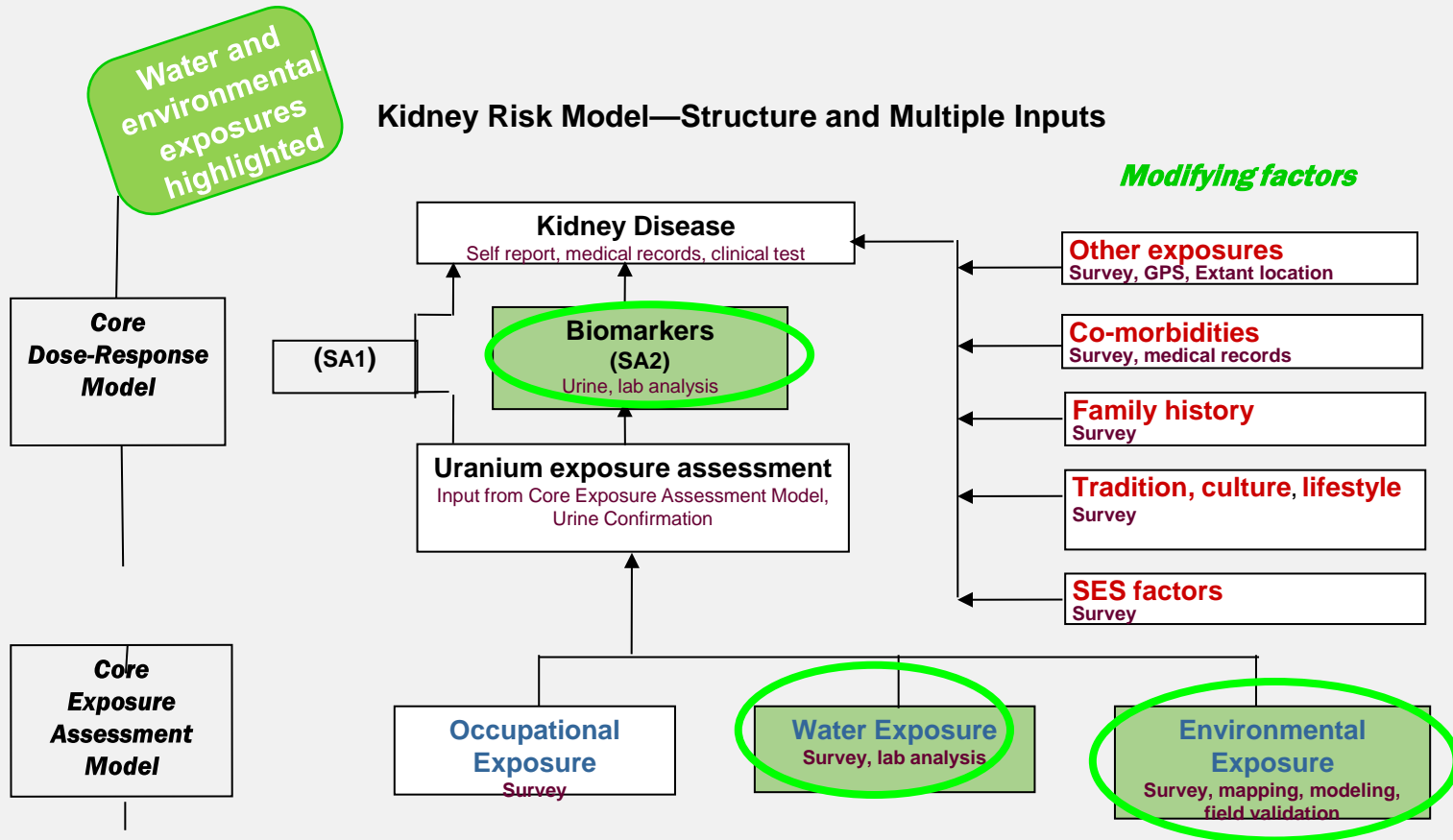
Diné Network for Environmental Health (DiNEH) Project: Documenting exposures to legacy uranium mining wastes on the Navajo Nation

Esther Erdei, Ph.D.



