COMIRB #26-1642
PI: Dr. Katherine James

Project Protocol: CLEAN W.A.T.E.R. (Community-Led Environmental Action for Neighborhood Water Accessibility, Treatment, and Equity Restoration) — Updated Participant Procedures

Version Date September 25, 2026
Principle Investigator: Katherine James, PhD, MS, MSPH

1. Background & Significance

1.1 Geological Vulnerability in the San Luis Valley (SLV)

The San Luis Valley (SLV) is a region of complex geological vulnerability, where bedrock and aquifer systems harbor significant concentrations of naturally occurring toxic metals, most notably arsenic and uranium[1]. This geochemical profile historically catalyzed extensive human mining activity, which in some instances resulted in profound environmental degradation. Legacy sites like the Summitville Mine serve as critical context for the remediation needs of the region[1]. Beyond arsenic and uranium, recent environmental surveillance identifies manganese and tungsten as contaminants of emerging concern within these groundwater systems, necessitating a comprehensive approach to exposure assessment[1].

1.2 The Regulatory Gap and Social Determinants

Rural residents in the SLV face a precarious "regulatory gap" due to their reliance on unregulated private wells[2]. Unlike municipal systems, these wells lack the oversight of the Safe Drinking Water Act, shifting the burden of monitoring and treatment onto individual households[2,3]. This vulnerability is exacerbated by social determinants of health unique to the SLV: geographic isolation, low population density, and limited access to healthcare and insurance[10]. The region's bi-ethnic population, characterized by a deep generational heritage, presents an elevated prevalence of type-2 diabetes and cardiovascular disease, conditions scientifically linked to chronic arsenic exposure[4,8,9,11]. Furthermore, the presence of manganese and tungsten is increasingly associated with cognitive function impairments and chronic kidney disease, creating a critical public health imperative for intervention[5,6,10,12].

1.3 Drought Exacerbation

Drought-driven stressors are actively intensifying toxic metal leaching and transport in the SLV through two primary mechanisms[13]:

- "Dark Snow" and Accelerated Runoff: Wildfires and increased particulate matter (PM) create "dark snow" events that lower albedo and accelerate snowmelt. This rapid melting drives snowmelt-induced flooding into abandoned mining infrastructure, such as the Nelson Tunnel EPA Superfund site, facilitating the transport of heavy metals directly into the local aquifer[13].
- Hydrological Stress: Prolonged drought and the subsequent over-pumping of groundwater cause significant drawdowns in the water table, which triggers the leaching of arsenic and other toxic metals from neighboring clay layers into the potable water supply[1].

1.4 Environmental health Framework

Utilizing the Colorado EnviroScreen tool, this project identifies exposure. Within the SLV, 41 of 41 census blocks are designated as rural and overlay precisely with areas of known metal contamination, signifying a convergence of social vulnerability and environmental risk[7].

2. Study Design & Methodology

2.1 Trial Architecture

The project evaluates household-level filtration interventions in mitigating external exposure in drinking water and, among participants who voluntarily provide urine samples, internal metal exposure. The intervention is implemented at the household level across two filtration pathways (under-sink or tabletop).

2.2 Participant Recruitment and Strategy

- Recruitment Strategy: The study leverages established rapport through the SLV Community Advisory Board (CAB). Community Navigators, hired locally, will lead recruitment to ensure cultural competency and trust. Local Community Navigators may use the following recruitment methods as needed:
    - Random selection of households in areas with known elevated arsenic or uranium from purchased address/email lists
    - Participants from Colorado Multiple Institutional Review Board (COMIRB)#21-3509 with previous water sample indicating elevated arsenic or uranium
    - Community-based in-person outreach
- Target Population: The project aims to enroll 100 for tabletop filtration and 80 for under-sink filters.

