Supplementary File S1

Prior postoperative acute kidney injury and acute kidney injury at a subsequent noncardiac operation: an All of Us cohort study

Supplementary Methods 1. Cohort and operation-pair construction

The study used the All of Us Research Program Controlled Tier v9 dataset C2025Q4R6, released June 26, 2026, with a data cutoff of January 1, 2025. Eligible operation records spanned August 2017 through the data cutoff. Adults were eligible only after both official consent dates.

Operations were identified independently through standardized procedure concepts and the original procedure codes supplied by contributing data sources, using the published 565-code Operative Stress Score (OSS) list. Three corrected other-cardiac codes were separated from that list, leaving a conservative 562-code noncardiac core. Standardized procedure concepts defined the primary cohort; the original source codes defined a planned sensitivity analysis of procedure-code capture.

Qualifying procedure rows on the same person-day were collapsed into one operation with the maximum OSS; same-day anesthesia coding was not required. Operation person-days were ordered for each person before eligibility was assessed, and every consecutive pair was formed. The later operation had to occur at least 90 days after the earlier operation. This rule prevented overlap between the earlier operation's seven-day outcome window and the later operation's 60-day reference window, but it did not establish renal recovery between operations.

Pairs were excluded if either operation included a direct renal-volume/removal or transplant procedure from the prespecified OSS list: CPT 50220, 50230, 50234, 50240, 50360, 50543, 50545, 50546, or 50548. Other urologic procedures were retained.

The operation and creatinine algorithms reproduced prespecified reference checks, but neither adapted v9 algorithm has been criterion-validated against manual chart review. The original-source-code and same-contributing-source analyses assess capture stability within All of Us rather than external validation.

Supplementary Methods 2. Creatinine reference, outcome, and observation

Each operation had its own preoperative reference and postoperative assessment window. The reference was the most recent valid serum creatinine in the preceding 60 days. Values reported in mg/dL were retained; values reported in micromoles per liter were divided by 88.4. Values below 0.2 mg/dL or at least 25 mg/dL and values without a verified unit were excluded. When multiple measurements shared the most recent eligible date, an available precise timestamp and then the higher normalized creatinine value resolved the tie.

A procedure or laboratory timestamp was treated as precise only when it was present and its clock time was not midnight. When both operation and laboratory times were precise, the reference measurement had to precede the operation and postoperative measurements had to follow it. Otherwise, the operation date was excluded: reference measurements came from calendar days -60 through -1 and postoperative measurements from days +1 through +7.

Postoperative measurements were censored at the next qualifying operation so that they were not attributed to the earlier operation. When another qualifying operation occurred within seven days and no valid creatinine separated the two operations, the earlier operation was not eligible for a paired endpoint.

Raw 2021 CKD-EPI creatinine-based estimated glomerular filtration rate (eGFR) values had to be greater than 0 and less than 300 mL/min/1.73 m². After that validity check, eligibility required eGFR of at least 15 mL/min/1.73 m² after rounding to the nearest whole value. The equation used the supported current v9 female and male concepts; unsupported sex concepts were not assigned an equation coefficient.

Creatinine-defined postoperative acute kidney injury (PO-AKI) was present when the maximum creatinine during the first 48 postoperative hours was at least 0.3 mg/dL above the preoperative reference, or when the maximum during the first seven postoperative days was at least 1.5 times the reference. Date-only records used postoperative days 1-2 for the absolute criterion. Stage 3 could be assigned by an absolute creatinine value of at least 4.0 mg/dL only after the operation met an AKI criterion. Urine-output and renal-replacement-therapy criteria were unavailable or not implemented. A pair entered the analytic cohort only when the endpoint was evaluable at both operations.

The absolute branch was anchored to the preoperative reference. It did not require the reference and postoperative measurements to be no more than 48 hours apart and did not search later rolling 48-hour intervals. It can therefore miss a later short-interval rise or classify a change that accumulated over a longer reference-to-postoperative interval. The seven-day branch likewise used the available maximum; the electronic record did not provide continuous daily observation.

For the observation diagnostic in Supplementary Table S1, the denominator in each prior-AKI group was all otherwise eligible operation pairs whose prior operation met the full endpoint eligibility rules. The subsequent-operation endpoint was considered observed only when the later operation met those same rules: a valid preoperative reference and postoperative measurement without unresolved overlap, a computable eGFR from supported inputs with a raw value greater than 0 and less than 300 mL/min/1.73 m², and a rounded eGFR of at least 15 mL/min/1.73 m². The numerator was the number of denominator pairs whose later operation met this full eligibility definition. This binary measure does not describe how often creatinine was tested within the window.

