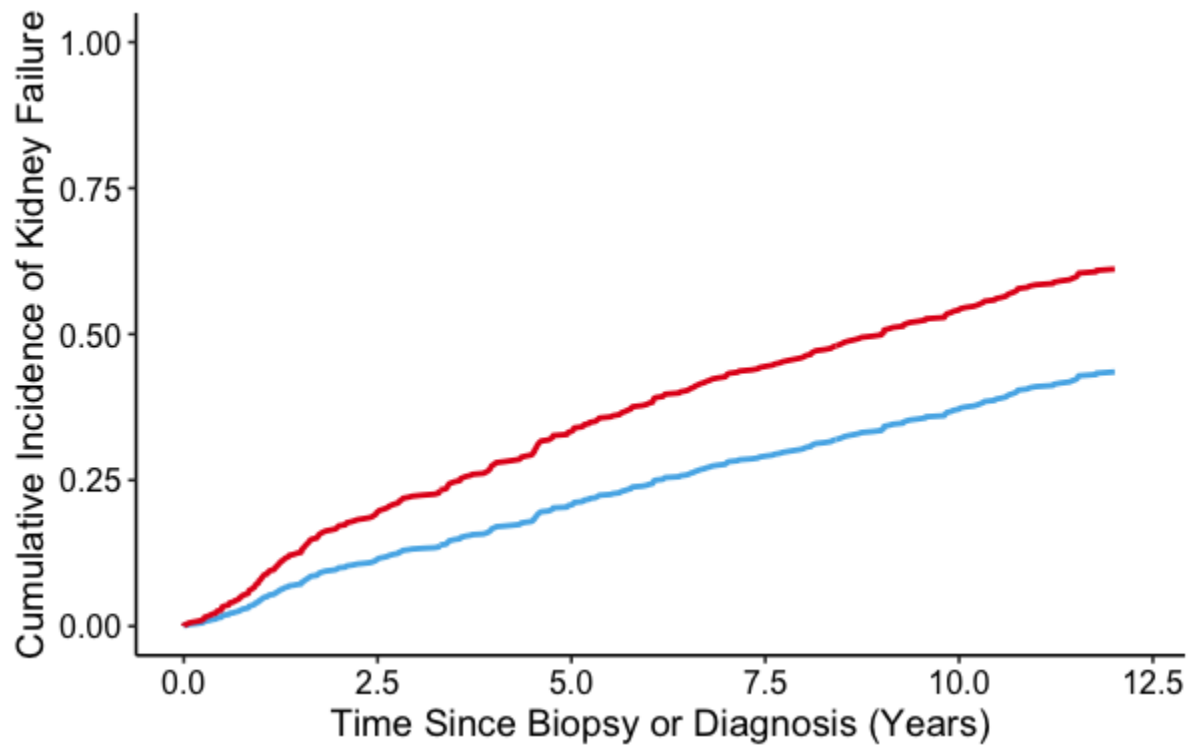
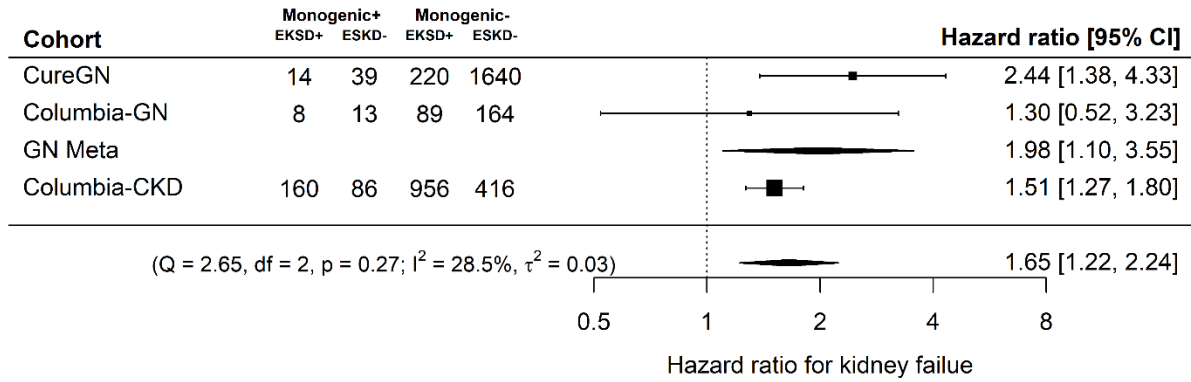


