Table S1: Descriptive Statistics for AASK and CRIC Data Individually

AASK Data	**Non-Black (N=0)**		**Black without APOL1 (N=424)**		**Black with APOL1 (N = 96)**	
	#, Mean	***% (SD)***	***#, Mean***	***% (SD)***	***#, Mean***	***% (SD)***
ESKD			54	13%	28	29%
AGE			54.7	(9.9)	53.9	(9.9)
SEX						
Male			266	62.7%	51	53.1%
Female			158	37.3%	45	46.9%
BASELINE PROTEINURIA LEVEL						
UPCR ≤ 0.220 mg/mg			319	75.2%	54	54.2%
0.220 mg/mg < UPCR ≤ 1 mg/mg			70	16.5%	32	33.3%
UPCR > 1 mg/mg			32	8.3%	12	12.5%
MEAN UPCR (mg/mg)			0.3	(0.8)	0.5	(0.9)
eGFR (cL/min/1.73 m^2)			38.5	(14.6)	33.6	(15.7)
DIABETES						
Has Diabetes			424	100%	96	100%

CRIC Data	**Non-Black (N=2911)**		**Black without APOL1 (N=1146)**		**Black with APOL1 (N = 278)**	
	#, Mean	***% (SD)***	***#, Mean***	***% (SD)***	***#, Mean***	***% (SD)***
ESKD	592	20%	376	33%	124	45%
AGE	59.6	(11.1)	58.9	(9.7)	54.0	(12.7)
SEX						
Male	1777	61%	565	49.3%	132	47.5%
Female	1134	39%	581	50.7%	146	52.5%
BASELINE PROTEINURIA LEVEL						
UPCR ≤ 0.220 mg/mg	1719	59.1%	624	54.5%	112	40.3%
0.220 mg/mg < UPCR ≤ 1 mg/mg	621	21.3%	262	22.9%	97	34.9%
UPCR > 1 mg/mg	571	19.6%	260	22.7%	69	24.8%
MEAN UPCR (mg/mg)	0.9	(2.3)	1.0	(2.2)	1.1	(2.1)
eGFR (cL/min/1.73 m^2)	51.0	(16.2)	40.0	(13.2)	40.8	(14.5)
DIABETES						
Has Diabetes	1389	47.7%	621	54.2%	114	41%
HISPANIC						
Yes	541	18.6%	7	0.6%	0	0%
HEALTH INSURANCE						
None	176	6%	56	4.9%	27	9.7%
Medicare	1070	36.8%	371	32.4%	69	24.8%
Medicaid / VA / Other	355	12.2%	313	27.3%	68	24.5%
Private	546	18.8%	133	11.6%	33	11.9%

Unknown / Missing	764	26.2%	273	23.8%	81	29.1%
INCOME						
$20,000 or under	679	23.3%	442	38.6%	101	36.3%
$20,001 - $50,000	677	23.3%	304	26.5%	67	24.1%
$50,001 - $100,000	667	22.9%	147	12.8%	43	15.5%
More than $100,000	503	17.3%	48	4.2%	9	3.2%
Unknown	385	13.2%	205	17.9%	58	20.9%
EDUCATION						
Less than High School	425	14.6%	311	27.1%	70	25.2%
High School Graduate	455	15.6%	267	23.3%	51	18.3%
Some College	734	25.2%	385	33.6%	102	36.7%
College Graduate or Higher	1297	44.6%	183	16%	55	19.8%
MARITAL STATUS						
Not Married	1018	35%	667	58.2%	170	61.2%
Married	1893	65%	479	41.8%	108	38.8%
ANKLE BRACHIAL INDEX						
ABI ≤ 0.9	347	11.9%	241	21%	43	15.5%
0.9 < ABI ≤ 1	483	16.6%	270	23.6%	65	23.4%
ABI > 1	2081	71.5%	635	55.4%	170	61.2%
BMI						
BMI < 25 kg/m^2	498	17.1%	136	11.9%	38	13.7%
25 kg/m^2 ≤ BMI < 30 kg/m^2	947	32.5%	200	23.5%	60	21.6%
30 kg/m^2 ≤ BMI < 40 kg/m^2	1161	39.9%	535	46.7%	124	44.6%
BMI ≥ 40 kg/m^2	305	10.5%	206	18%	56	20.1%
VISITED A NEPHROLOGIST						
Yes	1823	62.6%	769	67.1%	186	66.9%
DRINKING LAST 12 MONTHS						
Yes	2027	69.6%	602	52.5%	161	57.9%
MARIJUANA						
Yes	997	34.2%	402	35.1%	111	39.9%
EVER USE DRUGS						
Marijuana Only	658	22.6%	267	23.3%	68	24.5%
Cocaine, Heroin, or Speed	366	12.6%	144	12.6%	45	16.2%
No Drugs	1887	64.8%	735	64.1%	165	59.4%
CAUSE OF RENAL DISEASE						
Diabetes	706	24.3%	327	28.5%	52	18.7%
Hypertension	338	11.6%	231	20.2%	71	2525%
Other	533	18.3%	82	7.2%	25	9%
Don't Know	1334	45.8%	506	44.2%	130	46.8%
FAMILY HISTORY OF CAD						

