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Albuminuria With Preserved Estimated Glomerular Filtration Rate and Prevalent Cardiovascular Disease Among Adults in the United States: A Cross-Sectional Analysis of the National Health and Nutrition Examination Survey 2021-2023

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Abstract

Background: Albuminuria is a marker of kidney damage and cardiovascular risk, but routine creatinine-based assessment of estimated glomerular filtration rate (eGFR) does not detect it. We estimated how common albuminuria with preserved eGFR is among U.S. adults and examined its association with prevalent cardiovascular disease (CVD).

Materials and methods: We analyzed 5,282 nonpregnant adults aged ≥20 years from the National Health and Nutrition Examination Survey, August 2021-August 2023. Participants were classified into four phenotypes by eGFR (2021 race-free CKD-EPI creatinine equation; cut point 60 mL/min/1.73 m^2) and spot urine albumin-to-creatinine ratio (UACR; cut point 30 mg/g). Prevalent CVD was a self-reported diagnosis of heart failure, coronary heart disease, angina, myocardial infarction, or stroke. Associations were estimated with survey-weighted logistic regression, and the main estimates were independently reproduced in a second statistical software package. Secondary analyses estimated the share of affected adults with no diagnosed hypertension, diabetes, kidney disease, or CVD and the change in predicted 10-year total CVD risk when UACR was added to the American Heart Association Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) equations.

Results: Albuminuria with preserved eGFR was present in 7.8% of U.S. adults (95% confidence interval (CI): 6.9-8.7), or about 17.4 million people, and accounted for 79.1% of all adults with albuminuria. CVD prevalence was 22.2% in this group versus 6.4% in adults without kidney markers (adjusted odds ratio (OR): 1.86; 95% CI: 1.23-2.81). A simplified model with fewer parameters gave a similar result (OR: 1.87; 95% CI: 1.24-2.82). The odds of CVD did not differ significantly from those of adults with reduced eGFR without albuminuria (OR: 1.11; 95% CI: 0.72-1.72) and rose with albuminuria severity (OR: 1.13 per doubling of UACR). Among adults with albuminuria and preserved eGFR, 35.6% reported no diagnosis of hypertension, diabetes, kidney disease, or CVD, and only 3.2% had been told they had kidney disease. Adding UACR to PREVENT raised their mean predicted 10-year total CVD risk from 9.9% to 12.7% and moved 25.2% into a higher risk category.

Conclusions: About one in 13 U.S. adults has albuminuria with preserved eGFR. This phenotype was associated with prevalent CVD independently of traditional risk factors, and many affected adults had no diagnosis that would usually prompt urine albumin testing. Prospective studies should test whether wider UACR testing improves cardiovascular prevention.

Categories: Cardiology, Preventive Medicine, Nephrology
Keywords: albuminuria, cardiovascular disease, chronic kidney disease, cross-sectional study, estimated glomerular filtration rate, heart failure, nhanes, prevent equations, urine albumin-to-creatinine ratio

Introduction

Chronic kidney disease (CKD) is identified by either a reduced glomerular filtration rate or evidence of kidney damage, most often albuminuria [1]. Both markers independently predict all-cause and cardiovascular mortality [2]. In general-population cohorts, cardiovascular mortality rises with the urine albumin-to-creatinine ratio (UACR) independently of the estimated glomerular filtration rate (eGFR), including at UACR levels below the conventional albuminuria threshold of 30 mg/g [2,3]. This association holds in people with and without diabetes and extends to heart failure [4].

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In routine care, however, kidney health is assessed mainly with serum creatinine [5]. Creatinine is part of almost every basic metabolic panel, whereas UACR requires a separate urine test that is often not ordered [5,6]. In a U.S. national laboratory database of more than 28 million adults with diabetes or hypertension, only 21.0% had at least one UACR test between 2013 and 2019, compared with 89.6% who had an eGFR [5]. In a multinational consortium of clinical cohorts, the UACR testing rate was 35.1% among adults with diabetes and only 4.1% among adults with hypertension but no diabetes [6]. Adults whose kidney damage appears only as albuminuria, with an eGFR still ⩾60 mL/min/1.73 m^2, are therefore the most likely to go undetected [5,6]. Awareness of kidney disease among U.S. adults with CKD has also remained low for nearly two decades [7].

This testing gap matters for cardiovascular prevention. The American Heart Association (AHA) now describes cardiovascular, kidney, and metabolic disease as one connected syndrome [8]. The AHA Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) equations include eGFR in the base model and allow UACR as an optional additional predictor [9]. The 2024 Kidney Disease: Improving Global Outcomes (KDIGO) guideline advises testing people at risk of CKD with both eGFR and urine albumin (Practice Point 1.1.1.1) [1]. The August 2021-August 2023 National Health and Nutrition Examination Survey (NHANES) cycle provides recent, nationally representative data for estimating how much adding UACR changes predicted cardiovascular risk in adults with albuminuria and an eGFR ⩾60 mL/min/1.73 m^2 and how many of these adults reported no diagnosis of a condition that would prompt testing.

Using NHANES August 2021-August 2023, this study had four objectives: to estimate the weighted prevalence of four eGFR-albuminuria phenotypes among U.S. adults; to test whether albuminuria with preserved eGFR is associated with prevalent cardiovascular disease (CVD) after adjustment for major cardiovascular risk factors (the primary objective); to estimate the share of adults with this phenotype who have no diagnosed hypertension, diabetes, kidney disease, or CVD; and to quantify how adding UACR to the PREVENT equations changes predicted 10-year total CVD risk.

We tested three hypotheses. First, adults with an eGFR ⩾60 mL/min/1.73 m^2 and a UACR ⩾30 mg/g would have higher odds of prevalent CVD than adults with an eGFR ⩾60 mL/min/1.73 m^2 and a UACR <30 mg/g, even after adjustment for major risk factors. Second, their odds would not be lower than those of adults with reduced eGFR without albuminuria. Third, the association would increase across KDIGO albuminuria categories.

Materials And Methods

Study design and data source

This cross-sectional study used NHANES August 2021-August 2023, a survey of the civilian noninstitutionalized U.S. population conducted by the National Center for Health Statistics (NCHS). NHANES uses a stratified, clustered, four-stage probability sample and combines a household interview with a standardized physical examination and laboratory testing in a mobile examination center [10]. The NCHS Ethics Review Board approved the NHANES protocol (protocol #2021-05, listed for NHANES 2021-2022) [11], and participants gave written informed consent. This secondary analysis used de-identified public-use files and required no further ethics review. We merged 14 component files (DEMO, MCQ, BPXO, BMX, GHB, HDL, TCHOL, BIOPRO, ALB_CR, DIQ, SMQ, BPQ, KIQ_U, and HIQ) by respondent sequence number into one dataset of 11,933 participants and 185 variables. This report follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cross-sectional studies [12].