The exposure was PO-AKI after the prior operation. The outcome was PO-AKI after the subsequent operation, recomputed with that operation's own reference and postoperative window.

Supplementary Methods 3. Model, uncertainty, and analysis origin

The all-pair primary model used modified-Poisson regression with a log link. The design matrix was:

log E[subsequent PO-AKI] = intercept
+ prior PO-AKI
+ age at subsequent operation / 10 years
+ female sex
+ subsequent reference eGFR / 10 mL/min/1.73 m²
+ prior OSS
+ subsequent OSS
+ log2(interoperation interval in days)
+ subsequent-operation calendar year centered at 2020

Age and eGFR were scaled per 10 units, the interoperation interval was log2-transformed, calendar year was centered at 2020, and the model included an intercept. The primary model used sandwich uncertainty clustered by person with finite-sample correction. Risk ratios and 95% confidence intervals were obtained by exponentiating the prior-PO-AKI coefficient and its normal-Wald limits; P values were two-sided.

Three planned sensitivity analyses used the same formula. One used original source procedure codes to test procedure-code capture. One retained the earliest qualifying primary-cohort pair per person to remove repeat contributions. One required both operations to come from the same contributing data source to test source continuity. The first-pair model used the uncorrected heteroskedasticity-consistent sandwich estimator (HC0). The analysis plan requested HC3 leverage correction, but the statsmodels 0.14.6 Poisson implementation applied HC0; the reported first-pair interval therefore uses HC0. The other models used person-clustered sandwich uncertainty.

All model inputs were complete by design, and no values were imputed. All four models converged with full-rank design matrices and finite coefficients and covariance. Models were fit in Python 3.12.13 with statsmodels 0.14.6, NumPy 2.4.3, and pandas 2.3.3.

Cohort definitions and feasibility thresholds were set before repeat-operation counts were known. The positive crude association was then reviewed before the adjustment model and three sensitivity analyses were specified. Those models were specified before adjusted estimates were calculated.

Supplementary Results 1. Observation, procedure-code, and source checks

Supplementary Table S1. Selection, procedure-code, and provenance diagnostics

Diagnostic	Standardized procedure concepts	Original source procedure codes
Subsequent-endpoint observation after observed prior PO-AKI	36%	Not evaluated
Subsequent-endpoint observation after observed prior no PO-AKI	36%	Not evaluated
Observability risk ratio, prior PO-AKI vs no prior PO-AKI	0.99	Not evaluated
Pair count relative to standardized procedure concepts	1.00	1.17
Pair-date agreement at shared person and pair-order positions	Reference	89%
Largest contributing-data-source share	10%	12%

A contributing data source is an All of Us provenance group, not an identified hospital, facility, or clinician. Requiring both operations to come from the same contributing data source retained approximately 93% of primary-cohort endpoint-eligible pairs. These diagnostics address binary endpoint observation, procedure-code capture, and source concentration. They do not measure the frequency of creatinine testing within an observed postoperative window. The adjusted sensitivity estimates are reported in Table 2 of the manuscript. They test these three design concerns within the same data resource and are not independent replications.

The primary cohort included 1,448 of 21,247 otherwise eligible operation pairs (6.82%). Interpretation is therefore conditional on survival, return for another operation recorded in All of Us, and enough creatinine testing to evaluate both operation-specific endpoints. Similar binary observation by prior-AKI status does not exclude differential testing intensity within the observed windows.

Supplementary reporting, data, and code

This report follows the STROBE cohort-reporting guidance and its RECORD extension for studies using routinely collected health data.[1,2]

Participant-level All of Us data cannot leave the Researcher Workbench and are available only to authorized users under the applicable institutional Data Use and Registration Agreement. This study used Controlled Tier v9 C2025Q4R6. The cohort, exposure, outcome, and model definitions are reported in the manuscript and this supplement.

The analysis code uses an internal transcription of the published 565-code OSS supplement. The source article states that OSS intellectual-property rights are reserved by the University of Nebraska. Executable code and codelists are not publicly available because release requires both All of Us policy review and resolution of those rights. Complete creatinine concept/unit mappings and supported sex-concept mappings remain in the secure Workbench code and are not reproduced as

public codelists.

Only disclosure-controlled aggregates are reported. Dissemination is subject to the All of Us Research Program's acknowledgement, data-access, PubMed Central, ethical-conduct, and stigmatizing-research requirements.

Supplementary references

1. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PLoS Med. 2007;4:e297. doi:10.1371/journal.pmed.0040297

2. Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015;12:e1001885. doi:10.1371/journal.pmed.1001885