Yes	382	13.1%	169	14.7%	36	12.9%
FAMILY HISTORY OF RD						
Yes	329	11.3%	244	21.3%	73	26.3%
CONGESTIVE HEART FAILURE						
Yes	219	7.5%	162	14.1%	28	10.1%
STROKE						
Yes	217	7.5%	173	15.1%	31	11.2%
CARDIO-VASCULAR DISEASE						
Yes	901	31%	461	40.2%	90	32.4%
ATRIAL FIBRILLATION						
Yes	454	15.6%	247	21.6%	38	13.7%
HYPERTENSION						
Yes	2353	80.8%	1062	92.7%	263	94.6%
ANEMIA						
Yes	1098	37.7%	655	57.2%	145	52.2%
DEPRESSION						
Mild	2442	83.9%	965	84.2%	231	83.1%
Moderate	469	16.1%	181	15.8%	47	16.9%

Table S2: Relevant Hazard Ratios from Sensitivity Analysis

Increased risk of ESKD for APOL1 patients (expressed as hazard ratios), stratified by proteinuria levels. No substantial differences are seen between any of the sensitivity scenarios tested. Risk of ESKD associated with having APOL1 is higher if proteinuria levels are lower. Details on the different eGFR versions can be found in the appendix (calculations C1-C7)