Participants

The analytic sample included adults aged ⩾20 years who completed the examination, had a positive phlebotomy weight, were not pregnant, had valid serum creatinine and UACR results, and had a determinable CVD status (Figure *1*). Pregnant participants were excluded because pregnancy changes glomerular filtration and albumin excretion. Of 11,933 participants, 5,282 formed the analytic sample. The regression models used the 5,141 participants with complete covariate data. The remaining 141 participants (2.7%) had missing data for hypertension status (92), body mass index (BMI; 52), smoking status (seven), or diabetes status (one); some participants had missing data for more than one variable. Models 1, 2, and 3 used the same 5,141 participants so that their estimates are directly comparable.

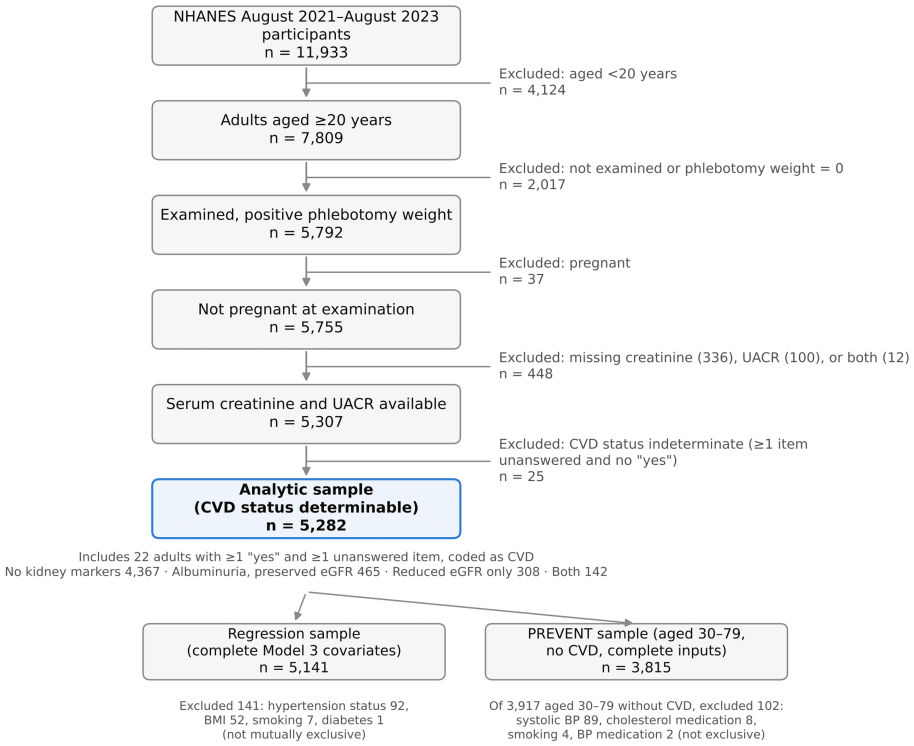


FIGURE 1: Selection of the analytic, regression, and PREVENT samples

Adults aged ≥20 years in NHANES August 2021-August 2023, with counts excluded at each step, the handling of incomplete CVD answers, and the final number in each phenotype.

BMI: body mass index, BP: blood pressure, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, NHANES: National Health and Nutrition Examination Survey, PREVENT: Predicting Risk of Cardiovascular Disease EVENTs, UACR: urine albumin-to-creatinine ratio

Exposure: eGFR-albuminuria phenotype

eGFR was calculated from serum creatinine (LBXSCR) with the 2021 race-free Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation [13]. UACR was the laboratory-reported value from a single spot urine sample. Participants were classified into four phenotypes: no kidney markers (eGFR ⩾60 mL/min/1.73 m^2 and UACR <30 mg/g; the reference group); albuminuria with preserved eGFR (eGFR ⩾60 mL/min/1.73 m^2 and UACR ⩾30 mg/g; the exposure of interest); reduced eGFR without albuminuria (eGFR <60 mL/min/1.73 m^2 and UACR <30 mg/g); and both markers (eGFR <60 mL/min/1.73 m^2 and UACR ⩾30 mg/g).

Within the group with eGFR ⩾60 mL/min/1.73 m^2, UACR was also classified by KDIGO albuminuria category (A2, 30 to <300 mg/g; A3, ⩾300 mg/g; the boundary value of 300 mg/g was assigned to A3) and analyzed as $\log_2$(UACR), so that each unit represents a doubling of UACR [1].

Outcome: prevalent CVD

Prevalent CVD was defined as a "yes" response to whether a doctor or other health professional had ever told the participant that they had congestive heart failure (MCQ160B), coronary heart disease (MCQ160C), angina (MCQ160D), heart attack (MCQ160E), or stroke (MCQ160F). Answers of "refused" or "don't know" were treated as missing. CVD was coded as present if any item was "yes" and as absent if all five items were "no." Of the 5,307 adults who met all other inclusion criteria, 5,260 answered all five items. Of the remaining 47, 22 answered "yes" to at least one item and were classified as having CVD; the other 25 had no "yes" responses and at least one unanswered item, so their CVD status could not be determined, and they were excluded. Both decisions were tested in sensitivity analyses. Individual CVD components are reported descriptively.

Covariates

Demographic covariates were age, sex, race and Hispanic origin (Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and other or multiracial), and family income-to-poverty ratio (<1.3, 1.3-3.49, and ⩾3.5). The income-to-poverty ratio was missing for 664 analytic adults (13.5% weighted). In the

prespecified Model 3, these adults were retained by adding a "missing" category. This category is a statistical construct rather than a socioeconomic group, and its estimate is not interpreted; other ways of handling missing income were examined in sensitivity analyses. BMI was calculated from measured height and weight.

Hypertension was defined as a mean systolic blood pressure ≥130 mm Hg or a mean diastolic blood pressure ≥80 mm Hg (average of up to three oscillometric readings), or current use of antihypertensive medication (BPQ150), following the 2017 American College of Cardiology (ACC)/AHA definition [14]. Diabetes was defined as a self-reported diagnosis (DIQ010), glycated hemoglobin (HbA1c) ≥6.5% [15], or current use of insulin or oral glucose-lowering medication. Current smoking was defined as having smoked at least 100 cigarettes in one's lifetime and now smoking every day or on some days. Lipid covariates were total cholesterol and high-density lipoprotein (HDL) cholesterol; self-reported use of prescribed cholesterol-lowering medication (BPQ101D) was also recorded. Access to care was defined as having any health insurance (HIQ011).

Recognition status

Adults were classified as having unrecognized risk if they reported no diagnosis of hypertension (BPQ020), diabetes (DIQ010; "borderline" was counted as not diagnosed), weak or failing kidneys (KIQ022), or any of the five CVD conditions. Kidney disease awareness was defined as a "yes" answer to KIQ022, as in prior NHANES studies [7]. This question measures awareness of kidney disease, not awareness of albuminuria, which NHANES does not ask about. A reported absence of diagnoses also does not mean that these conditions are absent.