2.3 Eligibility

1. Inclusion Criteria: Participants must:
    1. Be 18 years old or older
    2. Reside year-round in the San Luis Valley
    3. Use Private well as their primary household water
    4. Reside within a targeted high-risk geographic area
    5. Meet arsenic and uranium contaminant thresholds
        1. Kitchen-Sink Filtration: Arsenic >20 parts per billion (ppb) or Uranium >30 ppb
        2. Tabletop Filtration: Arsenic = 5-20ppb or Uranium 10-30ppb
2. Exclusion Criteria:
    1. Households already using NSF-53 certified filtration designed to remove metals
    2. Households unwilling to participate in longitudinal follow-up
3. Potential participants will undergo a three-step triage process to ensure resources reach the highest-risk areas:
    1. Onboarding and Exposure Survey: Verification of household reliance on private wells as a primary water source and assessment of known exposure variables.
    2. Geographic Targeting: Verification of residence within high-metal zones identified via historical data and predictive GIS mapping.
    3. Baseline Sampling: Initial well water results must fall within the above-mentioned arsenic and uranium contaminant thresholds.

2.4 Filtration Intervention Tiers

Three intervention tiers are deployed based on specific households infrastructure and meeting of metals exposure thresholds:

- Under-Sink Filter (USF): Epic Smart Shield under-sink filtration, or another protocol-approved certified system, installed at the primary kitchen cold-water tap for potable water use.
    - For households receiving the under-sink filtration intervention, the study team will provide installation instructions and participant maintenance materials. The filters are Epic Water Filters NSF-53 certified.
- Commercial Filter Pitcher (CFP): Provided for households where infrastructure cannot support an under-sink system, participants who are renters, or arsenic or uranium levels are just below EPA maximum contaminant levels.
    - For households receiving pitcher filtration intervention, the study team will provide instructions and filter replacement materials. The filters are Waterdrop pitcher filters that are NSF-53 certified.

2.5 Laboratory Analysis and Biomonitoring

Water samples are collected before and after filtration according to the study sampling schedule and processed through the ASU-Westerhoff Laboratory or the currently designated study laboratory. Urine samples are used to evaluate urinary metal concentrations and selected kidney-related biomarkers specified in the laboratory analysis plan; urine testing is not intended to diagnose disease. Urine samples will be analyzed at University of Colorado laboratory.

Water Samples: Water samples will be collected from households participating in the water filter implementation science study based on the following protocol. At each sampling point, two water samples will be collected, one pre-filtration from the tap and one post filtration from the pitcher. Flushed tap water samples will be collected directly from the primary drinking water tap using pre-cleaned, acid-washed high-density polyethylene (HDPE) bottles. Post filtration samples will be collected directly from the picture using the same HDPE bottles. All sample bottles will be prelabeled for ease of the participant and stored in a plastic bag with drop off at the local public health department within 1 day. Public health offices will scan the bar code for direct entry into the online chain of custody form. Samples will be picked up by courier within 2 weeks and shipped to ASU-Westerhoff Laboratory direct (24 hours). Upon receipt, samples will be preserved with ultrapure nitric acid (trace metal grade) to a pH <2 and stored at 4°C until analysis. Concentrations of metals and trace elements will be quantified using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) following U.S. Environmental Protection Agency Method 200.8. Samples will be analyzed for target metals arsenic, uranium, zinc, and tungsten along with other metals other environmentally relevant metrics (manganese, iron, antimony, hardness). Calibration will be performed using multi-element standard solutions with internal standards to correct for matrix effects and instrument drift. Quality assurance and quality control procedures will include method blanks, laboratory control samples, duplicate analyses, matrix spikes, and certified reference materials. Instrument detection limits, recovery rates, and analytical precision will be evaluated throughout the study to ensure data accuracy and reliability.