		MINIMAL PROTEINURIA		MODERATE PROTEINURIA		HIGH PROTEINURIA	
		Hazard Ratio	***95% CI***	***Hazard Ratio***	***95% CI***	***Hazard Ratio***	***95% CI***
	Non Time-Varying Model	*(UPCR ≤ 0.220 mg/mg)*		*(0.22 mg/mg < UPCR ≤ 1 mg/mg)*		*(UPCR > 1 mg/mg)*	
1	Primary Analysis (*eGFR = 2009 CKD-EPI_AS_NRF*)**	1.87	[1.23, 2.84]	1.41	[1.06, 1.87]	1.22	[0.93, 1.61]
2	eGFR = 2009 CKD-EPI_ASR Equation**	1.92	[1.27, 2.91]	1.41	[1.06, 1.87]	1.22	[0.93, 1.61]
3	eGFR = 2012 CKD-EPI_AS_NRF Equation*	2.00	[1.26, 3.16]	1.37	[1.00, 1.89]	1.24	[0.99, 1.66]
4	eGFR = 2012 CKD-EPI_ASR Equation*	2.03	[1.28, 3.21]	1.38	[1.00, 1.89]	1.24	[0.92, 1.66]
5	Using Albuminuria Instead of Proteinuria**	3.01	[1.87, 4.57]	1.16	[0.81, 1.65]	1.12	[0.85, 1.47]
6	Adjust for Biomedical Factors*	1.80	[1.13, 2.86]	1.48	[1.07, 2.03]	1.25	[0.93, 1.70]
7	Adjust for Sociodemographic Factors*	1.88	[1.18, 2.97]	1.31	[0.95, 1.80]	1.19	[0.88, 1.60]
8	Adjust for Biomedical and Sociodemographic Factors*	1.77	[1.12, 2.81]	1.43	[1.03, 1.97]	1.23	[0.91, 1.67]
	Time-Varying Model	*(UPCR ≤ 0.220 mg/mg)*		*(0.22 mg/mg < UPCR ≤ 1 mg/mg)*		*(UPCR > 1 mg/mg)*	
9	Primary Analysis (*eGFR = 2009 CKD-EPI_AS_NRF*)**	2.04	[1.10, 3.77]	1.70	[1.20, 2.40]	1.39	[1.11, 1.74]
10	eGFR = 2009 CKD-EPI_ASR Equation**	2.12	[1.15, 3.92]	1.70	[1.20, 2.40]	1.38	[1.10, 1.73]
11	eGFR = 2012 CKD-EPI_AS_NRF Equation*	2.39	[1.25, 4.54]	1.79	[1.22, 2.63]	1.28	[1.00, 1.63]
12	eGFR = 2012 CKD-EPI_ASR Equation*	2.44	[1.28, 4.64]	1.79	[1.22. 2.63]	1.28	[1.00, 1.64]
13	Proteinuria as a continuous value**	2.69	[1.32, 5.49]	1.90	[1.38, 2.62]	1.60	[1.32, 1.94]
14	Using Albuminuria Instead of Proteinuria**	2.12	[0.96, 4.70]	1.57	[1.13, 2.18]	1.38	[1.06, 1.79]
15	Adjust for Biomedical Factors*	2.29	[1.20, 4.36]	1.76	[1.19, 2.59]	1.41	[1.10, 1.81]
16	Adjust for Sociodemographic Factors*	2.24	[1.18, 4.27]	1.62	[1.10, 2.39]	1.32	[1.03, 1.69]
17	Adjust for Biomedical and Sociodemographic Factors*	2.23	[1.17, 4.25]	1.67	[1.14, 2.47]	1.40	[1.09, 1.79]

** CRIC and AASK studies both used (N = 4855)

* CRIC study only (N = 4335)

Sensitivity Analysis Details: The following descriptions describe how each model differs from the primary analysis presented in the main manuscript. Sensitivity analysis results 1-8 reflect the non time-varying model sensitivity analysis while sensitivity analysis results 9-17 reflect the time-varying model sensitivity results.

1) Primary analysis for the non time-varying models. Estimates derived from a Cox proportional hazards model, adjusting for age, sex, diabetes, estimated glomerular filtration rate, and urine protein to creatinine ratio. This version uses the 2009 CKD-EPI_AS_NRF equation for eGFR.
2) Use the 2009 CKD-EPI_ASR equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
3) Use the 2012 CKD-EPI_AS_NRF equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
4) Use the 2012 CKD-EPI_ASR equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
5) Instead of using Proteinuria at baseline visit, use Albuminuria.
6) Adjust for additional biomedical factors including ankle brachial index, BMI, history of visiting a nephrologist, drinking in the last 12 months, marijuana, other drug use (cocaine, heroin, speed), cause of renal disease, family history of CAD, family history of RD, congestive heart failure, stroke, cardio-vascular disease, atrial fibrillation, hypertension, anemia, and depression.
7) Adjust for sociodemographic factors including Hispanic, health insurance, income, education, and marital status.
8) Adjust for all biomedical and sociodemographic characteristics specified in models 8 and 9.
9) Primary analysis for the time-varying models. Estimates derived from a Cox proportional hazards model, adjusting for age, sex, diabetes, estimated glomerular filtration rate, and urine protein to creatinine ratio. This version uses the 2009 CKD-EPI_AS_NRF equation for eGFR.
10) Use the 2009 CKD-EPI_ASR equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
11) Use the 2012 CKD-EPI_AS_NRF equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
12) Use the 2012 CKD-EPI_ASR equation for eGFR instead of the 2009 CKD-EPI_AS_NRF equation.
13) Instead of categorizing proteinuria into categorical levels, use the log of UPCR and incorporate proteinuria in the model as a continuous variable
14) Instead of using Proteinuria, use Albuminuria. Baseline albuminuria is recorded. Albuminuria over time is estimated using calculation C.7.
15) Adjust for additional biomedical factors including ankle brachial index, BMI, history of visiting a nephrologist, drinking in the last 12 months, marijuana, other drug use (cocaine, heroin, speed), cause of renal disease, family history of CAD, family history of RD, congestive heart failure, stroke, cardio-vascular disease, atrial fibrillation, hypertension, anemia, and depression.
16) Adjust for sociodemographic factors including Hispanic, health insurance, income, education, and marital status.
17) Adjust for all biomedical and sociodemographic characteristics specified in models 8 and 9.