PREVENT risk estimation

We applied the sex-specific AHA PREVENT 10-year total CVD equations, with and without the optional UACR term [9], to adults aged 30-79 years without self-reported CVD who had complete data for all equation inputs (n = 3,815). Inputs were age, sex, total and HDL cholesterol, mean systolic blood pressure, diabetes, current smoking, eGFR, antihypertensive medication use, statin use, and the natural logarithm of UACR. BMI was included only in the PREVENT heart failure equations and was not used. Statin use was approximated by self-reported cholesterol-lowering medication because the NHANES prescription file was not part of the merged dataset. Input values outside the ranges allowed by the equations were set to the nearest limit (total cholesterol 130-320 mg/dL, HDL cholesterol 20-100 mg/dL, systolic blood pressure 90-200 mm Hg, eGFR 15-140 mL/min/1.73 m^2, and UACR 0.1-25,000 mg/g). This affected 287 adults (7.5%), most often because total cholesterol was below 130 mg/dL. Equation coefficients were taken from the preventr package (version 0.12.2) for R (R Foundation for Statistical Computing, Vienna, Austria). The October 2026 correction to PREVENT changed only the HbA1c and full equations; the base and UACR equations used here were not affected [16]. Our base equations matched an independent implementation, the pyprevent package (version 0.1.6) for Python (Python Software Foundation, Wilmington, DE, USA), for 200 simulated profiles (maximum difference <0.01 percentage points). Our UACR equations reproduced the PREVENT test cases, and an R recomputation reproduced every risk predicted in IBM SPSS Statistics (IBM Corp., Armonk, NY, USA) to within 0.001 percentage points.

Predicted risk was grouped as <5%, 5% to <7.5%, 7.5% to <20%, and ≥20%. Only the 7.5% cut point has guideline standing for PREVENT total CVD risk: the 2025 AHA/ACC high blood pressure guideline uses a 10-year PREVENT CVD risk ≥7.5% to guide drug treatment of stage 1 hypertension [17]. The other cut points mirror categories used with the pooled cohort atherosclerotic CVD (ASCVD) equations and are descriptive only; PREVENT-ASCVD thresholds were not applied to total CVD risk. In three sensitivity analyses, we restricted the sample to the 3,509 adults whose inputs were all within the stricter ranges of the preventr package (including systolic blood pressure ≤180 mm Hg), capped systolic blood pressure at 180 mm Hg, and set the statin term to zero.

Statistical analysis

All estimates used the phlebotomy subsample weight (WTPH2YR), masked variance strata (SDMVSTRA), and primary sampling units (PSUs; SDMVPSU). The phlebotomy weight was used because the exposure requires serum creatinine; NCHS provides this weight in this cycle for analyses of blood-based measures [10]. Variances were estimated by Taylor-series linearization. Subgroups were analyzed as domains (subpopulations) so that all PSUs remained in the variance calculation. The design had 15 strata and 30 PSUs, which gives 15 degrees of freedom (df). Confidence intervals (CIs) were based on the t distribution with 15 df. CIs for proportions used the logit transformation, except for the PREVENT reclassification proportions, which are Wald intervals from CSDESCRIPTIVES.

Participant characteristics were summarized as weighted means and percentages by phenotype. Weighted prevalence of each phenotype and of CVD was estimated with 95% CIs. Three sequential survey-weighted logistic regression models estimated odds ratios (ORs) for CVD by phenotype, with no kidney markers as the reference: Model 1 was unadjusted; Model 2 adjusted for age, sex, and race and Hispanic origin; and Model 3 additionally adjusted for income-to-poverty ratio, BMI, hypertension, diabetes, current smoking, and total

and HDL cholesterol. Model 3 estimates the association independent of traditional risk factors. Because some of these factors may lie on the causal pathway between kidney damage and CVD, Model 3 may underestimate the total association. A linear contrast compared albuminuria with preserved eGFR against reduced eGFR without albuminuria. A separate model with terms for low eGFR, albuminuria, and their product tested for multiplicative interaction. Single coefficients and contrasts were tested with design-based Wald t-tests (log OR divided by its linearization standard error, with 15 df), and the overall phenotype effect was tested with the adjusted Wald F test (three numerator df).

Model 3 contains 19 parameters, more than the 15 design df. Its design-based covariance matrix therefore has rank 15, and SPSS reports it as singular. This affects only joint tests of more than 15 parameters, such as an overall test of the whole model, which is therefore not reported. Single coefficients, single-df contrasts, and the three-df phenotype test remain estimable [18], and the phenotype part of the covariance matrix was well conditioned. We kept Model 3 as the primary model for three reasons. First, its adjustment set (the traditional cardiovascular risk factors) was fixed in the original analysis plan, and the rank limit comes from the survey design rather than the model: with 30 PSUs in 15 strata, covariance matrices from Taylor linearization or balanced repeated replication have a rank of at most 15 in any software. Eliminating the warning would have required removing at least four parameters from the confounder set to accommodate the variance estimator rather than the research question. Second, rank deficiency does not change how the variance of a single coefficient is estimated, and every test reported here has one or three numerator df [18]. Third, we checked the primary result with methods that do not use the singular matrix: a delete-one-PSU jackknife, whose covariance matrix is numerically of full rank; a Bonferroni-adjusted version of the phenotype test that uses only single-coefficient variances [18]; and four full-rank models (15 or fewer parameters) that keep age, sex, race and Hispanic origin, BMI, hypertension, diabetes, smoking, and cholesterol. These included a compact Model 3 and three models that omitted income. The compact Model 3 combines missing income with an income-to-poverty ratio ⩾1.3, combines non-Hispanic Asian adults with the other or multiracial group, and uses non-HDL cholesterol instead of total and HDL cholesterol. These checks were reported as sensitivity analyses and were not selected based on their results. Because the primary variance is estimated from only 15 stratum contrasts, we also computed a Satterthwaite-type effective df for the primary variance and used it to recompute the primary CI as a conservative check.

Sensitivity analyses repeated Model 3 (a) in adults aged ⩾40 years; (b) after excluding adults taking any antihypertensive or glucose-lowering medication, which removes most users of renin-angiotensin system inhibitors and sodium-glucose cotransporter 2 (SGLT2) inhibitors, drugs that lower UACR [1]; (c) with an atherosclerotic outcome (coronary heart disease, angina, myocardial infarction, or stroke) that excluded heart failure; (d) with heart failure alone; (e) with KDIGO A2 and A3 categories within eGFR ⩾60 mL/min/1.73 m^2; and (f) with $\log_2$(UACR) within eGFR ⩾60 mL/min/1.73 m^2. Missing data and outcome coding were examined by (g) multiple imputation by chained equations (20 imputations) of missing income, BMI, hypertension, diabetes, and smoking in all 5,282 analytic adults, with income in three categories and no missing category, and with estimates combined by Rubin's rules; (h) excluding adults with missing income (complete-case analysis); (i) omitting income from the model; (j) excluding the 22 partial CVD responders; and (k) counting the 25 indeterminate adults as non-cases. Excluded and included adults were compared on weighted characteristics.

For recognition status, we estimated the weighted proportion with unrecognized risk overall and by insurance status and income (income-to-poverty ratio <1.3 versus ⩾1.3); differences were tested with survey-weighted logistic regression. For PREVENT, we estimated by phenotype the mean predicted risk with and without UACR, the mean difference, and the proportions moved to a higher or lower risk category.