Urine Samples: Urine samples will be collected from the main household participant using trace-metal-free polypropylene collection urine cups following standardized biospecimen collection protocols. Immediately after spot urine sample collection, parafilm will be seal the sample and placed in a biohazard bag. Samples will be dropped off at the local public health office within 6

hours and immediately frozen. Within 2 weeks the sample will be shipped to University of Colorado. Upon receipt the samples will be stored at −80°C until analysis. Prior to laboratory analysis, samples will be thawed, mixed thoroughly, and prepared using validated dilution and digestion procedures as appropriate for the target analytes. Urinary concentrations of metals (arsenic, tungsten, uranium, and zinc) along with other environmentally relevant metals, will be quantified using ICP-MS. Analysis will be conducted using collision/reaction cell technology to minimize polyatomic interferences and improve analytical sensitivity. Calibration curves will be generated using certified multi-element standards, and internal standards will be used to correct for matrix effects and instrument drift. Quality assurance and quality control procedures will include laboratory blanks, duplicate samples, matrix spikes, certified reference materials, and ongoing calibration verification standards. Urinary creatinine will be measured using Jaffe methods to account for urine dilution and to facilitate normalization of metal concentrations. Analytical performance will be evaluated through assessment of detection limits, precision, and recovery rates to ensure the accuracy and reliability of biomonitoring results. Kidney markers (Neutrophil gelatinase-associated lipocalin (NGAL), microalbumin, and Kidney injury molecule-1 (KIM1)) will be analyzed using immunoassays Enzyme-Linked Immunosorbent Assay (ELISA).

2.6 Participant Communication Plan

Participants may receive:

- Recruitment email or telephone outreach
- Monthly reminder emails for online survey
- Sample collection or navigator visit reminders (every other month)
- Compensations notifications
- Interim appreciation/gratitude messages
- Study closeout communications containing:
    - Preliminary findings
    - Filter maintenance information
    - Replacement information
    - Local resources

2.7 Participant Follow-Up and Sample Collection Schedule

- Baseline visit
    - Includes:
    - Demographics
    - Water perceptions
    - Drinking habits
    - Exposure information
- Monthly follow-up surveys
    - Filter use
    - Adoption
    - Implementation
    - Maintenance
    - Water consumption behaviors
- Months 2, 4, and 6
    - Water samples are dropped off at a designated local public health department by the participant or picked up by a trained Community Navigator, according to the study schedule.

    - Urine samples may be dropped off at a designated local public health department within 6 hours of collection or provided directly to a trained Community Navigator for coordinated pickup.
- Closeout assessment
    - All monthly measures
    - Satisfaction
    - Future use intentions
    - Barriers and facilitators

2.9 Urine Biospecimen Collection and Transport

Urine collection, packaging, temporary storage, and transfer will follow the participant-facing collection guide and laboratory processes. Participants will receive a sterile collection cup, label, specimen bag, and instructions. The procedure is: wash hands; collect approximately 10 milliliters without allowing the container to touch the skin; complete urination in the toilet; screw the lid on tightly; wrap Parafilm around the lid/cup seam; record participant ID, date, and time; place the sealed cup in a provided specimen bag; close the bag securely; store the bag in a cool place; and deliver the sample to a designated local public health department within 6 hours of collection or provide it to a Community Navigator for coordinated pickup.

2.8 Filter Maintenance, Replacement, and Used-Filter Return

For households receiving the Epic Smart Shield under-sink filter, the study team will provide a participant maintenance guide covering installation, filter replacement, troubleshooting, and safe return of used filters. The study-directed replacement interval is every 4 months unless the study team directs earlier replacement based on water-testing results, filter performance, flow, or other protocol-defined criteria.

Used filters must remain intact and must not be cut open, dismantled, washed, cleaned, or placed in household trash or recycling during the study. The study team will provide designated bags for used filters. Participants will place the intact used filter in the provided bag, seal it, store it in a safe location, and return it to an approved CLEAN WATER drop-off location or directly to the Community Navigator as instructed. The study team will document filter return/replacement and determine appropriate downstream handling or recycling. The used filter may be further analyzed by ASU-Westerhoff laboratory to determine contaminant load.