Item S1: Calculations for eGFR and UPCR to UACR

Calculation C.1: eGFR Calculation: 2009 CKD-EPI_ASR [1,2]

This calculation considers age, sex, race, and creatinine when fitting the equation to estimate eGFR. All variables are used using the calculation for estimation.

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times 0.993^{age} \times (1.159 \text{ if black})$$

Where A, B, and C are the following:

Female

- Scr ≤ 0.7
    - A = 143.538
    - B = 0.7
    - C = -0.329
- Scr > 0.7
    - A = 143.538
    - B = 0.7
    - C = -1.209

Male

- Scr ≤ 0.9
    - A = 141
    - B = 0.9
    - C = -0.411
- Scr > 0.9
    - A = 141
    - B = 0.9
    - C = -1.209

Calculation C.2: eGFR Calculation: 2009 CKD-EPI_ASR_NB [1,2]

This calculation considers age, sex, race, and creatinine when fitting the equation to estimate eGFR. However, the race variable is not used when using the calculation for estimation.

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times 0.993^{age}$$

Where A, B, and C are the following:

Female

- Scr ≤ 0.7
  - A = 143.538
  - B = 0.7
  - C = -0.329
- Scr > 0.7
  - A = 143.538
  - B = 0.7
  - C = -1.209

Male

- Scr ≤ 0.9
  - A = 141
  - B = 0.9
  - C = -0.411
- Scr > 0.9
  - A = 141
  - B = 0.9
  - C = -1.209

Calculation C.3: eGFR Calculation: 2009 CKD-EPI_AS_NRF [2]

This calculation considers age, sex, and creatinine when fitting the equation to estimate eGFR. Race is excluded when fitting this equation. Age, sex, and creatinine are all used when estimating eGFR with this equation

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times 0.9938^{age}$$

Where A, B, and C are the following

Female

- Scr ≤ 0.7
  - A = 143.7
  - B = 0.7
  - C = -0.241
- Scr > 0.7
  - A = 143.7
  - B = 0.7
  - C = -1.200

Male

- Scr ≤ 0.9
  - A = 142
  - B = 0.9
  - C = -0.302
- Scr > 0.9
  - A = 142
  - B = 0.9
  - C = -1.200

Calculation C.4: eGFR Calculation: 2012 CKD-EPI_ASR [2]

This calculation considers age, sex, race, creatinine, and cystatin C when fitting the equation to estimate eGFR. All variables are used using the calculation for estimation.

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times \left(\frac{CysC}{0.8}\right)^{D} 0.9952^{age} \times (1.08 \text{ if black})$$

Where A, B, and C are the following:

Female

- Scr ≤ 0.7 and Cys C ≤ 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.248
  - D = -0.375
- Scr > 0.7 and Cys C ≤ 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.601
  - D = -0.375
- Scr ≤ 0.7 and Cys C > 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.248
  - D = -0.711
- Scr > 0.7 and Cys C > 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.601
  - D = -0.711

Male

- Scr ≤ 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.207
  - D = -0.375
- Scr > 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.601
  - D = -0.375
- Scr ≤ 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.207
  - D = -0.711
- Scr > 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.601
  - D = -0.711

Calculation C.5: eGFR Calculation: 2012 CKD-EPI_ASR_NB [2]

This calculation considers age, sex, race, creatinine, and cystatin C when fitting the equation to estimate eGFR. However, the race variable is not used when using the calculation for estimation.

