Navajo Birth Cohort Study initiated in 2010 to address the impacts of uranium exposure on child health outcomes

Birth Outcomes, Child Development

- **Home Environmental Assessment**
  - **Locations of nearly 600 homes**
  - **Indoor dust**
  - Radon
  - Gamma survey indoors and outdoors
  - **Drinking water**
- **Enrollment Survey**
  - Occupational history
  - Activity Survey
  - Family history of exposures
- **Biomonitoring (mom, baby)**
  - **Urine metals (36-element panel)**
  - **Whole blood (Pb, Cd, total Hg)**
  - **Serum (Cu, Se, Zn)**

Sample Collection Timepoints

	Blood	Urine
Mother	▪ Enrollment ▪ Delivery	▪ Enrollment ▪ Delivery
Father	▪ Enrollment	▪ Enrollment
Baby	▪ Birth (cord blood) ▪ 2-6 months ▪ 12 months	▪ Birth ▪ 2-6 months ▪ 12 months

NBCS → NBCS/ECHO

NBCS
Navajo
Birth Cohort Study

NBCS (2010-2018)

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

Enrolled 780 women during pregnancy, exposure assessment, assessment of child development through 1 year of age

NBCS/ECHO

Enrolled 481 (179 pregnant mothers and 302 children from NBCS

NBCS-ECHO Plus – 2019-2024

- Continue enrollment to 1200 (316 children and 20 new pregnant mothers)
- Add common elements developed by ECHO consortium (allows us to compare exposures/outcomes with national sample
- Assessment continues through the age of 9

ECHO (Environmental influences on Child Health Outcomes

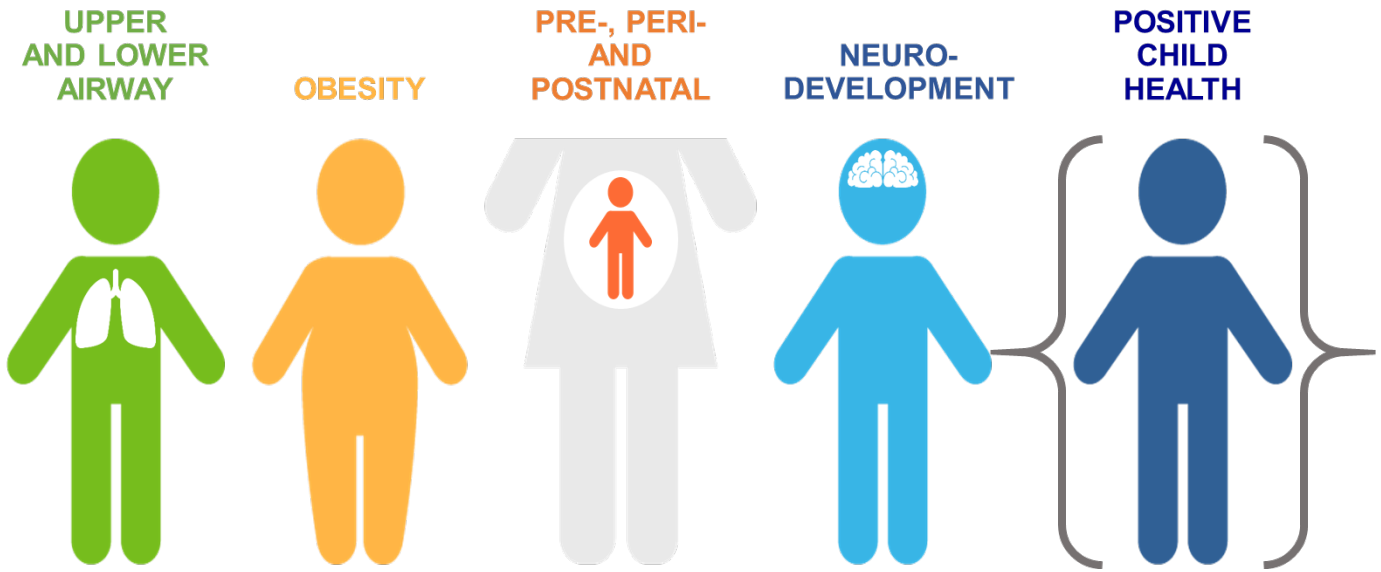
MISSION:
To enhance the health of children for generations to come

VISION:
To become one of our nation's pre-eminent research programs in child health