2.8 Biospecimen and Water Sample Tracking

The project is dedicated to maintaining data integrity and ethical specimen management. Chain-of-custody procedures apply to water samples, urine samples, and returned study filters as specified below.

- Participant ID assignment
- Barcode/sample labels
- Drop-off at designated local public health departments
    - Either by participant or hired local community navigator
- Courier transfer to the designated study laboratory
- Laboratory receipt and accessioning

Chain of custody documentation and electronic tracking are included in the tracking steps to ensure optimum sample and specimen management.

Participant-Facing Procedures Incorporated in This Protocol

Participant materials incorporated into this protocol include an Epic Smart Shield under-sink installation and maintenance guide, a study-directed filter replacement guide, a used-filter return procedure using study-provided bags and designated drop-off, and an English/Spanish urine collection guide. The urine guide instructs participants to collect approximately 10 milliliters, seal and label the cup, wrap Parafilm around the lid/cup seam, place the sealed sample in a provided specimen bag, store it in a cool place, and deliver it to a designated local public health department within 6 hours or provide it to a Community Navigator for coordinated pickup.

3. Statistical Analysis and Evaluation Framework

3.1 RE-AIM Framework Implementation

The CLEAN WATER project utilizes the Reach, Effectiveness, Adoption, Implementations, Maintenance (RE-AIM) framework to evaluate how effectively its scientific research is translated into active public health practice. The evaluation is structured across five core dimensions:

- **Reach:** Measured by the total number of households engaged, as well as community interaction with project webpages and educational downloads.
- **Effectiveness**: Assessed through quantitative changes in toxic metal concentrations in pre- and post-filtration water samples and, among voluntary urine participants, changes in urinary metal concentrations and specified kidney-related biomarkers; participant health knowledge may also be assessed.
- **Adoption:** Tracks the rate of filter implementation among eligible high-exposure households and the extent to which community-based organizations (CBOs) utilize project materials.
- **Implementation:** Monitors fidelity to the project model, specifically ensuring a high percentage of recipients reside within the 37 targeted census blocks.
- **Maintenance**: Focuses on continued filter use, completion of the study-directed 4-month replacement schedule or earlier replacement when indicated, appropriate troubleshooting, return of used filters, and qualitative feedback from the Community Advisory Board (CAB).

3.2 Success Metrics: Research 2 Action

Success is defined by the "Research 2 Action" framework, which focuses on the intentional translation of scientific research into immediate opportunities for community-led environmental intervention. Rather than solely documenting metal exposure, this approach utilizes the study's findings to directly remediate health risks by providing free, certified water filtration systems to households identified with elevated levels of arsenic, uranium, or lead. This framework is operationalized through the expertise of bilingual Community Navigators and the Community Advisory Board (CAB), ensuring that the research data is not only accessible but serves as a conduit for community momentum toward achieving health equity. By developing a sustainable implementation model and evaluating success through the RE-AIM framework, the project bridges the gap between scientific discovery and long-term public health practice in rural communities. Using the Research Action 2 framework we are framing this project as a necessary pilot for state-wide rural groundwater policy. By establishing a "proof of concept" for sustainable implementation, the project aims to produce peer-reviewed models for rural sustainability.

4. Risks & Benefits

4.1 Participant Risks

Participation may involve minor risks associated with providing water and urine samples, temporary storage and transport of specimens, and installation or maintenance of household filtration equipment. Plumbing work may result in minor leaks or property damage if performed incorrectly; participants may stop and contact the study team rather than modify plumbing themselves. The primary psychosocial risk is emotional discomfort or anxiety upon receiving results indicating elevated metal concentrations in a primary water source.

4.2 Direct Participant Benefits

1. Comprehensive Water Testing: Free study analysis for arsenic, uranium, lead, manganese, tungsten, and other metals included in the approved laboratory panel.
2. Free Filtration Infrastructure**:** Provision and professional installation filters.
3. Individual Results: Participants will receive individual water-testing results as specified by the study and consent materials. Urinary metals and kidney-related biomarkers are research measurements and are not intended to diagnose disease.
4. Incentive: A $100 participation incentive per household to compensate for time and study participation, consistent with the approved consent materials.

