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BACKGROUND

- When compared to the general population, PWH are at greater risk to develop CKD and end stage kidney disease.
- An assessment of urinary protein and albumin excretion, a marker of tubular and glomerular disease, respectively, can serve as an important prognostic measure of progression of CKD.
- Excess proteinuria and albuminuria serve as markers of kidney damage and are used to predict progression of kidney disease.

METHODS

- REPRIEVE (NCT02344290) is a randomized ASCVD prevention trial of PWH between ages 40 and 75 on stable ART.
- This is the baseline analysis report for the Kidney Ancillary Study to REPRIEVE. The analyses in this report examine proteinuria and albuminuria and how these values vary by clinical risk factors.
- All analyses are limited to Kidney Ancillary Study population and include participants with samples drawn on or before the start of treatment, who enrolled in REPRIEVE A5332 after protocol version 3 at 42 sites participating in the Kidney Ancillary Study.
- Definitions:
 - Proteinuria (urine protein to creatinine ratio):**
 - normal to mildly increased (<150mg/g)
 - moderately increased (150-500mg/g)
 - severely increased (>500mg/g)
 - Albuminuria (urine albumin to creatinine ratio):**
 - normal to mildly increased (<30mcg/mg)
 - moderately increased (30-300mcg/mg)
 - severely increased (>300mcg/mg)
- Statistical analysis:* We summarize participant characteristics overall and by urinary protein category. Single and multivariable log binomial regression was performed for each binary outcome. Moderately and severely increased were combined for modeling of proteinuria and albuminuria.

RESULTS

Table 1: Characteristics of Participants by Proteinuria Category

Characteristic*	Normal to Mildly Increased (n=1963)	Moderately Increased (n=656)	Severely Increased (n=74)
Age in years	49 (44, 53)	49 (45, 54)	48 (44, 53)
Natal female sex	641 (36%)	327 (53%)	45 (61%)
Race			
White	641 (33%)	167 (25%)	18 (24%)
Black or African American	926 (47%)	318 (48%)	39 (53%)
Asian	289 (15%)	150 (23%)	14 (19%)
GBD Super Region			
High Income	1243 (63%)	296 (45%)	33 (45%)
Lat America/Caribbean	110 (6%)	32 (5%)	2 (3%)
Southeast/East Asia	272 (14%)	149 (23%)	14 (19%)
Sub-Saharan Africa	338 (17%)	179 (27%)	25 (34%)
Diabetes	11 (1%)	4 (1%)	0 (0%)
Hypertension	589 (30%)	214 (33%)	20 (27%)
Obesity (BMI ≥ 30kg/m²)	507 (26%)	128 (20%)	13 (18%)
Current/former smoker	884 (45%)	284 (43%)	26 (36%)
eGFR (mL/min per 1.73m²)	98 (82, 111)	99 (84, 113)	91 (72, 112)
Current CD4 ct (c/mm³)	629 (468, 826)	595 (437, 775)	609 (443, 778)
HIV VL <400 cp/mL	1638 (98%)	495 (98%)	56 (98%)

*Continuous variables are described as Median (Q1, Q3). Other variables reported as count and percentage. The HIV viral load data reflects missing values for 465 participants.

In the REPRIEVE cohort, proteinuria and albuminuria were present among 27% and 9% of PWH despite 98% having HIV VL < 400 cp/mL.