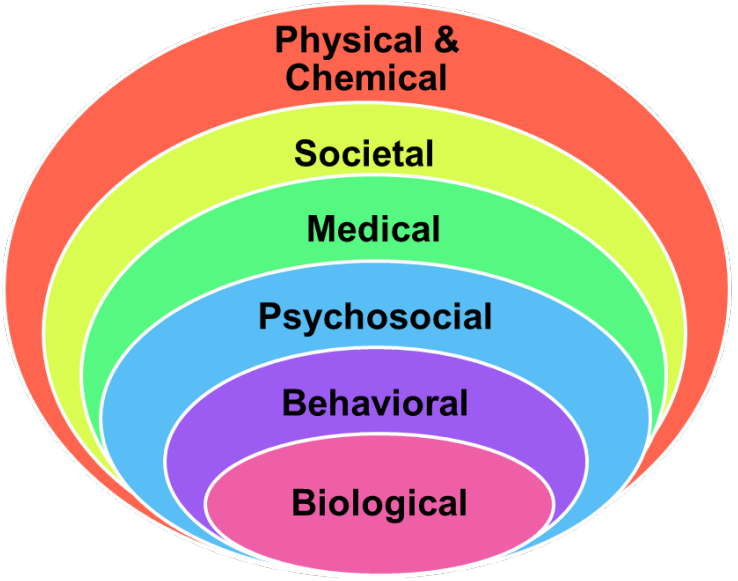
LONG-TERM GOALS:
Scientific: To inform high-impact programs, policies, and practices that improve child health

Strategic: To establish best practices for how to conduct Team Science in the 21st century

Focus on key pediatric outcomes



Data Collection



Pregnancy
- Surveys and questionnaires
- Blood and urine for metals

At delivery:
- Collect blood and urine for metals

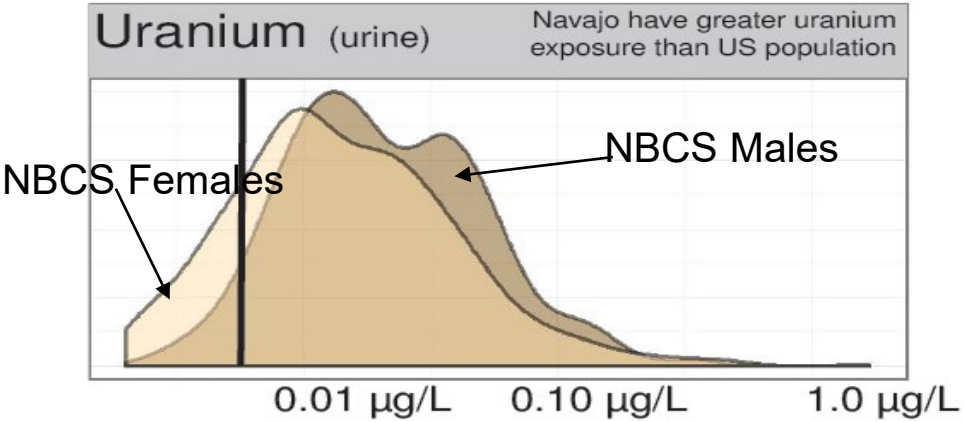
From birth through 8 years of age:
- Collect data from surveys and questionnaires
- Collect blood and urine every year
- Annual ASQ assessment
- Between the ages of 3-5 and again between the ages of 6-8 we conduct physical and neurodevelopmental assessments.

Art by Mallery Quetawki

Exposures seen from biomonitoring of key metals

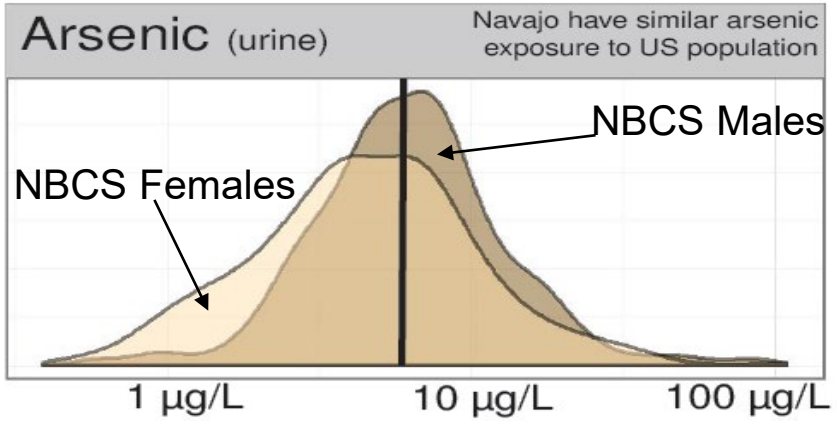
Uranium (kidney toxicity; estrogen mimicker)