DiNEH Project Risk Model

Sources of inputs to estimate each participant's total exposure

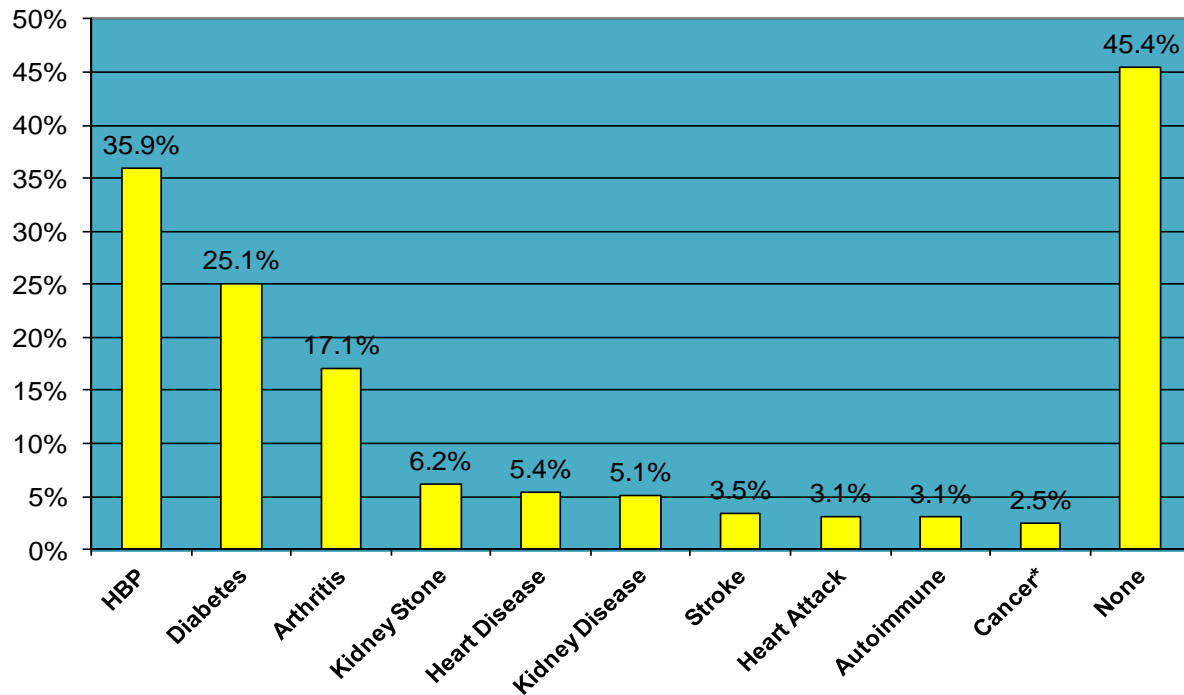




DiNEH Survey Responses – Phase I

Prevalence of Self-Reported Health Conditions Among 1,304 DiNEH Survey Participants

(*Cancer prevalence based on 1,011 participants surveyed)



