

Assessment of Differential Uranium Exposure and its Association with Hypertension and Elevated Blood Pressure in American Indian Communities in the Strong Heart Family Study

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Research Question: Is uranium exposure associated with increased blood pressure and incident hypertension in American Indian communities in the Strong Heart Family Study?

BACKGROUND

Cardiovascular disease is the leading cause of death among American Indians (AI) and hypertension (HTN) is an important risk factor for cardiovascular disease. AI populations in the Strong Heart Study have also been found to have increased levels of urinary uranium (U) compared to the general U.S. population.¹ This is likely due to elevated levels of U in groundwater and drinking water, which is exacerbated by a long history of U mining on tribal land, lack of access to regulated water sources,² and fertilizer usage.³ Other metals have been shown to be associated with elevated blood pressure (BP) and HTN incidence,^{4,5} and U has several toxic health effects such as nephrotoxicity. Little is known about the effects of U on HTN and BP, especially within AI communities who face a large burden of both.



Strong Heart Study

The largest epidemiologic study of cardiovascular disease in American Indians



The Strong Heart Study (SHS) is a community-based participatory cohort study investigating cardiovascular disease in AIs in participating tribes in Arizona, Oklahoma, and North and South Dakota. The Strong Heart Family Study (SHFS) is an ancillary study assessing gene-environment interactions for incident diabetes.

Study Design

Phase 3, Baseline - pilot study (1998-1999): Urinary U, baseline BP, and confounder data collected

Phase 4, Baseline - full study (2001-2003): Urinary U, baseline BP, and confounder data collected

Phase 5, Follow-Up (2006-2009): Blood pressure data collected

TABLES AND FIGURES

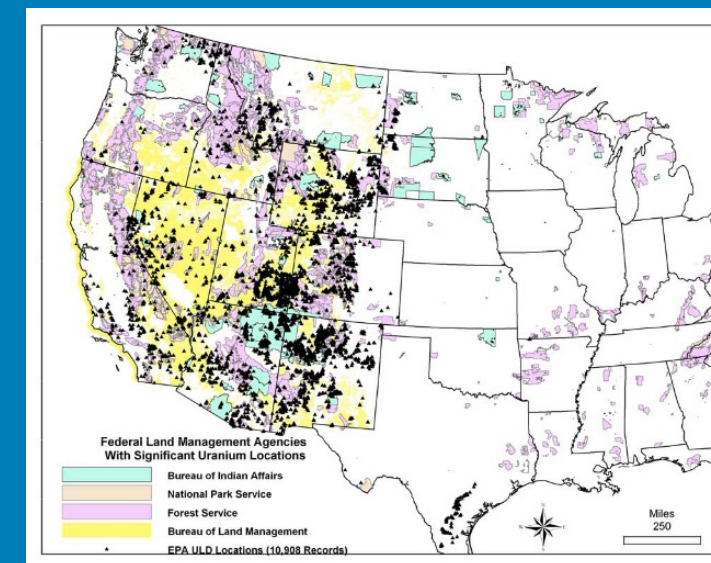


Figure 1. Uranium locations.⁶

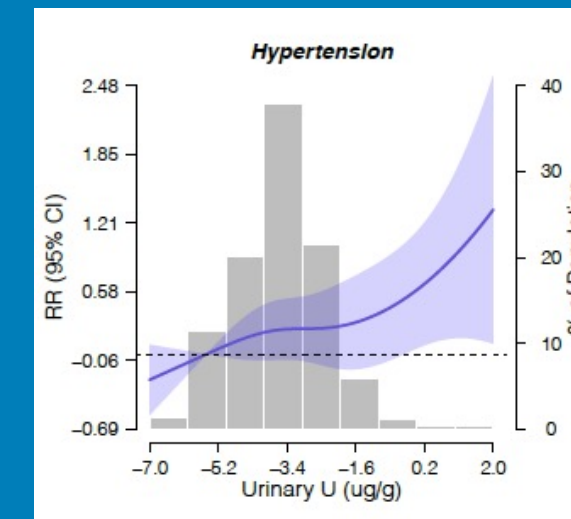


Figure 2. Relative risk of hypertension per log urinary U (ug/g creatinine). Solid line = relative risk; shaded area = 95% CI. RR was calculated using restricted cubic splines for U with knots at the 10th, 50th, and 90th percentiles.