- Black vertical line represents the 50th percentile for US population
- NBCS median urinary uranium concentrations exceed the US median (36% of men and 26% of women have urine uranium above national norms



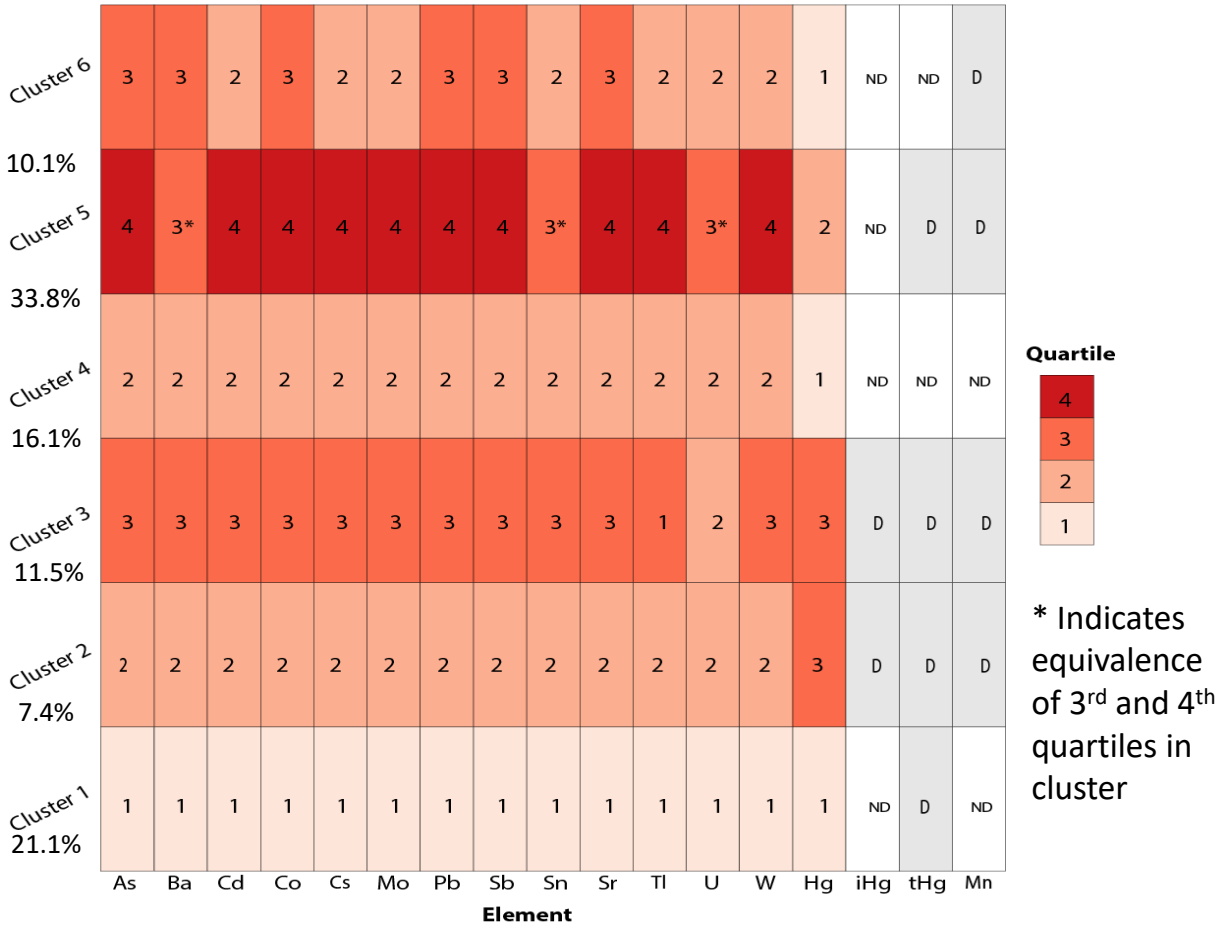
Arsenic (cancer, immunotoxicity)