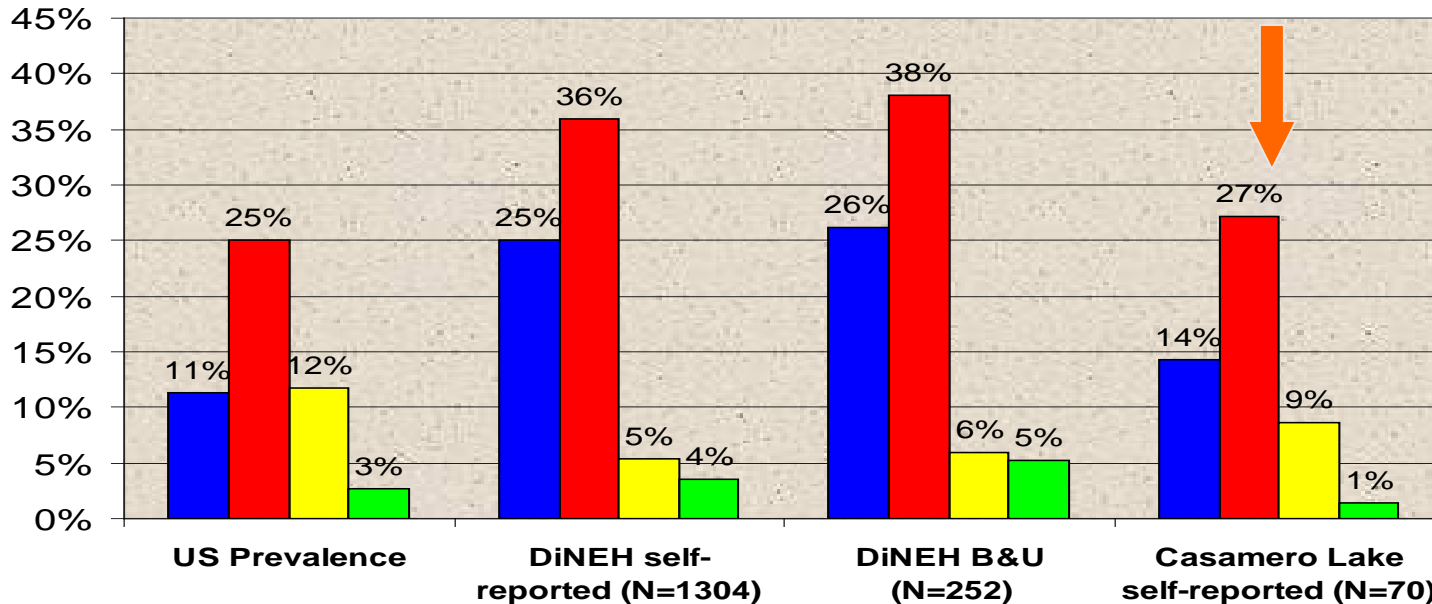
- High prevalence of cardiovascular disease and diabetes in DiNEH participants
- Do chronic exposures to U mine wastes exacerbate existing disparities in metabolic diseases?



DINEH Survey Results for Casamero Lake Chapter: Health Problems



**Prevalence* of Self-reported Health Problems,
Casamero Lake Chapter Participants Compared with
Rates for U.S., All DiNEH Participants, and
DiNEH Blood and Urine Participants**



For further comparison: Navajo diabetes prevalence, 1991-1993 = 22% (all ages), 40% (≥ 40 yrs) (Navajo Nutrition Study, 1997).