4.3 Community-Level Benefits

Data from CLEAN W.A.T.E.R. serves as the empirical foundation for the "Housing Resilience Roadmap," a broader initiative to identify drought-driven housing adaptations. Furthermore, the project produces community-vetted educational materials and an evidence-based implementation model for rural groundwater mitigation.

5. Data Security & Confidentiality

5.1 Digital Security Protocols

The project adheres to stringent digital security standards to protect participant privacy. All field data entry is conducted via secure, encrypted platforms (REDCap) using managed devices. The storage of Personally Identifiable Information (PII) on personal devices is strictly prohibited.

Commented [EI1]: We're only using REDCap correct? Shuild I delete Qualtrics?

5.2 Anonymization and Informed Consent

As this project involves non-exempt human subjects research, all participants undergo a rigorous informed consent process. The project team will generate de-identified data sets for sharing with community partners and the Colorado Department of Public Health & Environment (CDPHE).

5.3 Data Storage and Security

The data storage and confidentiality protocols for the CLEAN WATER project are designed to meet rigorous institutional and federal standards to protect participant privacy.

All project data is stored securely using a VPN through CU Anschutz, ensuring that access is restricted to authorized research personnel only. The following measures further safeguard the data:

- **Secure Entry Systems:** Community Navigators and project staff enter all survey and field data directly into REDCap. Data entry is expected within 48 to 72 hours of collection to minimize the time information exists outside the primary security system.
- **Device Policy:** There is a strict prohibition against storing any Personally Identifiable Information (PII) or Personal Health Information (PHI) on personal devices. iPads and

other data collection technology provided to field staff must be returned to research staff at the conclusion of the study.

- **Data Integrity:** Any inconsistencies or missing entries in the database are resolved within five business days to maintain a clean and secure dataset.

5.4 Confidentiality and Privacy Protections

The project employs multiple layers of legal and procedural protections to maintain participant confidentiality:

- **Certificate of Confidentiality:** This project has been issued a federal Certificate of Confidentiality, which provides a high level of protection by prohibiting researchers from disclosing identifying information or biospecimens in most federal, state, or local legal proceedings.
- **De-identification:** While raw data is collected for research purposes, any information shared with community partners, state health departments, or published in journals is strictly de-identified.
- **Restricted Access:** Access to records that identify participants is limited to the study team, the Institutional Review Board (IRB), and designated federal offices like the CDC or FDA that oversee research subject protections.
- **Informed Consent:** Participants are explicitly informed about what data is collected—including demographics, water and urine test results, and survey responses—and how these rules protect their privacy under HIPAA and other relevant laws

6. References

1. Smith RG, Lopez AM, Honeyman AS, Carney D, Fendorf S, Lombard MA, et al. Anthropogenic and geogenic factors affecting groundwater arsenic and potential drinking water exposure in the San Luis Valley, Colorado. Environmental Science & Technology. 2026. doi: 10.1021/acs.est.6c02761.

2. US Environmental Protection Agency. Private Drinking Water Wells. Available at: https://www.epa.gov/privatewells. Accessed October 15, 2026.

3. US Environmental Protection Agency. Overview of the Safe Drinking Water Act. Available at: https://www.epa.gov/sdwa/overview-safe-drinking-water-act. Accessed October 15, 2026.

4. World Health Organization. Arsenic. December 7, 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/arsenic. Accessed October 15, 2026.

5. World Health Organization. Manganese in Drinking-water: Background Document for Development of WHO Guidelines for Drinking-water Quality. Geneva: World Health Organization; 2021. WHO reference number WHO/HEP/ECH/WSH/2021.5. Available at: https://www.who.int/publications/i/item/WHO-HEP-ECH-WSH-2021.5.