RESULTS

Figure 1: Distribution of Proteinuria Among 2693 Participants

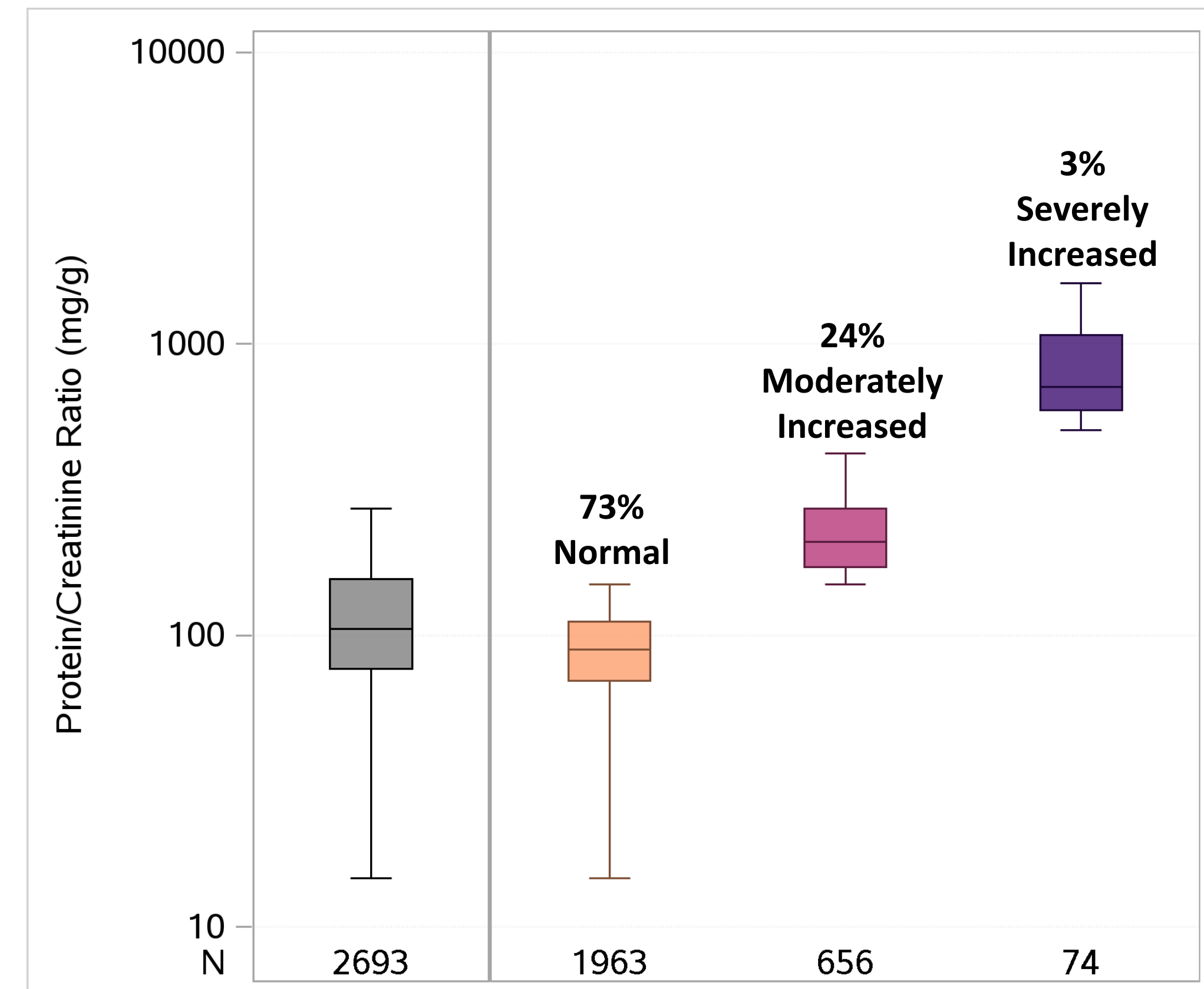