- Distribution of urine total arsenic in NBCS females and males
- NBCS median urinary total arsenic concentrations are similar to the US median
- Exposure sources very different – in US, population exposures primarily seafood, rice



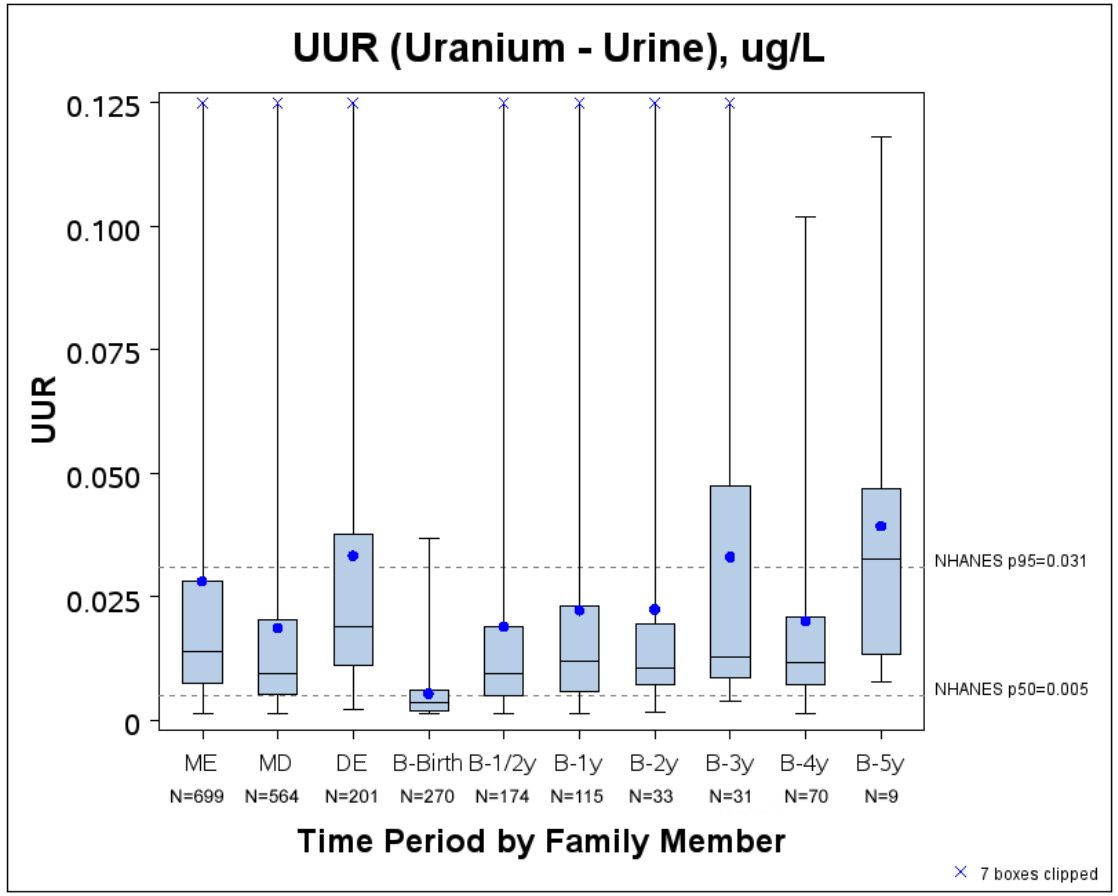
Exposures reflect patterns of mixtures

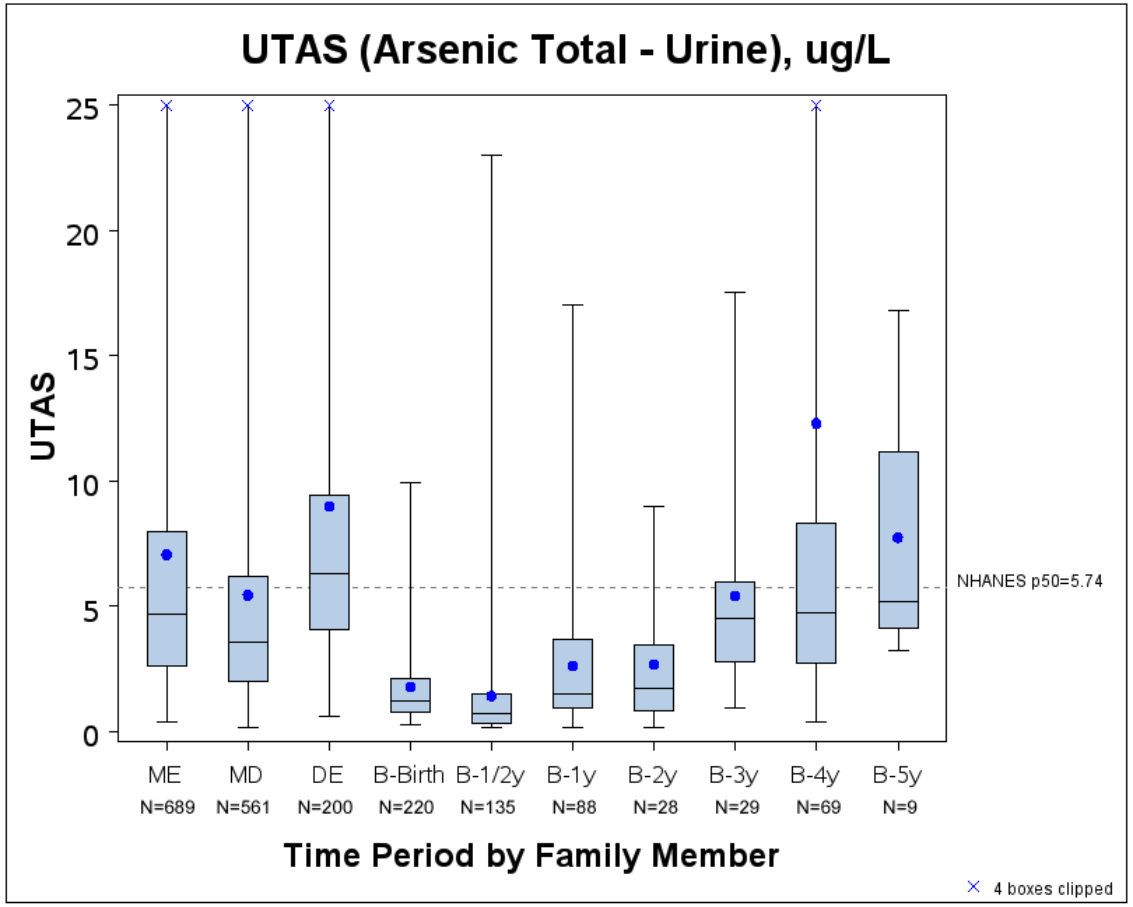
- More than 20% of moms have low exposures
- Overall rate of preterm birth in cohort 7%
- ~45% have mixture exposures that create a 3-fold greater risk of preterm birth (clusters 5 & 6)
- Mercury modulates the risk downward



Summary of mean posterior probability from the fully adjusted model and relative risk of preterm birth by exposure cluster					
Exposure Cluster	**Group Size (N)**	**Empirical Probability**	**Mean Posterior Probability (95% CI)**	**Relative Risk (95% CI)**	**Probability EC_i>EC1**
1	88	0.034	0.045 (0.018-0.081)	*Reference Group*	*Reference Group*
2	31	0.032	0.049 (0.012-0.109)	1.362 (0.25-3.638)	50.46
3	48	0.042	0.059 (0.023-0.108)	1.647 (0.44-3.936)	65.97
4	67	0.090	0.093 (0.049-0.148)	2.587 (0.9-5.678)	92.57
5	141	0.092	0.097 (0.065-0.134)	2.706 (1.059-5.768)	96.26
6	42	0.119	0.117 (0.058-0.19)	3.295 (1.046-7.437)	95.74
*Posterior probability >0.95 that EC is above 1 compared to reference cluster (EC2).					

NBCS/ECHO: Exposures begin in childhood
By age 4, children are reaching adult concentrations





- 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

Detailed Neurodevelopmental Assessments (between ages of 3-5 and again at 7-8)

Domain	Measure
Cognitive	DAS-II
Language	OWLS-2
Adaptive skills	Vineland
Social-Emotional	CBCL, SRS-2 (questionnaires)
Behavioral Observation	TOF, CARS-2
Medical	Medical and Developmental History, Physical Exam
Social cognitive functioning	Eye tracking measure