Analyses were performed in SPSS Statistics version 31.0.1 (IBM Corp. Released 2025. IBM SPSS Statistics for Windows, Version 31.0.1. Armonk, NY) with the Complex Samples procedures (CSPLAN, CSTABULATE, CSDESCRIPTIVES, and CSLOGISTIC). All derived variables (sample flags, phenotype, CVD, and covariates) were independently recoded from the raw NHANES variables in R (version 4.3.3) and matched the SPSS coding for every participant. Estimates were then recomputed with the R survey package (version 4.2.1) [19]. Of 96 estimates taken from a single complete SPSS run, 95 matched the precision SPSS prints, and one PREVENT confidence limit differed by 0.0001 percentage points because the SPSS syntax rounds the PREVENT coefficients. The delete-one-PSU jackknife standard error of the primary log OR was within 0.3% of the linearization standard error. Multiple imputation used the mice package (version 3.16.0). Unweighted counts not printed by the Complex Samples procedures were obtained with the SPSS DESCRIPTIVES and FREQUENCIES procedures. All tests were two-sided with $\alpha = 0.05$. The complete SPSS syntax and the R and Python verification code are available from the corresponding author upon reasonable request.

Results

Participants

The 5,282 adults in the analytic sample represented about 224.2 million U.S. adults (Figure *1*). Their weighted mean age was 48.8 years, and 50.9% were women. Overall, 9.4% (95% CI: 8.3-10.6) reported prevalent CVD (657 cases). Compared with the analytic sample, the 473 examined, nonpregnant adults excluded for missing laboratory or CVD data were older (51.3 versus 48.8 years) and more often had

hypertension (58.2% versus 48.7%) and CVD (14.4% versus 9.4%). Compared with adults included in the models, the 141 adults excluded for missing covariates were younger (42.8 versus 49.0 years) and more often women (60.5% versus 50.7%), with similar CVD prevalence (7.2% versus 9.5%).

Prevalence of eGFR-albuminuria phenotypes

Albuminuria with preserved eGFR was the most common abnormal kidney phenotype. It was present in 7.8% (95% CI: 6.9-8.7) of U.S. adults, or about 17.4 million people. Reduced eGFR without albuminuria was present in 4.2% (95% CI: 3.4-5.1; about 9.4 million), and both markers were present in 2.1% (95% CI: 1.6-2.7; about 4.6 million). Any albuminuria was present in 9.8% of adults, and 79.1% (95% CI: 73.8-83.5) of them had an eGFR ⩾60 mL/min/1.73 m^2. Therefore, four of every five adults with albuminuria would not be identified by eGFR alone.

Participant characteristics

Adults with albuminuria and preserved eGFR were older than those without kidney markers (mean age 55.6 versus 46.6 years) but about 15 years younger than those with reduced eGFR without albuminuria (70.6 years) (Table *1*). Their mean eGFR (95.7 mL/min/1.73 m^2) was close to that of the reference group (98.8 mL/min/1.73 m^2). Compared with the reference group, they more often had hypertension (70.5% versus 44.6%) and diabetes (41.8% versus 10.6%), had a higher mean systolic blood pressure (130.2 versus 119.4 mm Hg), and more often smoked (18.4% versus 14.2%). Most (91.6%) had health insurance.

Characteristic	Overall	No kidney markers (ref.)	Albuminuria, preserved eGFR	Reduced eGFR only	Both markers
Unweighted n	5,282	4,367	465	308	142
Weighted % of U.S. adults	100	86.0	7.8	4.2	2.1
Age, y, mean	48.8	46.6	55.6	70.6	68.1
Age, y, SE	0.5	0.5	1.1	0.9	0.6
Female, %	50.9	50.6	51.7	59.5	44.2
Non-Hispanic White, %	60.7	60.6	54.8	73.2	60.5
Non-Hispanic Black, %	10.7	10.0	13.1	15.6	20.6
Hispanic, %	16.7	17.5	16.8	5.1	5.1
Non-Hispanic Asian, %	6.2	6.3	7.9	1.6	7.3
Other or multiracial, %	5.7	5.6	7.5	4.5	6.4
Income-to-poverty ratio <1.3, %	16.3	16.0	18.6	16.4	21.8
Health insurance, %	90.7	90.1	91.6	98.6	97.4
BMI, kg/m^2, mean	29.7	29.5	30.8	30.6	31.4
BMI, kg/m^2, SE	0.3	0.3	0.4	0.3	0.8
Systolic BP, mm Hg, mean	120.8	119.4	130.2	125.0	135.0
Systolic BP, mm Hg, SE	0.4	0.4	1.7	1.3	1.7
Hypertension, %	48.7	44.6	70.5	72.7	89.0
Antihypertensive medication, %	24.7	19.8	45.0	58.7	80.3
Diabetes, %	14.6	10.6	41.8	29.0	49.7
HbA1c, %, mean	5.7	5.6	6.7	6.0	6.6
HbA1c, %, SE	<0.1	<0.1	0.1	0.1	0.1
Current smoking, %	14.3	14.2	18.4	10.8	13.7
Total cholesterol, mg/dL, mean	188.2	189.3	186.9	178.4	168.5
Total cholesterol, mg/dL, SE	1.2	1.2	3.2	2.7	7.5
HDL cholesterol, mg/dL, mean	53.6	53.8	52.4	52.4	51.5

HDL cholesterol, mg/dL, SE	0.4	0.5	0.9	1.0	1.0
Cholesterol-lowering medication, %	22.5	18.4	39.8	53.3	67.6
eGFR, mL/min/1.73 m², mean	95.5	98.8	95.7	51.7	44.5
eGFR, mL/min/1.73 m², SE	0.5	0.5	1.4	0.6	1.7
UACR, mg/g, median	7.4	6.6	59.3	8.7	82.7
UACR, mg/g, 25th percentile	4.8	4.6	41.2	6.0	46.3
UACR, mg/g, 75th percentile	13.0	10.6	121.9	13.2	233.8
Composite CVD, unweighted cases	657	367	124	101	65
Composite CVD, %	9.4	6.4	22.2	30.8	43.8
Composite CVD, 95% CI lower limit, %	8.3	5.5	16.7	23.7	33.8
Composite CVD, 95% CI upper limit, %	10.6	7.3	28.9	38.8	54.3

TABLE 1: Weighted characteristics and prevalent CVD of U.S. adults by eGFR-albuminuria phenotype (NHANES August 2021-August 2023)

Percentages, means, SEs, and percentiles are weighted with WTPH2YR; n and CVD cases are unweighted. CVD confidence limits are logit-transformed 95% CIs with 15 degrees of freedom. Missing values (unweighted, of 5,282): systolic BP 136, hypertension status 92, BMI 52, cholesterol-lowering medication 22, smoking seven, insurance six, antihypertensive medication five, diabetes and HbA1c one each, and total and HDL cholesterol none; the income-to-poverty ratio was missing for 664 (13.5% weighted). Adults with missing income were kept in Model 3 through a "missing" category that is not interpreted; adults missing any other model covariate were excluded from the models (n = 141). Missing data were addressed in sensitivity analyses.