Figure 2: Distribution of Albuminuria Among 2791 Participants

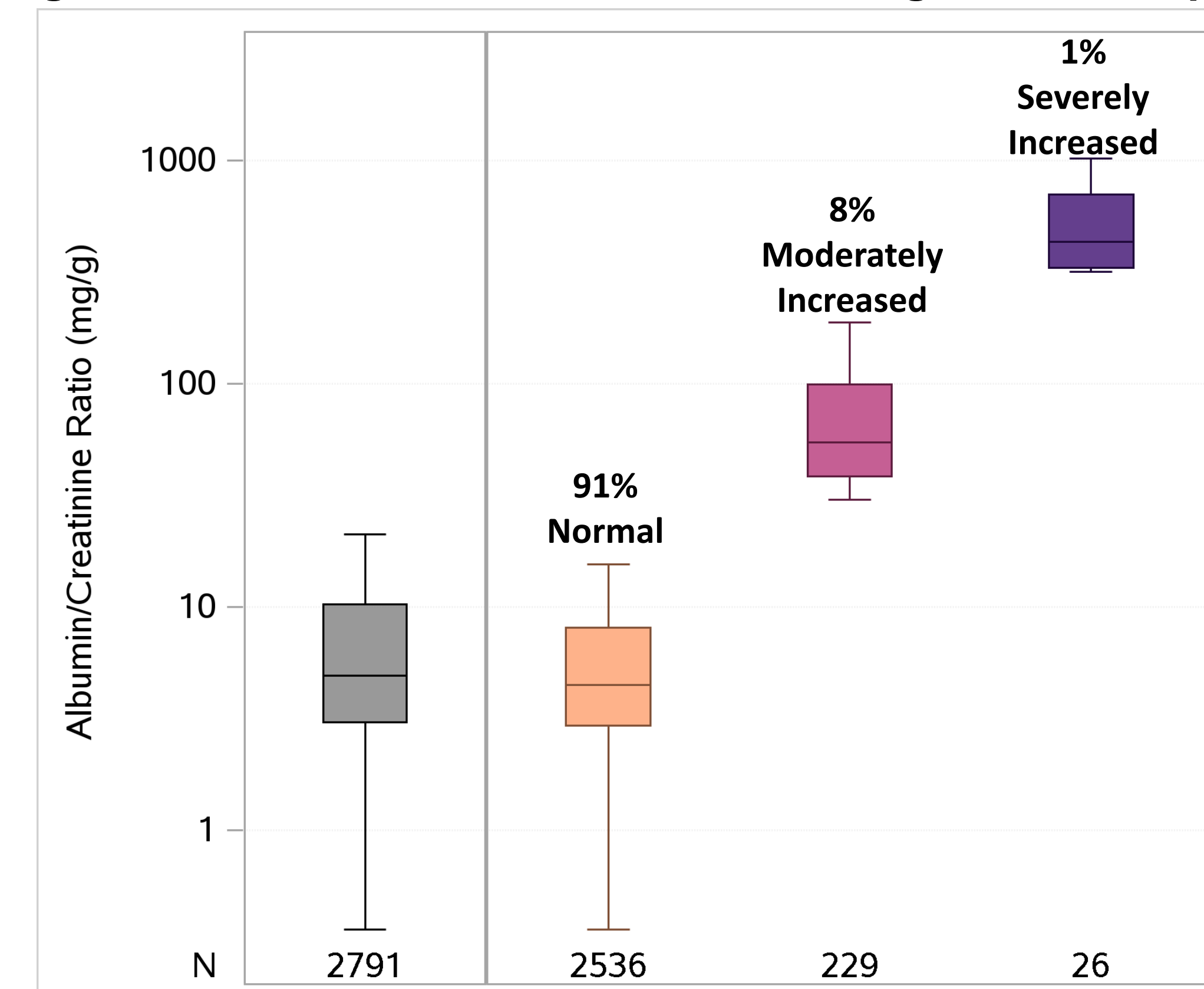


Figure 3: Adjusted