ND Assessment Summary

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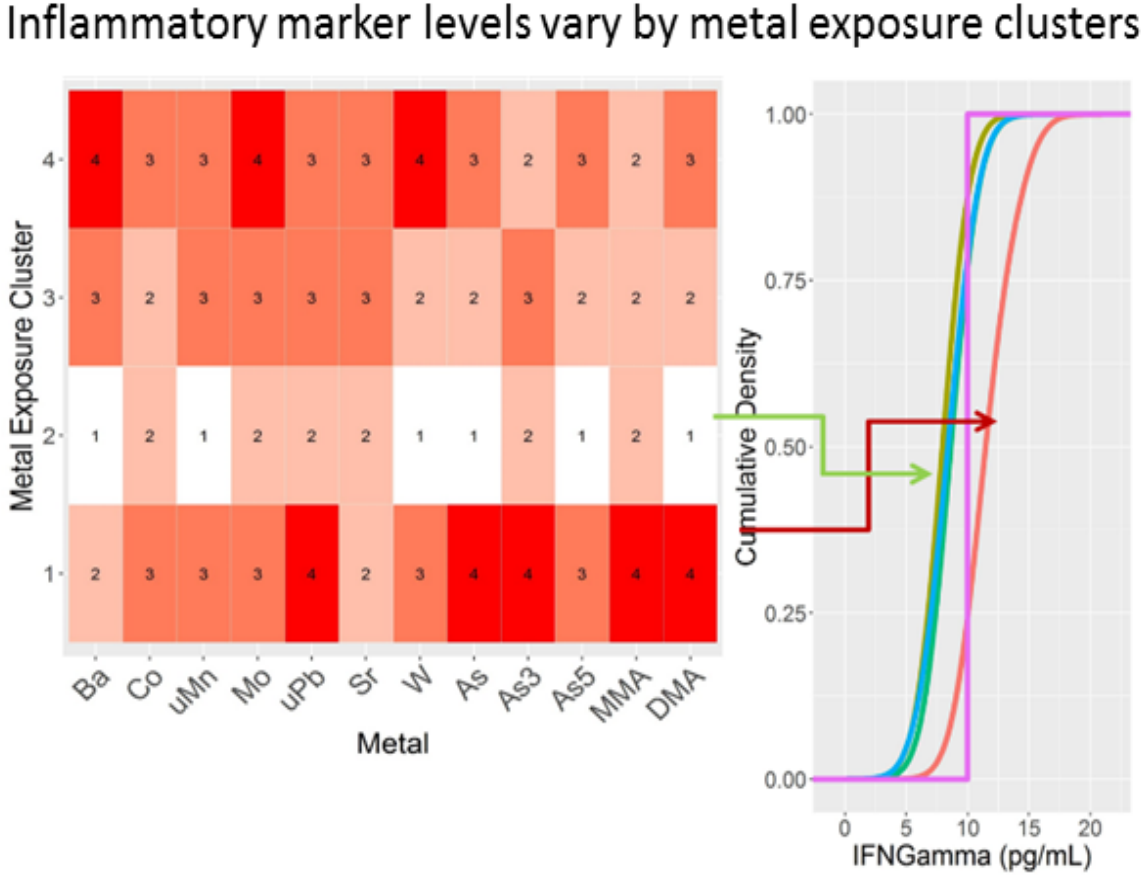
- Navajo preschoolers performed within the average ranges across multiple direct assessments and parent-report measures, except on the verbal domains across both modalities.

- High prevalence of language disorder independent of intellectual disability, general developmental delay, and autism spectrum disorder (validity of test instrument?, other reasons?)