BMI: body mass index, BP: blood pressure, CI: confidence interval, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, HbA1c: glycated hemoglobin, HDL: high-density lipoprotein, NHANES: National Health and Nutrition Examination Survey, ref.: reference group, SE: standard error, UACR: urine albumin-to-creatinine ratio

Prevalent CVD and its association with phenotype

CVD prevalence increased across phenotypes: 6.4% in adults without kidney markers, 22.2% in those with albuminuria and preserved eGFR, 30.8% in those with reduced eGFR without albuminuria, and 43.8% in those with both markers (Table *1*). Among the five CVD components, heart failure showed the largest relative difference: 10.7% (95% CI: 7.3-15.5) in adults with albuminuria and preserved eGFR versus 1.4% (95% CI: 1.1-1.9) in adults without kidney markers.

Albuminuria with preserved eGFR was associated with CVD in all three models (Table *2*, Figure *2A*). The OR decreased from 4.25 without adjustment to 2.78 after adjustment for demographics and to 1.86 (95% CI: 1.23-2.81; Wald t = 3.19, 15 df; p = 0.006) after full adjustment, supporting the first hypothesis. The compact 15-parameter Model 3 gave nearly the same estimate (OR: 1.87; 95% CI: 1.24-2.82), as did the three other full-rank models (ORs 1.88-1.89; lower confidence limits 1.21-1.22) (Table *3*). The jackknife standard error was within 0.3% of the linearization standard error. With the conservative effective df of 4.4 instead of 15 (one stratum contributed 39% of the primary variance), the 95% CI widened to 1.10-3.13 (Wald t = 3.19, 4.4 df; p = 0.029).

Comparison	Model	OR	95% CI lower limit	95% CI upper limit	Wald t	p-value
Albuminuria, preserved eGFR versus no kidney markers	Model 1	4.25	2.89	6.25	8.02	<0.001
Albuminuria, preserved eGFR versus no kidney markers	Model 2	2.78	1.78	4.33	4.91	<0.001
Albuminuria, preserved eGFR versus no kidney markers	Model 3	1.86	1.23	2.81	3.19	0.006
Reduced eGFR only versus no kidney markers	Model 1	6.40	4.47	9.16	11.02	<0.001
Reduced eGFR only versus no kidney markers	Model 2	2.02	1.40	2.92	4.07	0.001
Reduced eGFR only versus no kidney markers	Model 3	1.67	1.16	2.40	2.98	0.009
Both markers versus no kidney markers	Model 1	10.96	6.77	17.74	10.60	<0.001
Both markers versus no kidney markers	Model 2	4.19	2.49	7.03	5.90	<0.001
Both markers versus no kidney markers	Model 3	2.53	1.42	4.51	3.42	0.004
Albuminuria, preserved eGFR versus reduced eGFR only (contrast)	Model 3	1.11	0.72	1.72	0.52	0.61
eGFR × albuminuria interaction (ratio of ORs)	Model 3	0.82	0.40	1.68	-0.60	0.56

TABLE 2: ORs for prevalent CVD by eGFR-albuminuria phenotype across sequential survey-weighted logistic regression models

Wald t: design-based Wald t test (log OR divided by its Taylor-series linearization standard error) with 15 design degrees of freedom; p-values are two-sided, and CIs use the same t distribution. All models were fit on the same 5,141 adults with complete covariates. Model 1 is unadjusted; Model 2 adjusts for age, sex, and race and Hispanic origin; Model 3 adds income-to-poverty ratio, BMI, hypertension, diabetes, current smoking, and total and HDL cholesterol. Overall phenotype effect (adjusted Wald F test, three and 13 degrees of freedom): Model 1 $F = 65.91$, $p < 0.001$; Model 2 $F = 16.28$, $p < 0.001$; Model 3 $F = 5.62$, $p = 0.011$. The contrast was estimated from Model 3, and the interaction was estimated from a separate model with the Model 3 covariates. Model 3 has more parameters than design degrees of freedom; see the Materials & Methods section and the full-rank rows of Table 3. CVD prevalence by phenotype is shown in Table 1.

BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, HDL: high-density lipoprotein, OR: odds ratio

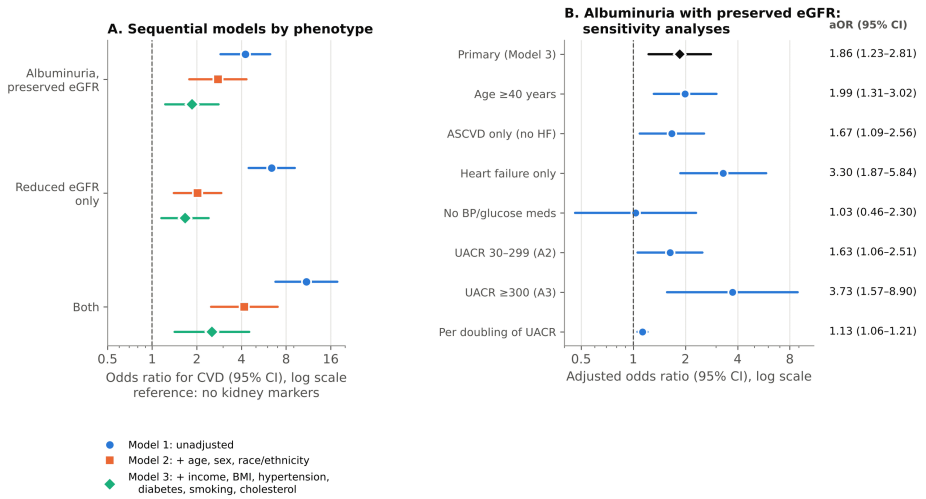


FIGURE 2: Adjusted odds of prevalent CVD

(A) ORs by phenotype across sequential models, with no kidney markers as the reference. (B) Sensitivity analyses for albuminuria with preserved eGFR (Model 3). Log scale; bars show 95% CIs. A2 and A3, KDIGO albuminuria categories (UACR in mg/g).

aOR: adjusted odds ratio, ASCVD: atherosclerotic cardiovascular disease (coronary heart disease, angina, myocardial infarction, or stroke), BMI: body mass index, BP/glucose meds: antihypertensive or glucose-lowering medication, CI: confidence interval, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, HF: heart failure, KDIGO: Kidney Disease: Improving Global Outcomes, ORs: odds ratios, UACR: urine albumin-to-creatinine ratio