Supplementary Files:

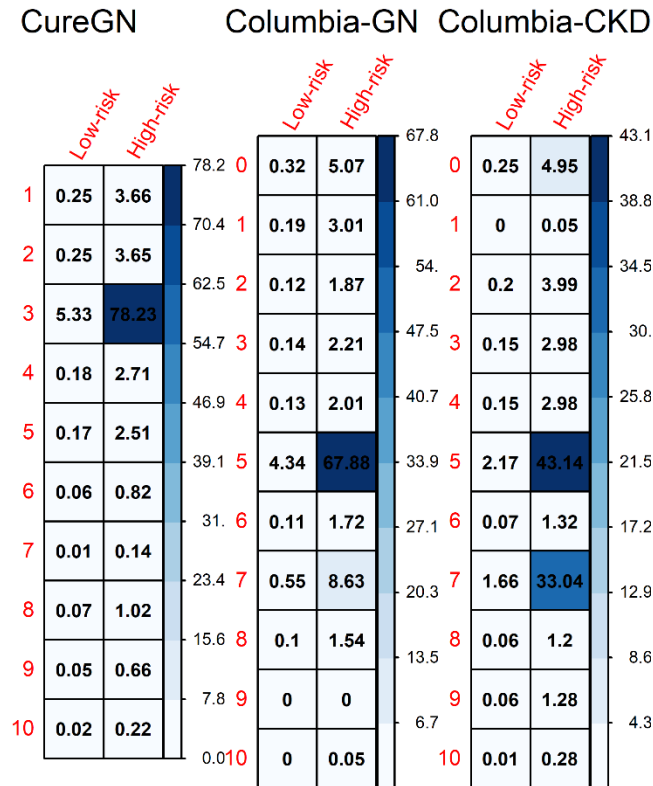
Supplementary Figure 1. Conditionally adjusted event curves showing kidney failure rates based on monogenic kidney disorders in the Columbia-GN cohort presented at the same time scale as the CureGN cohort.



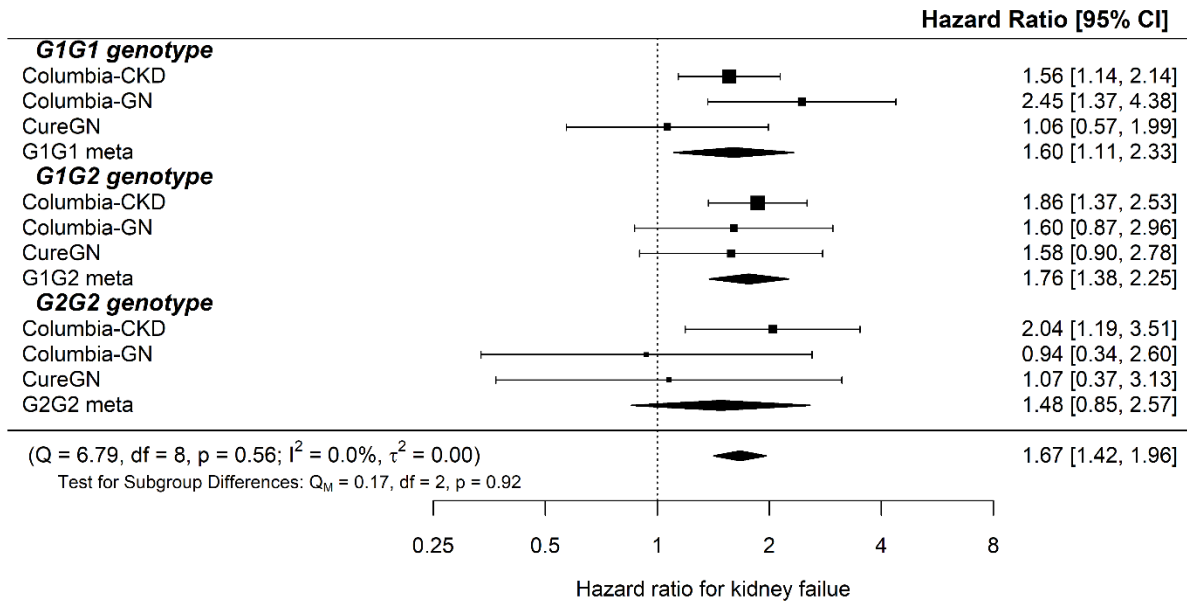
Supplementary Figure 2. Sensitivity analysis: restricted maximum likelihood random-effects meta-analysis of kidney failure risk across all three cohorts evaluating the effect of monogenic glomerular disorders using the fully adjusted Cox models and the use of the complete case analyses of Columbia-GN and Columbia-CKD that include eGFR and UACR values. Sub-analysis of genetic glomerular disorders within CureGN and Columbia-GN is also included.