Relative Risk of Elevated Proteinuria

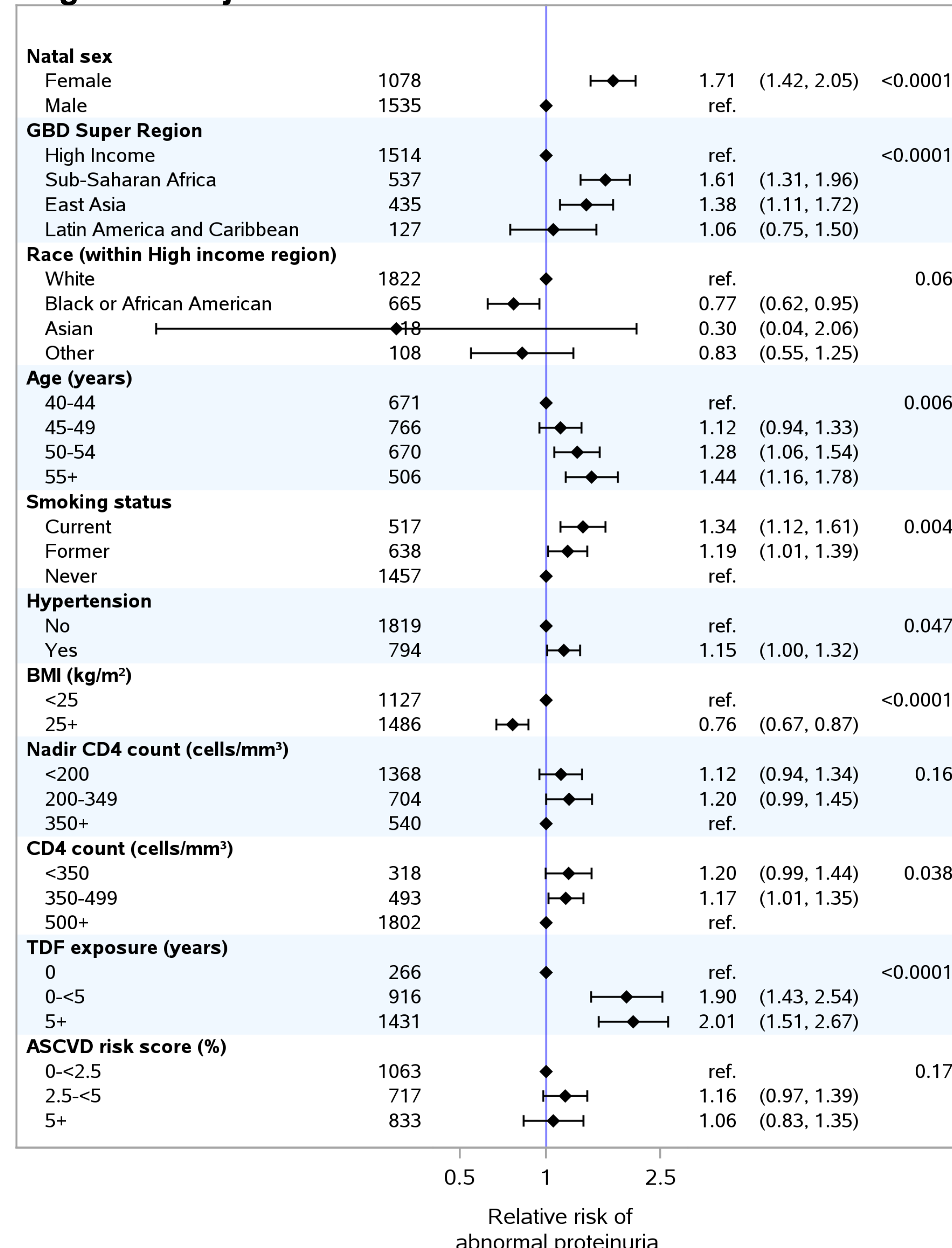
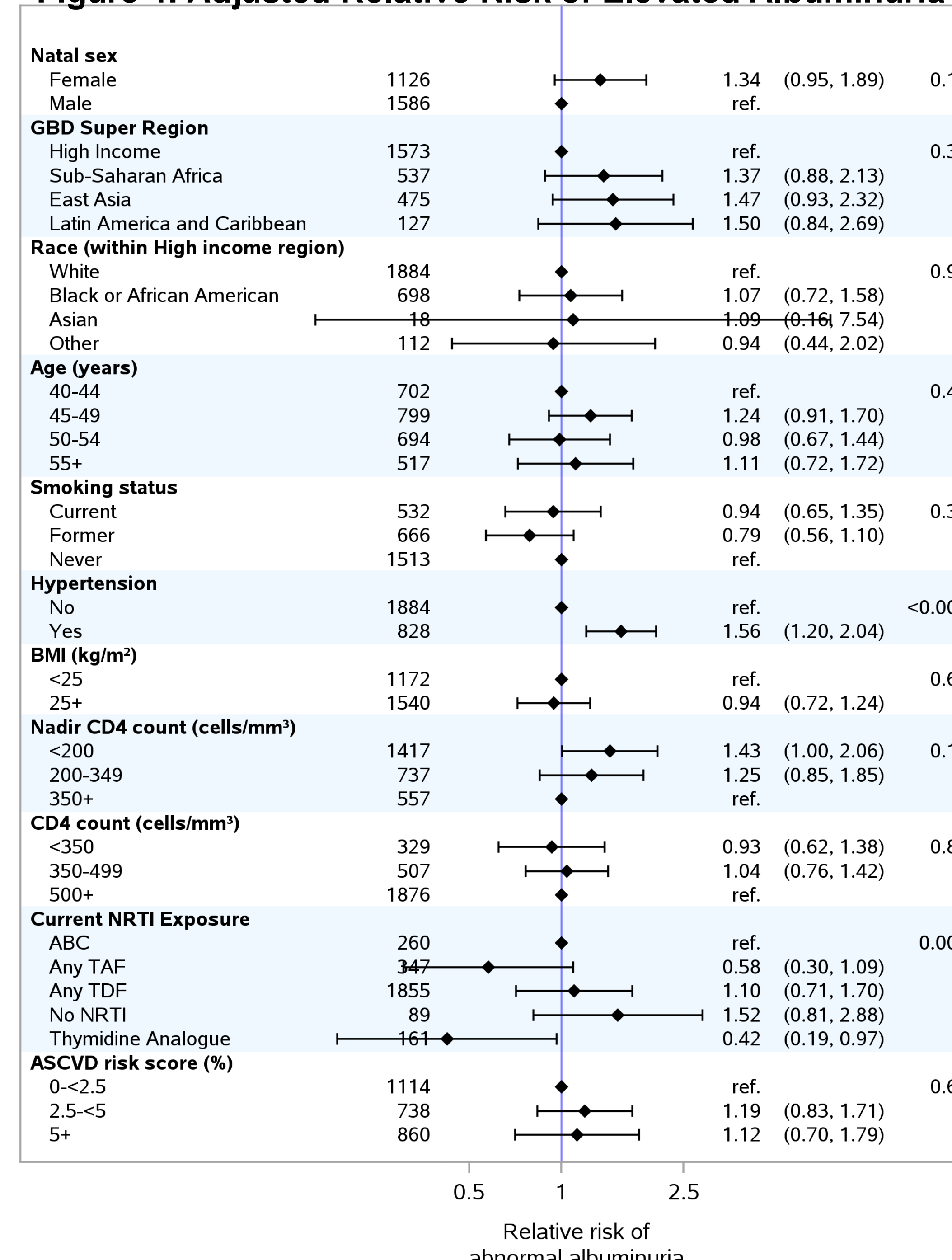