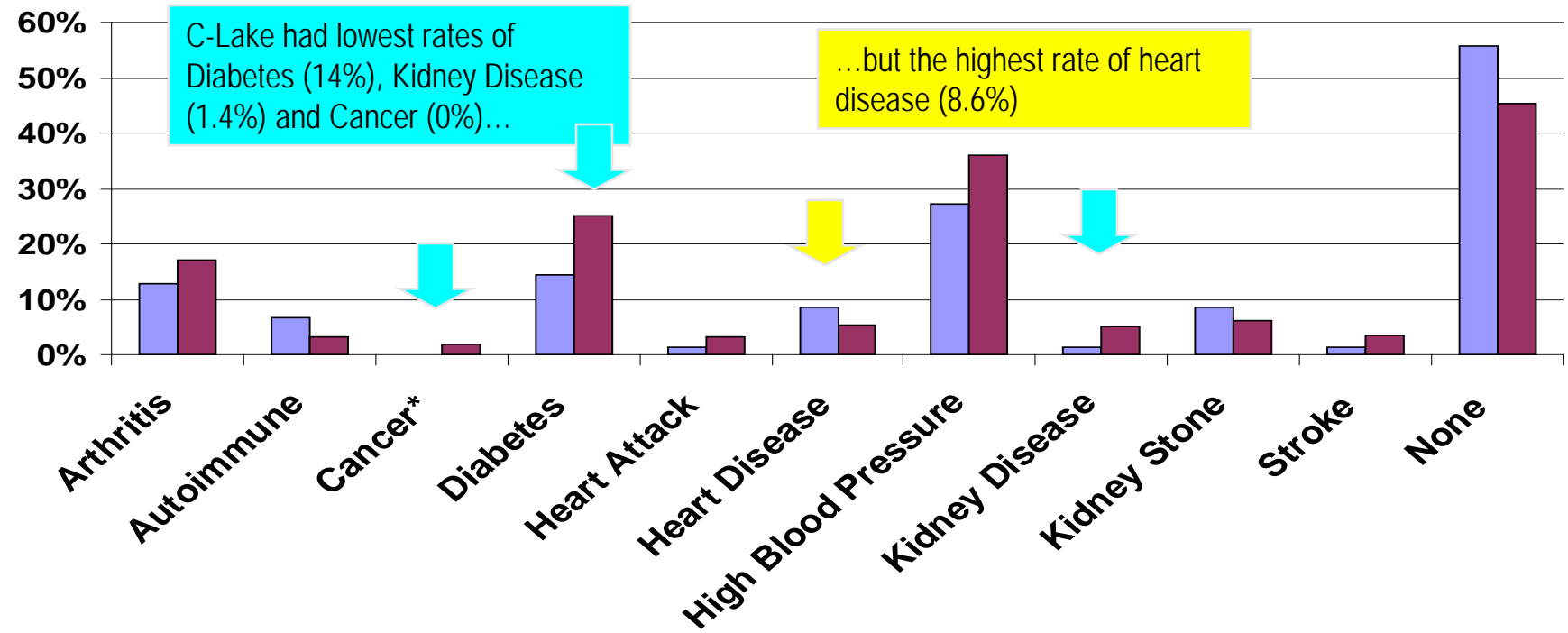
- Diabetes II
- Hypertension
- Heart Disease
- Stroke

*Prevalence = percentage of the population having a particular disease or condition at any given time



All Health Problems Reported by Casamero Lake Residents v. All Chapters

Casamero Lake All Chapters



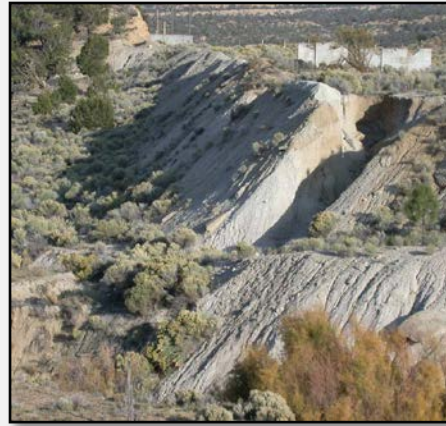
C-Lake had lowest rates of Diabetes (14%), Kidney Disease (1.4%) and Cancer (0%)...

...but the highest rate of heart disease (8.6%)

Goal of the DiNEH Phase II sub-study



- Direct response to community members' requests for research on immune system function during the capacity building and environmental risk evaluation work
- Address possible pathways within the human body in association with environmental uranium and other heavy metal (V, Pb, Hg, Ni, Cu, and As) exposures
- Find early indicators of health effects from legacy exposures



DiNEH Project Phase II

Biological sample collection



- Samples collected from 267 individuals, evenly distributed across 20 chapters (chart)
- 14 community-based collection events
- IHS collaboration through CUE-JTH Program
- Early markers, showing alterations in immune cell distribution and activity
- Biomonitoring to determine urinary metals/metalloids – U, total As, Ni, Cu, V



