

Association Between Urinary Biomarkers & Volatile Toxicants and Disability: NHANES 2013–2018 Analysis

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Introduction

Environmental toxicants heavy metals and volatile organic compounds (VOCs) are increasingly recognized as contributors to neurological dysfunction and disability. Cadmium, thiocyanate (a smoking/cyanide biomarker), manganese, and VOC metabolites are pervasive in the U.S. population, yet their combined and non-linear influence on functional disability remains poorly characterized in nationally representative data.

Objective

To quantify associations between urinary biomarkers of environmental toxicant exposure and disability in U.S. adults using 2013–2018 NHANES data identifying key predictors, evaluating non-linear dose-response relationships, comparing machine learning with survey-weighted regression, and assessing interaction effects between co-occurring toxicants.

Methods

Data Source: NHANES 2013–2018 cycles; N = 26,150 adults with complete urinary biomarker and disability questionnaire data

Outcome: Disability = self-reported difficulty in ≥ 1 functional domain (mobility, cognition, vision, hearing, self-care, or communication)

Exposures: Urinary metals, metalloids, and VOC metabolites, creatinine-adjusted and log-transformed to correct right-skew

Statistical Models: Survey-weighted multivariable logistic regression (accounting for NHANES complex sampling design) and Random Forest classification

Dose-Response: Restricted cubic splines to test for non-linearity across the exposure range

Interaction: Relative Excess Risk due to Interaction (RERI) to quantify supra-additive effects between co-exposures

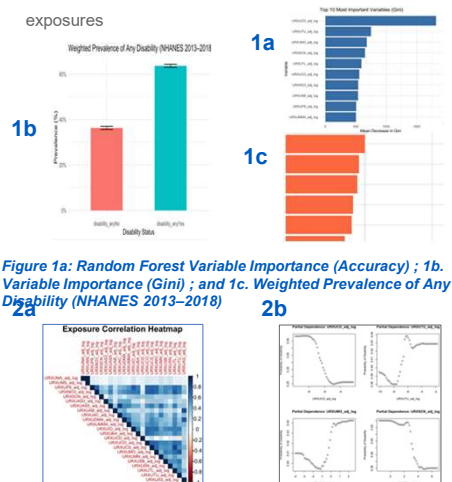


Figure 1a: Random Forest Variable Importance (Accuracy); 1b. Variable Importance (Gini); and 1c. Weighted Prevalence of Any Disability (NHANES 2013–2018)

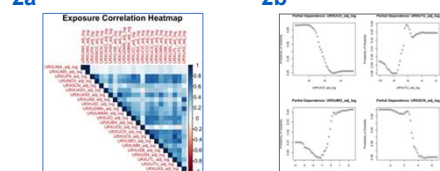


Figure 2a: Correlation matrix of log-transformed urinary biomarkers. Figure 2b: Partial dependence plots — isolated effects of cadmium, tungsten, molybdenum, and thiocyanate

3a



Figure 3a: Non-linear dose-response curves (restricted cubic splines) for thiocyanate and cadmium relative to the median exposure level (OR = 1).

3b



Figure 3b: Survey-weighted odds ratios (95% CI) for disability across urinary metal, metalloid, and VOC metabolite exposures.

Results

Model & Population Overview.

- 63% of the 26,150 NHANES 2013–2018 participants reported ≥ 1 functional limitation — mobility, cognition, vision, hearing, self-care, or communication (Figure 1c)
- Random Forest variable importance ranked urinary cadmium (URXUCD) as the dominant predictor of disability by both accuracy and Gini metrics, well ahead of any other biomarker (Figure 1a–b)
- Correlated biomarker clusters (arsenic species, VOC metabolites) were well tolerated by the Random Forest model; cadmium was comparatively independent of other exposures (Figure 2a)
- Partial dependence plots showed cadmium's conditional effect plateauing at high concentrations, while tungsten and molybdenum showed non-monotonic (U-shaped) patterns (Figure 2b)
- The Random Forest model achieved excellent discrimination (AUC = 0.798; Figure 4), correctly distinguishing disability status ~80% of the time

Dose-Response & Interaction Effects

- Cadmium showed a strong non-linear dose-response: risk accelerated sharply above the median, reaching OR = 28 at the 95th percentile vs. median consistent with a toxic threshold effect (Figure 3a)

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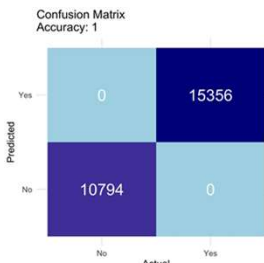


Figure 4: ROC curve for the Random Forest classification model (AUC = 0.798), indicating excellent discrimination between adults with and without disability.

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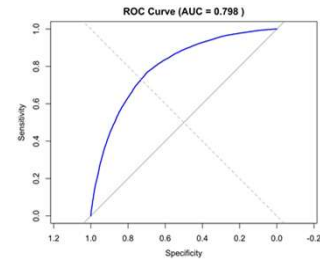
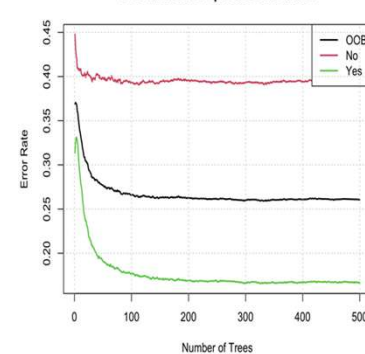


Figure 5: Confusion matrix for the Random Forest model on training data (accuracy = 1.0) — a perfect training fit that motivated out-of-bag validation (Figure 6).

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Figure 6: Out-of-bag (OOB) and class-specific error rates vs. number of trees. Error stabilizes well below the training-set perfect fit, confirming the model is not simply overfit.



Inferences

- Cadmium shows a threshold-type toxic effect: risk stays modest near the median but accelerates sharply beyond it, consistent with cadmium's known bioaccumulation, nephrotoxicity, and neurotoxicity. Smoking-linked thiocyanate independently raises disability risk (OR 1.25), reinforcing smoking as a modifiable driver separate from cadmium's contribution.
- Random Forest and survey-weighted regression converge on cadmium, thiocyanate, and manganese as top risk factors; where their dose-response patterns diverge at extreme concentrations, this likely reflects confounding by correlated co-exposures rather than a true protective effect, and is a target for multi-pollutant follow-up. Excellent model discrimination (AUC = 0.798) supports urinary biomarker panels as a feasible population-level screening tool.

Conclusion

- Multiple urinary biomarkers, especially cadmium, were associated with increased disability risk, supporting interventions to reduce environmental metal exposure and smoking.

References

- Dai L, Zhou Q, Gao Y, Su G, Jiang Q, Xia L, Yang P, Association of exposure to urinary and blood heavy metals with visual disability among U.S. adults in NHANES 2013–2018. *Front Public Health*. 2025;13:1583105.
- Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Cadmium*. U.S. Department of Health and Human Services; 2012.