Analysis	n	OR	95% CI lower limit	95% CI upper limit	Wald t	p-value
Primary analysis (Model 3)	5,141	1.86	1.23	2.81	3.19	0.006
Full rank: compact Model 3	5,141	1.87	1.24	2.82	3.24	0.006
Full rank: race in four groups, no income, total and HDL cholesterol	5,141	1.88	1.21	2.93	3.04	0.008
Full rank: race in four groups, no income, non-HDL cholesterol	5,141	1.88	1.22	2.90	3.11	0.007
Full rank: race in five groups, no income, non-HDL cholesterol	5,141	1.89	1.22	2.92	3.10	0.007
Adults aged ≥40 years	3,877	1.99	1.31	3.02	3.52	0.003
Excluding antihypertensive or glucose-lowering medication users	3,302	1.03	0.46	2.30	0.08	0.94
Outcome without heart failure (CHD, angina, MI, stroke)	5,138	1.67	1.09	2.56	2.56	0.022
Heart failure only	5,138	3.30	1.87	5.84	4.46	<0.001
eGFR ≥60 only: KDIGO A2 (UACR 30 to <300 mg/g)	4,708	1.63	1.06	2.51	2.41	0.030
eGFR ≥60 only: KDIGO A3 (UACR ≥300 mg/g)	4,708	3.73	1.57	8.90	3.23	0.006
eGFR ≥60 only: per doubling of UACR	4,708	1.13	1.06	1.21	3.91	0.001
Missing data: multiple imputation of missing covariates	5,282	1.82	1.19	2.78	3.00	0.009
Missing data: excluding adults with missing income (complete case)	4,502	1.96	1.25	3.05	3.21	0.006
Missing data: income omitted from the model	5,141	1.89	1.21	2.95	3.04	0.008
Outcome coding: excluding partial CVD responders	5,121	1.80	1.18	2.74	2.97	0.010
Outcome coding: indeterminate CVD counted as non-cases	5,166	1.82	1.17	2.82	2.91	0.011

TABLE 3: Sensitivity analyses: adjusted odds of CVD for albuminuria with preserved eGFR (Model 3)

Wald t: design-based Wald t test (log OR divided by its Taylor-series linearization standard error) with 15 design degrees of freedom; p-values are two-sided. For multiple imputation (20 imputed datasets), the estimate and standard error were combined by Rubin's rules and referred to the same t distribution. Full-rank rows: the compact Model 3 (15 parameters) uses race and Hispanic origin in four groups (non-Hispanic Asian combined with other or multiracial), income-to-poverty ratio <1.3 versus ≥1.3 or missing, and non-HDL cholesterol in place of total and HDL cholesterol; the other three full-rank models (15, 14, and 15 parameters) omit income and use the race grouping and cholesterol terms shown in each row. All four were estimated in SPSS and reproduced in R. These four models are the only models here with no more parameters than design degrees of freedom. All other models have 16-19 parameters, so their design-based covariance matrices are rank-deficient, and SPSS reports them as singular (see Materials & Methods). Rows marked eGFR ≥60 only are restricted to adults with eGFR ≥60 mL/min/1.73 m², with UACR <30 mg/g as the reference for A2 (408 exposed adults) and A3 (45 exposed adults). Outcome-coding rows excluded the 22 partial responders classified as having CVD, or counted the 25 indeterminate adults as non-cases. Missing-data and outcome-coding rows were estimated in SPSS and reproduced in R, except for multiple imputation, which was run in R (mice and survey packages); income was categorized into three categories, with no missing category in the imputation and complete-case rows.

CHD: coronary heart disease, CI: confidence interval, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, HDL: high-density lipoprotein, KDIGO: Kidney Disease: Improving Global Outcomes, MI: myocardial infarction, OR: odds ratio, UACR: urine albumin-to-creatinine ratio

In Model 3, the odds of CVD did not differ significantly between adults with albuminuria and preserved eGFR and those with reduced eGFR without albuminuria (OR: 1.11; 95% CI: 0.72-1.72; Wald t = 0.52, 15 df; p = 0.61). This interval is compatible with odds ranging from 28% lower to 72% higher, so the data neither confirm nor refute the second hypothesis. The overall phenotype effect remained significant (adjusted Wald F = 5.62 with three and 13 df, p = 0.011; Bonferroni-adjusted Wald t tests, largest t = 3.42, adjusted p = 0.011; compact model, adjusted Wald F = 6.45, p = 0.007). The interaction estimate (ratio of ORs: 0.82; 95% CI: 0.40-1.68; Wald t = -0.60, 15 df; p = 0.56) showed no evidence of departure from multiplicative joint effects, but the estimate was too imprecise to rule out such a departure.

Sensitivity analyses

The association was similar in adults aged ≥40 years and when heart failure was removed from the outcome (Table *3*, Figure *2B*). It was strongest for heart failure alone (OR: 3.30; 95% CI: 1.87-5.84). Among adults with

eGFR ⩾60 mL/min/1.73 m², the odds of CVD rose with albuminuria severity, from an OR of 1.63 for KDIGO A2 to 3.73 for A3, and by 13% per doubling of UACR, supporting the third hypothesis. Among adults taking no antihypertensive or glucose-lowering medication, the estimate was close to the null value and imprecise (OR: 1.03; 95% CI: 0.46-2.30); this subgroup had only 12 CVD cases with albuminuria and preserved eGFR. The primary estimate changed little when missing covariates were multiply imputed (OR: 1.82; 95% CI: 1.19-2.78), when adults with missing income were excluded (OR: 1.96; 95% CI: 1.25-3.05), when income was omitted (OR: 1.89; 95% CI: 1.21-2.95), and under alternative CVD coding (OR: 1.80 after excluding partial responders; OR: 1.82 after counting indeterminate adults as non-cases).

Unrecognized risk

Among adults with albuminuria and preserved eGFR, 35.6% (95% CI: 29.4-42.4), or about 6.2 million people, reported no diagnosis of hypertension, diabetes, kidney disease, or CVD. Only 3.2% (95% CI: 1.5-6.4) of the whole group had ever been told they had weak or failing kidneys; among all adults with albuminuria, this awareness was 10.9% (95% CI: 7.2-16.0). Adults with unrecognized risk had a mean age of 48.1 years and a median UACR of 52.5 mg/g. At the examination, 39.9% (95% CI: 29.0-52.0) of them met the blood pressure threshold for hypertension, 5.8% (95% CI: 3.2-10.2) met the diabetes criteria, almost all by HbA1c ⩾6.5%, and 12.9% (95% CI: 6.6-23.4) were current smokers.

The proportion of adults with unrecognized risk did not differ significantly by insurance status (35.5% insured versus 37.1% uninsured; survey-weighted logistic regression, Wald t = -0.21 for insured status, 15 df; p = 0.84). Among adults with reported income, it was higher in those with an income-to-poverty ratio ⩾1.3 than in those with a ratio <1.3 (40.8% versus 21.8%; Wald t = -3.19 for a ratio <1.3, 15 df; p = 0.006). In other words, lower-income adults in this group more often reported a diagnosed condition.