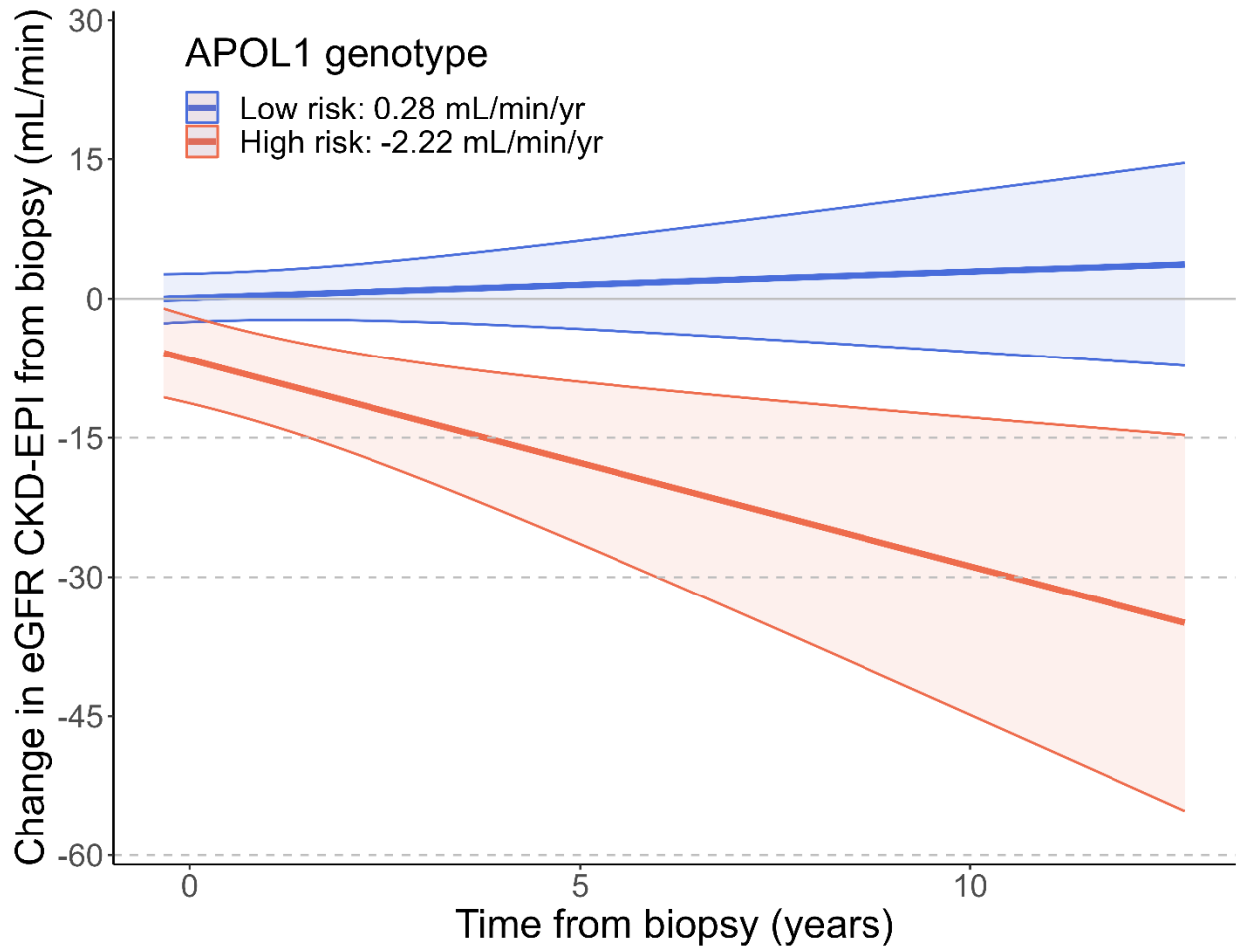
Supplementary Figure 3. Correlation plots between *APOL1* kidney risk genotype (x-axis) and genetic ancestry clusters (y-axis) using chi-squared tests across the 3 studies. Higher values show higher correlation strength.