Figure 4: Adjusted Relative Risk of Elevated Albuminuria



FINDINGS

- Among REPRIEVE participants in the Kidney Ancillary Study, all were receiving ART, median CD4 count was 623 cells/mm³, 98% with HIV VL < 400cp/mL, eGFR 98 mL/min.
- The baseline prevalence of proteinuria and albuminuria was 27% and 9%, respectively.
- For participants with severely increased proteinuria, median eGFR was lower than for other groups (91 vs 98 mL/min). This was not observed among participants with severely increased albuminuria.
- Women were more likely to have excess proteinuria compared to men (35% vs. 21%) and albuminuria (11% vs. 8%).
- 38% and 37% of participants from Sub-Saharan Africa and Asian sites, respectively, had excess proteinuria. Similarly, albuminuria was more common from these sites compared to High Income regions.
- Among participants receiving tenofovir disoproxil fumarate, 32% had excess proteinuria and 10% excess albuminuria.
- Nadir and current CD4 counts were numerically lower for persons with excess proteinuria.
- In adjusted analysis, these factors remained associated with proteinuria (Fig 3):
 - Female sex
 - Enrollment from Sub-Saharan Africa and Asian sites
 - Older age
 - Current smoking
 - Diagnosis of hypertension
 - BMI < 25 kg/m²
 - Exposure to tenofovir disoproxil fumarate
- In adjusted analysis, these factors remained associated with albuminuria (Fig 4):
 - Diagnosis of hypertension
 - Certain NRTI exposures

CONCLUSIONS

- The proportion of PWH with suppressed viremia in the REPRIEVE cohort with excess proteinuria was 27%, a significant proportion of the cohort.
- Several factors related to excess proteinuria were as previously reported, including older age, diagnosis of hypertension, current smoking, and use of tenofovir disoproxil fumarate.
- The association with female sex and enrollment from Sub-Saharan Africa and Asian sites require additional analysis and an assessment of why these differences were noted. Potential explanations include:
 - Exposure to additional factors causing proteinuria.
 - Lack of access to prevention services.
- Excess albuminuria was present in 9% of the cohort.
 - Hypertension was independently associated with albuminuria.
 - There were also differences based on NRTI use.
- Future analyses will focus on the relationship of excess proteinuria and albuminuria or progressive kidney function declines and the role of statins to prevent CKD.

ADDITIONAL KEY INFORMATION

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