PREVENT risk with and without UACR

The PREVENT sample included 3,815 adults aged 30-79 years without CVD, representing 156.0 million adults. In those with albuminuria and preserved eGFR, adding UACR raised mean predicted 10-year total CVD risk from 9.9% to 12.7% (difference: 2.83 percentage points; 95% CI: 2.51-3.15) (Table *4*, Figure *3*). One in four (25.2%; 95% CI: 18.2-32.3), or about 2.7 million adults, moved to a higher risk category, and none moved to a lower category. The share at or above the 7.5% treatment threshold rose from 49.9% to 57.5%. In the subgroup with unrecognized risk, mean predicted risk rose from 6.1% to 8.0%, and 20.4% moved to a higher category. In adults without kidney markers, adding UACR slightly lowered mean predicted risk (from 5.0% to 4.6%), and 7.1% moved to a lower category. For adults with albuminuria and preserved eGFR, results were similar when the analysis was limited to adults with all inputs in range (n = 3,509; mean risk 9.2% to 11.8%; 24.0% moved up), when systolic blood pressure was capped at 180 mm Hg (24.9% moved up), and when the statin term was set to zero (mean risk 10.4% to 13.4%; 23.4% moved up). These figures describe changes in model predictions, not observed events.

Measure	All adults	No kidney markers	Albuminuria, preserved eGFR	Albuminuria, preserved eGFR, unrecognized risk	Reduced eGFR only	Both markers
Unweighted n	3,815	3,301	292	120	158	64
Base equation risk, mean %	5.9	5.0	9.9	6.1	16.0	19.5
UACR equation risk, mean %	5.7	4.6	12.7	8.0	14.3	24.1
Difference, percentage points	-0.16	-0.41	2.83	1.90	-1.66	4.59
Difference, 95% CI lower limit	-0.20	-0.44	2.51	1.44	-1.96	2.85
Difference, 95% CI upper limit	-0.11	-0.38	3.15	2.35	-1.36	6.32
Moved to a higher category, %	2.6	0.7	25.2	20.4	0	18.0
Moved higher, 95% CI lower limit	2.3	0.4	18.2	9.5	NA	8.9
Moved higher, 95% CI upper limit	3.0	1.1	32.3	31.3	NA	27.1
Moved to a lower category, %	6.8	7.1	0	0	16.6	0
Moved lower, 95% CI lower limit	6.0	6.2	NA	NA	7.7	NA
Moved lower, 95% CI upper limit	7.5	7.9	NA	NA	25.4	NA
Risk ≥7.5%, base equation, %	28.5	24.1	49.9	32.0	78.9	85.5
Risk ≥7.5%, UACR equation, %	26.4	21.4	57.5	39.2	70.8	94.6

TABLE 4: PREVENT 10-year total CVD risk with and without UACR by phenotype (adults aged 30-79 years without CVD)

Adults aged 30-79 years without self-reported CVD who had complete inputs for the total CVD equations (n = 3,815; 156.0 million weighted). Difference: mean risk from the UACR equation minus mean risk from the base equation, in percentage points, with a design-based 95% CI. Risk categories: <5%, 5% to <7.5%, 7.5% to <20%, and ≥20%; only ≥7.5% is a guideline threshold for PREVENT total CVD risk [17]. Statin use was approximated by self-reported cholesterol-lowering medication. Moved higher or lower: weighted proportion whose category changed when UACR was added, with Wald 95% CIs from SPSS CSDESCRIPTIVES (reproduced in R). Unrecognized risk: no reported diagnosis of hypertension, diabetes, kidney disease, or CVD. No hypothesis tests were performed for this table. Reclassification is model-based: it shows how predictions change, not improved calibration, discrimination, or outcomes.

CI: confidence interval, CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, NA: not applicable because no participant moved in that direction, PREVENT: Predicting Risk of Cardiovascular Disease EVENTs, UACR: urine albumin-to-creatinine ratio

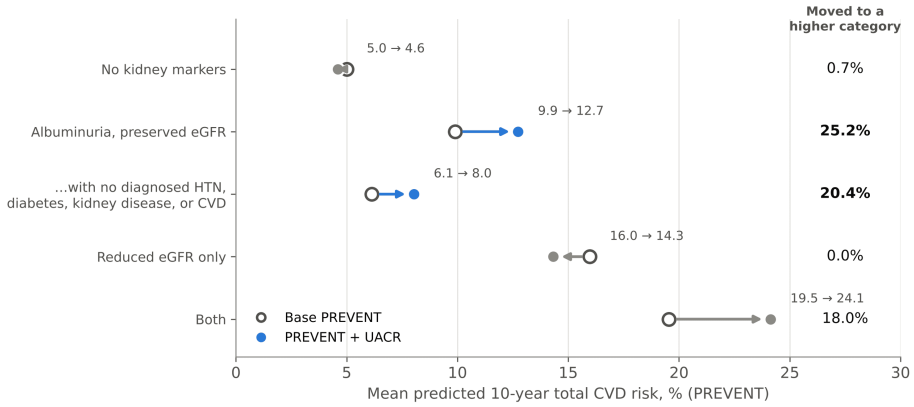


FIGURE 3: PREVENT 10-year total CVD risk with and without UACR

Mean predicted risk under the base equation (open circles) and the UACR-enhanced equation (filled circles) in adults aged 30-79 years without CVD (n = 3,815). The right column gives the share moved to a higher predicted-risk category. Predictions describe model behavior, not observed events.

CVD: cardiovascular disease, eGFR: estimated glomerular filtration rate, HTN: hypertension, PREVENT: Predicting Risk of Cardiovascular Disease EVENTs, UACR: urine albumin-to-creatinine ratio

Discussion

Principal findings

In this nationally representative sample from the August 2021-August 2023 NHANES cycle, about one in 13 U.S. adults (7.8%, about 17.4 million) had albuminuria with preserved eGFR. This group made up four of every five adults with albuminuria, and creatinine-based testing alone would not identify them. After adjustment for traditional risk factors, the phenotype was associated with 86% higher odds of prevalent CVD. The odds of CVD in this group did not differ significantly from those in adults with reduced eGFR without albuminuria, but the comparison was too imprecise to establish that the two phenotypes carry similar risk. The association increased with albuminuria severity and was strongest for heart failure. More than a third of affected adults reported no diagnosis of hypertension, diabetes, kidney disease, or CVD, and fewer than one in 25 had been told they had kidney disease. Adding UACR to PREVENT raised predicted risk in this group by almost three percentage points and moved one in four into a higher risk category.

Comparison with prior studies

The direction of the association is consistent with evidence from cohort studies. In the CKD Prognosis Consortium meta-analysis of general-population cohorts, higher UACR predicted cardiovascular mortality independently of eGFR, and the two markers were associated with mortality in a multiplicative manner without interaction [2]. Our fully adjusted interaction estimate (ratio of ORs: 0.82; 95% CI: 0.40-1.68) showed no significant departure from this multiplicative pattern, although it was too imprecise to confirm it. The Prevention of Renal and Vascular End-Stage Disease study showed that urinary albumin excretion predicted cardiovascular death in the general population even at levels then considered normal [3]. The Heart Outcomes Prevention Evaluation study linked albuminuria to cardiovascular events, death, and heart failure in people with and without diabetes [4]. The heart failure OR of 3.30 in our study is consistent with this literature and with the PREVENT UACR add-on equations, which also predict heart failure [9].

