with 22% increased likelihood of achieving target BP by 6 months [OR(95% CI): 1.22(1.05, 1.42)]. Participants receiving SPCs (vs multi-pills) experienced more rapid BP reduction in the first 6 months (-2.0 vs. -1.2 mmHg monthly change; p-diff<0.001). Over long-term follow-up, participants using SPCs achieved significantly lower SBP at each timepoint. The risk of the primary CV composite endpoint and SAEs was not significantly different between groups. DISCUSSION/SIGNIFICANCE OF IMPACT: SPC therapy resulted in more rapid and sustained BP reduction and a greater likelihood of achieving BP control compared with multi-pill therapy without increase in SAEs. Future research is needed to identify optimal strategies for implementing SPC-based approaches at the population-level and optimize public health benefits of intensive BP control.

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Associations of urine uranium with kidney function and metabolomics†

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OBJECTIVES/GOALS: We evaluated the associations of urine uranium with incident chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73m2), incident albuminuria (albumin-to-creatinine ratio >30 mg/g), and baseline and follow-up plasma metabolite levels in participants without diabetes across the Great Plains and Southwest. METHODS/STUDY POPULATION: We evaluated participants with available urine uranium estimates, eGFR, uACR, and other variables of interest. In incident case analyses, participants were free of CKD (N=1,845) and albuminuria (1,693) at baseline (2001-2003). We used generalized estimating equations, clustering on family identifier, to estimate risk ratios (RRs) of incident CKD and albuminuria per doubling of urine uranium adjusted for sex, age, eGFR or uACR, study center, educational level, smoking status, BMI, and arsenic exposure. Nontargeted metabolomic profiling was analyzed by gas chromatography-mass spectrometry. In metabolome-wide association analyses, we used adjusted linear mixed models to estimate the association of urine uranium (N=1,223) with relative changes in metabolite concentrations over time. RESULTS/ANTICIPATED RESULTS: Overall, the median (IQR) age was 35.9 (23.7, 46.8) years and 60% participants were female. The number of incident CKD cases was 28 (mean follow-up 5.6 years), and the number of albuminuria cases was 140. The adjusted RR (95% CI) per doubling of urine uranium was 0.90 (0.71, 1.15) for incident CKD and 1.00 (0.92, 1.08) for incident albuminuria. In metabolome-wide analyses, urine uranium was associated with a relative change in 8 unique metabolites and 31 unknown metabolomic features (p-value <0.05), with 5 unique metabolites (threonic acid, N-acetylornithine, isocitric acid, cellobiose, and 6-deoxyglucose) and 7 unknown metabolomic features reaching false discovery rate significance (BH-adjusted p-value <0.05). DISCUSSION/SIGNIFICANCE OF IMPACT: Urine uranium was not associated with incident CKD nor with albuminuria. We identified 5 unique metabolites associated with urine uranium. Our findings are relevant for uranium-related kidney disease in people without diabetes, but require additional confirmation due to potential reverse causality and lack of drinking water uranium exposure.

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Assessing the effectiveness of interruptive EHR alerts via individually randomized trials in the presence of post-randomization contamination†

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OBJECTIVES/GOALS: Randomized evaluation of interruptive EHR alerts in improving service delivery or patient health outcomes is usually carried out within the EHR system and in routine hospital operations. However, this study setting leads to increased risk of contamination, where factors outside the original design affect estimation and testing of treatment effect. METHODS/STUDY POPULATION: We focused on the effect of contamination on the design and analysis of individually randomized controlled trials (iRCTs) for the study of the effectiveness of EHR alerts. More specifically, we looked at post-randomization contamination due to clinician-induced correlations. To account for this kind of contamination, we extended the iRCT design to include clinicians' random effects under the linear mixed effects model (LMEM) framework. We then proceeded to derive sample size and power formulas under different LMEM correlation structures. Using extensive simulation studies, we evaluated the derived formulas and assessed the effect of using a naive two-sample t-test that ignores post-randomization contamination. RESULTS/ANTICIPATED RESULTS: We observed that the level of contamination on sample size, power, and type I error due to clinician-induced correlations was driven by three parameters: variances of the clinicians' random intercepts and slopes, and the correlation between them. These parameters reflect the way and extent to

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