6. World Health Organization. Guidelines for Drinking-water Quality. 4th ed, incorporating the first and second addenda. Geneva: World Health Organization; 2022. Available at: https://www.who.int/publications-detail-redirect/9789240045064.

7. Colorado Department of Public Health and Environment. EnviroScreen. Available at: https://climate.colorado.gov/enviroscreen. Accessed October 15, 2026.

8. Wang W, Xie Z, Lin Y, Zhang D. Association of inorganic arsenic exposure with type 2 diabetes mellitus: a meta-analysis. Journal of Epidemiology and Community Health. 2014;68(2):176–184. doi: 10.1136/jech-2013-203114.

9. Moon KA, Guallar E, Umans JG, Devereux RB, Best LG, Fabsitz RR, et al. Association between exposure to low to moderate arsenic levels and incident cardiovascular disease. Annals of Internal Medicine. 2013;159(10):649–659. doi: 10.7326/0003-4819-159-10-201311190-00719.

10. Fox J, Macaluso F, Moore C, Mesenbring E, Johnson RJ, Hamman RF, James KA. Urine tungsten and chronic kidney disease in rural Colorado. Environmental Research. 2021;195:110710. doi: 10.1016/j.envres.2021.110710.

11. Hamman RF, Marshall JA, Baxter J, Kahn LB, Mayer EJ, Orleans M, Murphy JR, Lezotte DC. Methods and prevalence of non-insulin-dependent diabetes mellitus in a biethnic Colorado population: The San Luis Valley Diabetes Study. American Journal of Epidemiology. 1989;129(2):295–311.

12. Liu W, Xin Y, Li Q, Shang Y, Ping Z, Min J, et al. Biomarkers of environmental manganese exposure and associations with childhood neurodevelopment: A systematic review and meta-analysis. Environmental Health. 2020;19:104. doi: 10.1186/s12940-020-00659-x

13. Reynolds RL, Goldstein HL, Moskowitz BM, et al. Dust deposited on snow cover in the San Juan Mountains, Colorado, 2011–2016: Compositional variability bearing on snow-melt effects. Journal of Geophysical Research: Atmospheres. 2020. https://doi.org/10.1029/2019JD032210

Statistical Analysis Plan

Statistical Objectives
Primary objective
To quantify the effectiveness of household filtration interventions in reducing arsenic and uranium concentrations in drinking water.
Secondary objectives

1. Evaluate filtration effectiveness for arsenic, uranium, tungsten, zinc, manganese, and other measured metals.
2. Characterize changes in filtration effectiveness across months 3, 5, and 7.
3. Evaluate longitudinal changes in urinary arsenic, uranium, tungsten, and zinc concentrations among participants who voluntarily provide urine specimens.
4. Examine associations between water metal concentrations and urinary metal concentrations.
5. Assess longitudinal changes in urinary NGAL, KIM-1, and microalbumin.
6. Evaluate associations between urinary metal concentrations and kidney-related biomarkers.
7. Assess filter adoption, implementation fidelity, maintenance, and continued use.

Outcome Definitions
4.1 Primary Water Outcomes
The primary water outcomes will be arsenic and uranium removal efficiency.
For metal (m), household (i), and time (t):
RE=100*frac (PFM-PoFM)/PFM
where:

- RE = percentage removal efficiency.
- PFM = pre-filtration metal concentration.
- PoFM = post-filtration metal concentration.

Removal efficiency will be calculated only when the pre-filtration concentration is positive and sufficiently quantifiable.
Because percentage removal can be unstable at very low baseline concentrations, the primary statistical comparisons will also examine paired concentration differences and post-to-pre concentration ratios.
Arsenic and uranium will be treated as co-primary analytes, with the multiplicity strategy finalized before analysis.