The low awareness found here also matches earlier work. Among NHANES adults with CKD stages G3-G4 who were at high risk of kidney failure, Chu and colleagues found that only 49.0% were aware of their disease in 2011-2016, with no change over time after adjustment [7]. Low testing may contribute. In a national laboratory database, about one in five adults with diabetes or hypertension had UACR testing between 2013 and 2019 [5], and in a multinational consortium, only 4.1% of adults with hypertension but no diabetes were tested [6]. In our study, the share with unrecognized risk did not differ significantly by insurance status, but few affected adults were uninsured, and the comparison was imprecise. This study therefore cannot determine whether the gap lies in testing practice or in access to care.

Interpretation

Several mechanisms could link albuminuria to CVD, although a cross-sectional association does not establish cause. Albuminuria may reflect generalized endothelial dysfunction and low-grade inflammation that also affect the coronary and cerebral circulation [20]. It may also mark end-organ damage from long-standing hypertension or hyperglycemia [20]. Because this study is cross-sectional, reverse causation is also possible: in heart failure, albuminuria is closely associated with clinical and biomarker evidence of systemic

congestion [21]. The especially strong association with heart failure should be interpreted with this in mind.

The near-null estimate among adults taking no antihypertensive or glucose-lowering medication should be interpreted cautiously. That subgroup had only 12 CVD cases with the exposure, so its 95% CI (0.46-2.30) is compatible with both no association and an effect as large as the primary estimate. The finding may also mean that the association is concentrated in adults with established hypertension or diabetes, in whom albuminuria marks end-organ damage [20]. Prospective data are needed to distinguish these explanations.

Adding UACR changed predicted risk in both directions. It raised predicted risk in adults with albuminuria and lowered it modestly in adults with low UACR. Among adults with albuminuria and preserved eGFR, the share at or above the 7.5% treatment threshold rose from 49.9% to 57.5% once UACR was included. In the subgroup with unrecognized risk, one in five moved to a higher category; because these adults reported no relevant diagnosis, routine care may not prompt a risk assessment. These shifts follow from the structure of the UACR equation: its positive ln(UACR) term raises predicted risk whenever UACR is high, so an upward shift in this group is expected [9]. Without follow-up for events, this study cannot show whether the UACR-enhanced estimates are better calibrated or discriminate better than the base equation.

Implications

These findings are consistent with the KDIGO practice point to test people at risk with both eGFR and urine albumin [1] and with the AHA framework of cardiovascular, kidney, and metabolic disease as one syndrome [8]. About two-thirds of affected adults already reported a diagnosis (hypertension, diabetes, kidney disease, or CVD) for which KDIGO advises albuminuria testing [1], so fuller use of existing guidance could reach them. Identifying the remaining third would require broader testing. Approximately 40% met the blood pressure threshold for hypertension at the examination. Whether broader testing, or using the UACR-enhanced PREVENT equation for treatment decisions, improves outcomes or is cost-effective cannot be judged from cross-sectional data and requires prospective evaluation.

Strengths and limitations

The strengths of this study include a nationally representative and contemporary sample; use of the 2021 race-free CKD-EPI creatinine equation; derived variables recoded from the raw files and estimates reproduced in R; multiple sensitivity analyses, including four full-rank models, a jackknife check, and multiple imputation; and a PREVENT implementation checked against pyprevent (base equations), the preventr test cases (UACR equations), and an R recomputation.

This study also has limitations. First, its cross-sectional design means that the temporal order of exposure and outcome cannot be established, and reverse causation is possible, especially for heart failure. Second, phenotypes were based on a single creatinine measurement and a single spot UACR. They do not meet the KDIGO criterion of persistence for three months, so they describe kidney phenotypes rather than diagnosed CKD [1], and transient albuminuria would misclassify some adults.

Third, outcomes and diagnoses were self-reported. CVD and recognition status depend on recall, and a reported absence of diagnosis does not mean the absence of disease. Twenty-two adults with incomplete CVD answers were classified from a single "yes" answer, and 25 were excluded as indeterminate; neither decision materially changed the estimate. Survival bias may also have excluded adults who died of CVD before the survey.

Fourth, missing data and selection may have affected the results. Adults excluded for missing laboratory or CVD data were older and more often had hypertension and CVD than the analytic sample, so the absolute prevalence of CVD may be underestimated. NCHS weights adjust for unit nonresponse, but not for these item-level exclusions [10]. ORs were stable under multiple imputation and a complete-case income analysis, but multiple imputation assumes that data are missing at random given the measured variables [22]. Medication data were also limited because the prescription file was not merged. Users of renin-angiotensin system or SGLT2 inhibitors could be excluded only through a broader proxy, and statin use in PREVENT was approximated by any cholesterol-lowering medication.

Fifth, some subgroups were small, and the survey design provided limited df. The reduced-eGFR phenotypes and the medication-free subgroup had few events. The design provides 15 df, whereas Model 3 and the sensitivity models have 16-19 parameters, so their design-based covariance matrices are rank-deficient, and SPSS reports them as singular. Single coefficients, single-df contrasts, and the three-df phenotype test remain estimable; the primary standard error agreed with the jackknife standard error, and the primary OR agreed with estimates from all four full-rank models. However, no overall model test can be reported. With few PSUs, the variance estimates themselves are imprecise: one stratum contributed 39% of the primary variance (effective df, 4.4), and with this df, the primary 95% CI widens to 1.10-3.13 (Wald $t = 3.19$, 4.4 df; $p = 0.029$) [18]. SPSS also issued step-halving convergence warnings for the contrast, interaction, and age ⩾40 models; R reached the same estimates with converged fits.

Finally, unweighted response rates in this cycle were low, at 34.6% for the interview and 25.7% for the

examination, although NCHS weighting adjusts for nonresponse [10]. PREVENT was developed to predict future events [9]; here, it describes how predicted risk shifts, not observed outcomes, so reclassification cannot be interpreted as improved calibration, discrimination, or outcomes [23]. Input values outside the permitted ranges were set to the nearest permitted limits (7.5% of the PREVENT sample), and restricting the analysis to adults with all inputs within range gave similar results. Residual confounding by unmeasured factors, such as diet, physical activity, and disease duration, is also possible.

Conclusions

Albuminuria with preserved eGFR is common among U.S. adults and accounts for most adults with albuminuria in the population, so creatinine-based testing alone would miss most affected adults. In this study, the phenotype was associated with prevalent CVD independently of traditional risk factors, and the association increased with albuminuria severity. Whether its risk differs from that of reduced eGFR without albuminuria could not be determined. Many affected adults reported no diagnosis that would usually prompt testing, and few had been told they had kidney disease.

Adding UACR to the PREVENT equations increased predicted risk in this group and moved a substantial share of affected adults into a higher-risk category. These cross-sectional findings support measuring UACR alongside eGFR in at-risk adults, as current guidance advises. Prospective studies with repeated UACR measurements and outcome data are needed to confirm the association with incident cardiovascular events and to test whether broader testing and UACR-enhanced risk estimation improve prevention.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. National Center for Health Statistics Ethics Review Board issued approval 2021-05. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **AI use statement:** The authors have declared that no AI tools were used during the work or in the drafting of this article. The authors take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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