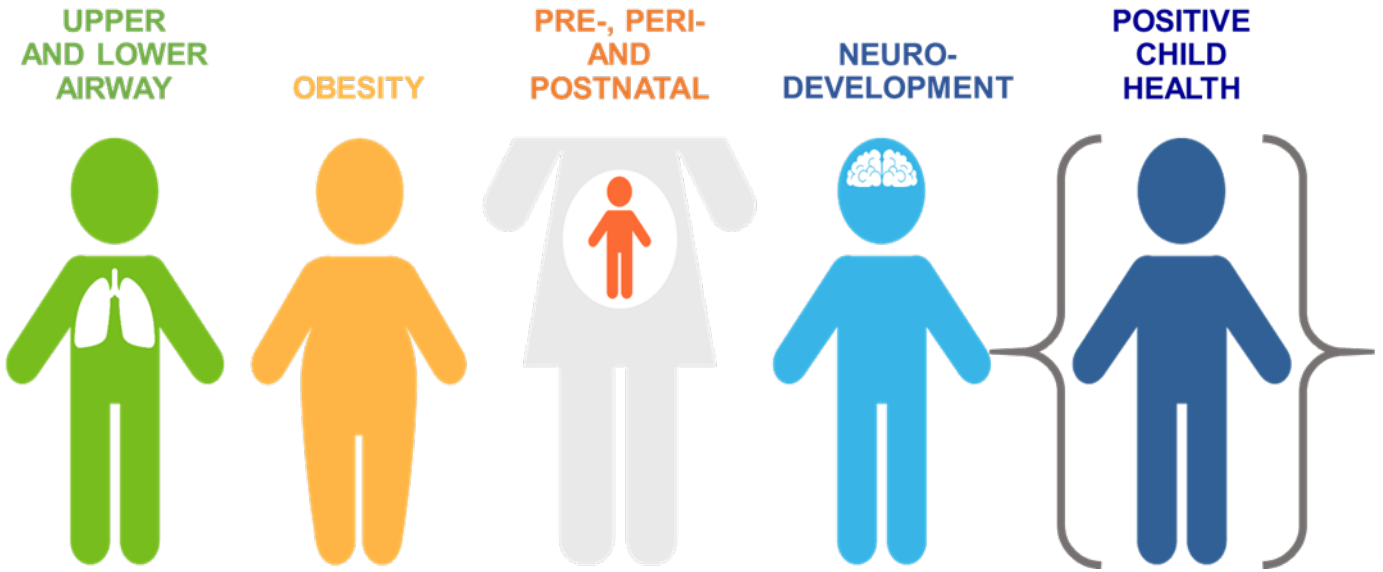
Associations between metal exposures and inflammatory responses in NBCS Mothers

- Maternal inflammation has been associated with increased risk of having a child with a neurodevelopmental disorder
- Biomarkers of inflammation are associated with chronic health conditions including cardiovascular disease, cancer, diabetes, chronic kidney disease and autoimmune disorders



Continuation of study……

- Assess the relationship between exposures and ND and other health outcomes.
- Compare NBCS to national sample to increase understanding of the influence of early life environmental exposures on health trajectory of Navajo children.



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NBCS-ECHO Flow Chart - basis for discussing most appropriate interactions for NBCS-ECHO

Recruitment
- In hospital Ob/Gyn waiting room
- Literature in Peds clinics
- Currently done by UNM or SRIC staff &/or NNDOH CHER

Enrollment
- Verification of pregnancy and notification of enrollment- NBCS-ECHO staff
- Consent & HiPAA – requires a private space (partitioned, office or conference room); done by UNM,NNDOH & SRIC staffs

Biological Sample Collection (Enrollment)
- Blood and urine collected in lab (or in home by NBCS staff) and processed by hospital lab staff trained by UNM

Biological Sample Collection (36 wk/ Delivery)
- Mom urine during 36 week visit to avoid blood contamination
- Mom blood at admission to L&D
- Cord blood and meconium during delivery by L&D staff

Infant Biospecimen Collection
- 2-6 months well-baby visit- NBCS blood and urine in peds or lab trained by UNM staff
- 12 mo urine and blood – peds or lab trained by UNM staff
- If collected during home visit, NBCS-ECHO staff coordinates with lab for processing

Medical Records Abstraction
- Performed by NBCS staff for Mother during pregnancy
- Mother at delivery
- Baby through 8th year

Annual child collections in ECHO (age 2-8)
- Surveys done in clinic or at home by UNM, SRIC and/or NNDOH staff
- Lab samples collected in peds or in lab
- If specimens collected during home visit, NBCS-ECHO staff coordinates with lab for processing

Note:
- All sample collection and processing done by lab staff occurred with intensive UNM training/certification.
- Currently there are 4 developmental assessments, often done by UNM or SRIC staff will conduct all in NBCS-ECHO, either in our space, pediatrics, or home
- UNM/SRIC/NNDOH staff will include phlebotomists and be trained to collect urine samples in home as well.
- NBCS-ECHO staff will also be trained in sample processing
- NBCS-ECHO staff will also be trained in med record abstraction
- **Neurodevelopmental Assessments (age 3-5 and 7-8), completed by UNM and UCSF clinicians. These assessments are completed for several participants over a 2-3 day visit where the clinicians can utilize our office space, an available conference room or exam room and the NNDOH CHR office.**