Secondary Water Outcomes
Secondary water outcomes include:

- Concentrations of tungsten, zinc, manganese, iron, antimony, and other measured analytes.
- Absolute reductions in metal concentrations.
- Post-filtration metal concentrations.
- Proportions of samples meeting prespecified drinking water benchmarks.
- Changes in removal efficiency over follow-up.
- Potential changes in filtration performance following filter replacement.

Regulatory benchmarks will be identified for each analyte where applicable. The analysis will distinguish enforceable standards from advisory or health-based reference values.

Urinary Metal Outcomes
Urinary metal concentrations will include arsenic, uranium, tungsten, zinc, and other metals measured in the laboratory panel. The primary biomonitoring approach will use natural log-transformed urinary concentrations, with urinary creatinine incorporated to address variation in urine dilution. Creatinine-adjusted concentrations will also be presented in descriptive and sensitivity analyses. Total urinary arsenic will not automatically be interpreted as equivalent to inorganic arsenic exposure.

Kidney Biomarker Outcomes
The kidney-related biomarkers will include:

- Neutrophil gelatinase-associated lipocalin (NGAL).
- Kidney injury molecule-1 (KIM-1).
- Urinary microalbumin.

Biomarker distributions will be examined and log-transformed where appropriate. These measurements will be interpreted as research biomarkers, not diagnostic indicators of kidney disease.

Descriptive Statistical Analysis
Participant and household characteristics will be summarized overall and by filtration pathway. Continuous variables will be summarized using means and standard deviations for approximately symmetric distributions, or medians and interquartile ranges for skewed distributions. Categorical variables will be reported as counts and percentages. Baseline water metal concentrations will be summarized by filtration pathway and metal. The proportion of measurements below the laboratory detection or quantification limit will be reported for each analyte.

Primary Analysis: Water Filtration Effectiveness
The principal analysis will compare paired pre-filtration and post-filtration concentrations for arsenic and uranium.
For each analyte and sampling period, the analysis will estimate:

- Median percentage removal efficiency.

- Absolute pre-to-post concentration change.
- Geometric mean post-to-pre concentration ratio.
- Proportion of paired samples showing a reduction in concentration.

For concentrations that are positive and reliably quantified, paired differences on the natural logarithmic scale.

The exponentiated mean log difference will estimate the geometric mean post-to-pre concentration ratio. Values below detection limits will be handled using prespecified censored-data methods where appropriate rather than automatically assigning zero. To account for repeated measurements within households, a longitudinal mixed-effects model will be fitted where the data support the models. Sampling month will initially be modeled categorically to avoid assuming a linear trend. Separate models will be fitted for arsenic and uranium.

Secondary Analysis: Filtration Pathways

Water metal reductions will be described separately for:

1. Under-sink filtration.
2. Tabletop/pitcher filtration.

Differences between pathways will be explored using regression models adjusted for relevant baseline characteristics, including baseline metal concentration and household water characteristics where available. Because filtration pathways are not randomly assigned and eligibility thresholds differ, between-pathway estimates will not be interpreted as causal comparisons of filter technologies.

Longitudinal Urinary Metal Analysis

Urinary metal concentrations will be analyzed among participants who voluntarily provide specimens. Where repeated urine measurements are available, linear mixed-effects models will estimate changes over time. Urinary creatinine will be included as a covariate in the principal model when appropriate, with creatinine-standardized analyses used as sensitivity analyses. Changes will be expressed as estimated geometric mean ratios and percentage changes with 95% confidence intervals. Analyses will account for the possibility that urinary metal concentrations reflect multiple exposure sources beyond household drinking water.

Water–Urine Exposure Associations

Associations between drinking water metal concentrations and urinary metal concentrations will be assessed using multivariable regression. Where timing permits, post-filtration water concentrations and household drinking water consumption will be evaluated as predictors of subsequent urinary metal concentrations. Potential covariates include age, sex, household water consumption, baseline exposure, relevant dietary or occupational exposures, and other measured factors identified before analysis. Repeated observations will be handled using mixed-effects models. These analyses will be considered exploratory because the study does not include random assignments to filtration pathways or an untreated comparison group.