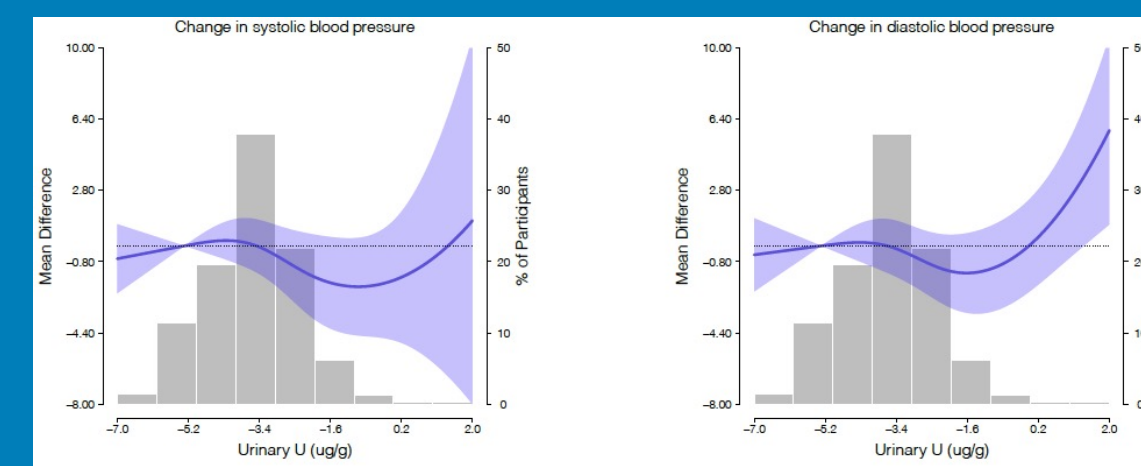


Figure 3. Mean difference in systolic and diastolic BP per log urinary U (ug/g creatinine). Solid lines = relative risk; shaded area = 95% CI. RR was calculated using restricted cubic splines for U with knots at the 10th, 50th, and 90th percentiles.

Table 1. Risk ratios (95% confidence intervals) for incident hypertension at follow-up.

Uranium Quartiles (cases/non cases)	Model 1		Model 2		Model 3	
	RR	95% CI	RR	95% CI	RR	95% CI
1 (52/312)	1.00	Referent	1.00	Referent	1.00	Referent
2 (66/298)	1.26	0.93, 1.71	1.28	0.94, 1.73	1.30	0.96, 1.78
3 (66/298)	1.26	0.91, 1.74	1.28	0.93, 1.77	1.32	0.95, 1.83
4 (69/295)	1.33	0.96, 1.85	1.38	0.99, 1.91	1.44	1.04, 1.99
IQR (253/1203)	1.11	0.96, 1.28	1.13	0.97, 1.31	1.14	0.99, 1.33

Table 2. Change in systolic blood pressure between baseline and follow-up.

Log Uranium	Model 1		Model 2		Model 3	
	β	95% CI	β	95% CI	β	95% CI
Log Uranium	-0.52	-1.06, 0.01	-0.54	-1.08, -0.00	-0.37	-0.91, 0.16
Uranium Quartiles						
1	1.00	Referent	1.00	Referent	1.00	Referent
2	0.02	-1.76, 1.80	0.02	-1.78, 1.81	0.18	-1.62, 1.98
3	-0.29	-2.01, 1.43	-0.33	-2.05, 1.38	-0.02	-1.80, 1.76
4	-1.97	-3.81, -0.13	-2.02	-3.86, -0.18	-1.49	-3.34, 0.35
IQR	-0.02	-0.05, 0.00	-0.02	-0.05, -0.00	-0.02	-0.04, 0.01

METHODS

The study population included 1456 participants from the SHFS who did not have diabetes or hypertension at baseline, and who had complete data for BP, urinary U (ug/g creatinine), and relevant confounders. HTN was defined as systolic BP \geq 140 mmHg, diastolic BP \geq 90 mmHg, or taking HTN medication. We used generalized estimating equations with independence correlation structure conditional on family membership to estimate the association of U exposure with systolic BP and diastolic BP using linear regressions, and HTN incidence using Poisson regression with robust variance. Model 1 adjusted for age, sex, study center, and smoking status. Model 2 further adjusted for GFR, pre-diabetes status, and BMI. Model 3 further adjusted for log-adjusted arsenic and cadmium.

- U is associated with increased risk of hypertension.
- U is associated with a decrease in systolic BP and has no statistically significant effect on diastolic BP.

DISCUSSION

There was an increased relative risk of incident hypertension comparing the highest to lowest urinary U quartiles. Systolic BP decreased at follow-up comparing the highest to lowest urinary U quartiles, but this association was attenuated when other metals were added into the model. These findings suggest a moderate increased risk for hypertension at chronic levels of uranium exposure typical of the Southwest and Great Plains in the US. This association of urinary U with hypertension is inconsistent with the decreased systolic BP levels at follow-up. Additional research is needed to disentangle these inconsistencies.

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