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times \left(\frac{CysC}{0.8}\right)^{D} 0.9952^{age}$$

Where A, B, and C are the following:

Female

- Scr ≤ 0.7 and Cys C ≤ 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.248
  - D = -0.375
- Scr > 0.7 and Cys C ≤ 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.601
  - D = -0.375
- Scr ≤ 0.7 and Cys C > 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.248
  - D = -0.711
- Scr > 0.7 and Cys C > 0.8
  - A = 130.815
  - B = 0.7
  - C = -0.601
  - D = -0.711

Male

- Scr ≤ 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.207
  - D = -0.375
- Scr > 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.601
  - D = -0.375
- Scr ≤ 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.207
  - D = -0.711
- Scr > 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.601
  - D = -0.711

Calculation C.6: eGFR Calculation: 2012 CKD-EPI_AS_NRF [2]

This calculation considers age, sex, race, creatinine, and cystatin C when fitting the equation to estimate eGFR. However, the race variable is not used when using the calculation for estimation.

$$eGFR = A \times \left(\frac{Scr}{B}\right)^{C} \times \left(\frac{CysC}{0.8}\right)^{D} 0.9961^{age}$$

Where A, B, and C are the following:

Female

- Scr ≤ 0.7 and Cys C ≤ 0.8
  - A = 130.005
  - B = 0.7
  - C = -0.219
  - D = -0.323
- Scr > 0.7 and Cys C ≤ 0.8
  - A = 130.005
  - B = 0.7
  - C = -0.544
  - D = -0.323
- Scr ≤ 0.7 and Cys C > 0.8
  - A = 130.005
  - B = 0.7
  - C = -0.219
  - D = -0.778
- Scr > 0.7 and Cys C > 0.8
  - A = 130.005
  - B = 0.7
  - C = -0.544
  - D = -0.778

Male

- Scr ≤ 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.144
  - D = -0.323
- Scr > 0.9 and Cys C ≤ 0.8
  - A = 135
  - B = 0.9
  - C = -0.544
  - D = -0.323
- Scr ≤ 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.144
  - D = -0.778
- Scr > 0.9 and Cys C > 0.8
  - A = 135
  - B = 0.9
  - C = -0.544
  - D = -0.778

Calculation C.7: UPCR to UACR Approximation Equation [3]

The following equation, can be used to approximate urine albumin to creatinine ratio (UACR) using urine protein to creatinine ratio (UPCR) in mg/g. We used this equation determine cutoffs for three categorical albuminuria levels (minimal, moderate, and severe) used in our sensitivity analysis. The selected cutoffs for the criteria were UPCR of 220 mg/g and 1000 mg/g which align with UACR of approximately 60 mg/g and 80 mg/g respectively.

Sumida K, Nadkarni GN, Grams ME, et al. Conversion of Urine Protein-Creatinine Ratio or Urine Dipstick Protein to Urine Albumin-Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis: An Individual Participant-Based Meta-analysis. Ann Intern Med 2020; 173: 426–435.

$$
\begin{aligned}
&Predicted\ UACR \\
&= \exp\left(5.392 + 0.3072 \times log\left(min\left(\frac{UPCR}{50}, 1\right)\right)\right. \\
&+ 1.5793 \times log\left(max\left(min\left(\frac{UPCR}{500}, \quad 1\right), \quad 0.1\right)\right) \\
&\left.+ 1.1266 \times log\left(max\left(\frac{UPCR}{500}, 1\right)\right)\right)
\end{aligned}
$$

References

[1] Levey AS, Stevens LA. Estimating GFR Using the CKD Epidemiology Collaboration (CKD-EPI) Creatinine Equation: More Accurate GFR Estimates, Lower CKD Prevalence Estimates, and Better Risk Predictions. *Am J Kidney Dis* 2010; 55: 622–627.

[2] Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. *N Engl J Med* 2021; 385: 1737–1749.

[3] Sumida K, Nadkarni GN, Grams ME, et al. Conversion of Urine Protein-Creatinine Ratio or Urine Dipstick Protein to Urine Albumin-Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis : An Individual Participant-Based Meta-analysis. *Ann Intern Med* 2020; 173: 426–435.