Chapter	# DiNEH Survey Participants (1,304)	# DiNEH Participants in B&U Collections (267)
Baca-Prewitt	96	32
Becenti	60	22
Casamero Lake	70	14
Church Rock	69	13
Coyote Canyon	65	18
Crownpoint	71	20
Iyanbito	61	17
Lake Valley	61	9
Littlewater	65	11
Mariano Lake	69	19
Nahodishgish	60	15
Ojo Encino	65	2
Pinedale	64	5
Pueblo Pintado	65	9
Smith Lake	69	19
Standing Rock	72	17
Thoreau	66	18
Torreon	67	0
White Rock	26	1
Whitehorse Lake	63	6



DINEH PROJECT RESULTS (AVERAGE AGE 55)

**ACTIVE-MINING ERA EXPOSURES
(WORKERS* AND FAMILIES) →
INCREASED KIDNEY DISEASE,
ADD TO OTHER KNOWN RISKS**

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



**ONGOING ENVIRONMENTAL LEGACY
EXPOSURES → INCREASED RISK
FOR HYPERTENSION, AUTOIMMUNITY,
AND MULTIPLE CHRONIC DISEASES**

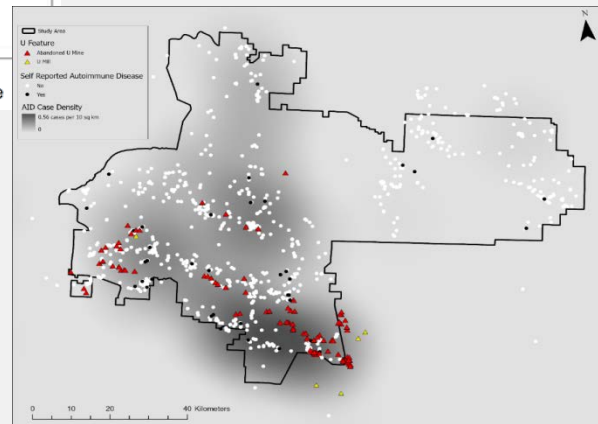
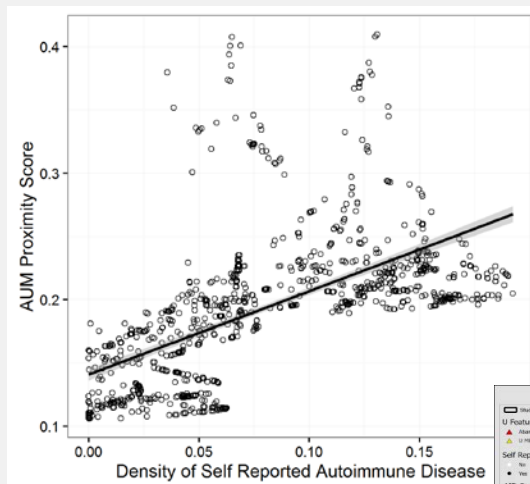
Based on proximity to waste and self-reported activities
creating contact with waste
Autoimmunity also linked to uranium in drinking water

Hund et al., 2015, Journal of Royal Statistical Society, Series A, Statistics in Society
Erdei et al., 2019, Journal of Autoimmunity

Evidence of immune dysregulation in Diné adults – uranium associated increase in autoantibodies



- Self-reported autoimmune disease diagnosis -- associated with proximity to AUM (n=1,304).
- Prevalence = 3.1% in both phases, lower than published national rates (3.0%-7.5%)
- Aggregation of AID cases – increased in Chapter with abandoned U mines/milling sites (map)



Autoantibody production and detection

- 239 samples analyzed at IHS LabCorp in Phoenix, AZ
 - (CLIA certified clinical diagnostic laboratory)
- Antinuclear antibody (ANA) testing using flow cytometry-based microbead assay
- Fluorescence staining and microscopy (traditional method; figure, top right) vs. new faster technique by IHS LabCorp
- Microbeads – special panel of autoantigens tested; positive response to specific autoantibodies may indicate connective tissue disease, Sjögren's syndrome, all clinically relevant.
- ~27.2% of individuals (n=239; average age 55 ± 14 yrs) had detectable anti-nuclear antibodies
- ANA positivity associated with proximity to waste sites, certain metals in drinking water