Kidney Biomarker Analysis

Associations between urinary metal concentrations and kidney-related biomarkers will be evaluated using regression models. Separate analyses will be performed for NGAL, KIM-1, and microalbumin. For repeated measurements, mixed-effects models will be used. Potential confounders will be selected based on biological relevance and data availability. Results will be presented as adjusted effect estimates with 95% confidence intervals. Because urinary creatinine may be related to kidney function, creatinine adjustment strategies will be evaluated carefully, and sensitivity analyses will assess their influence on estimated associations. No causal or diagnostic conclusions will be drawn solely from observed biomarker associations.

Implementation Science Analysis: RE-AIM
The study will evaluate five RE-AIM dimensions.

- Reach: Number and proportion of eligible households recruited, enrolled, and retained, along with geographic distribution across targeted communities.
- Effectiveness: Reduction in drinking water metal concentrations and changes in urinary metal concentrations and kidney-related biomarkers.
- Adoption: Proportion of eligible households receiving and using their assigned filtration systems.
- Implementation: Installation completion, reported filter use, protocol adherence, sample collection completion, and fidelity to geographic targeting.
- Maintenance: Continued filter use, adherence to replacement schedules, filter returns, troubleshooting, and intention to continue using filtration after the study.

Implementation indicators will be summarized using counts, proportions, and 95% confidence intervals where meaningful. Monthly repeated survey outcomes may be analyzed using generalized estimating equations or mixed-effects regression models.

Missing Data and Laboratory Detection Limits
Missingness will be characterized by assessment period, filtration pathway, and specimen type. Reasons for missing samples will be documented where available. Mixed-effects models will use available repeated observations under their applicable missing-data assumptions. Sensitivity analyses will evaluate the potential impact of incomplete follow-up, particularly for voluntary urine collection. Laboratory measurements below detection or quantification limits will be flagged and summarized. Appropriate censored-data methods or prespecified sensitivity analyses will be used depending on the proportion of censored observations. Laboratory quality-control failures will be handled according to documented quality-assurance procedures.

Statistical Inference and Multiple Comparisons
Effect estimates will be reported with 95% confidence intervals. Statistical testing will use two-sided tests with a nominal significance level of 0.05. Because arsenic and uranium are proposed as co-primary analytes, the final SAP will specify whether both must demonstrate effectiveness or whether a multiplicity adjustment, such as Holm's procedure, will be applied. Secondary metal, biomonitoring, and kidney biomarker analyses will be identified as exploratory unless a formal testing hierarchy is approved. Interpretation will prioritize effect magnitude, uncertainty, and public health relevance.

Sensitivity Analyses
Sensitivity analyses will include:

1. Alternative handling of concentrations below detection limits.
2. Models using absolute rather than relative metal reductions.
3. Analyses restricted to households with complete follow-up.
4. Adjustment for baseline metal concentrations.
5. Assessment of seasonal and sampling-period variation.
6. Assessment of filter replacement and reported adherence.
7. Alternative urinary creatinine adjustment strategies.
8. Analyses excluding samples with documented laboratory quality-control concerns.

Statistical Software
Analyses will be conducted using R, Stata, SAS, or equivalent validated statistical software. Statistical scripts, derived variables, exclusion criteria, and analysis decisions will be documented to ensure reproducibility.

Reporting
Results will be reported by filtration pathway, sampling period, and metal.
The statistical report will include:

- Participant flow and analytical sample sizes.
- Baseline household and exposure characteristics.
- Paired water metal concentration results.
- Metal removal efficiency estimates.
- Longitudinal filtration performance.
- Urinary metal concentration findings.
- Kidney biomarker analyses.
- RE-AIM implementation indicators.
- Missing-data and sensitivity analyses.

The final interpretation will distinguish demonstrated filtration performance from exploratory evidence of changes in internal metal exposure and kidney-related biomarkers.