Supplementary Figure 4. Restricted maximum likelihood random-effects meta-analysis of kidney failure risk in the CureGN, Columbia-GN and Columbia-CKD cohorts based on specific *APOL1* kidney risk genotypes using the fully adjusted Cox models.



Supplementary Figure 5. Rate of eGFR decline in CureGN based on *APOL1* kidney risk genotype from time of kidney biopsy.



Supplementary Table 4: Expanded baseline characteristics by genetics features across the three cohorts. Abbreviations: minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), IgA nephropathy (IgAN), congenital anomalies of the kidney and urinary tract (CAKUT), autosomal dominant polycystic kidney disease (ADPKD), autosomal recessive polycystic kidney disease (ARPKD).

	CureGN				Columbia-GN				Columbia-CKD				
	Full Cohort	Monogenic	APOL1 High-risk	ACMG SF	No Genetic Disorder	Full Cohort	Monogenic	APOL1 High-risk	No Genetic Disorder	Monogenic	APOL1 High-risk	No Genetic Disorder	
Participants, n	1913	53 (3%)	122 (6%)	100 (5%)	1651 (86%)	1098	39 (4%)	68 (6%)	997 (91%)	2716	279 (10%)	130 (5%)	2313 (85%)
Age at enrollment, median (IQR)	34 (15 - 53)	32 (14 - 46)	32 (17 - 46)	34 (17 - 57)	35 (15 - 54)	43.59 (31.80 - 54.79)	45 (29 - 54)	41 (30 - 47)	43 (32 - 55)	46.82 (27.73 - 61.20)	42 (28 - 58)	47 (31 - 57)	47 (27 - 62)
Age at biopsy, median (IQR)	33 (14 - 52)	30.8 (13.1 - 44.6)	29 (15.0 - 43.8)	33.3 (16.0 - 56.9)	33 (13.0 - 52.0)	34.44 (24.70 - 48.18)	37.7 (24.4 - 50.6)	35.84 (24.61 - 42.63)	33.85 (26.60 - 49.98)	NA	NA	NA	NA
Pediatric at biopsy, n (%)	638 (33%)	17 (30%)	44 (36%)	27 (27%)	552 (33%)	126 (11%)	6 (15%)	3 (4%)	67 (7%)	NA	NA	NA	NA
Developed Kidney Failure, n (%)	234 (12%)	14 (26%)	41 (34%)	10 (10%)	176 (11%)	393 (36%)	15 (38%)	41 (60%)	343 (34%)	1472 (54%)	174 (62%)	108 (83%)	1195 (52%)
Age at kidney failure, median (IQR)	37.18 (18.69 - 56.64)	36.92 (19.80 - 49.88)	32.32 (19.50 - 48.07)	39.45 (21.32 - 61.22)	37.67 (18.45 - 57.49)	43.93 (31.84 - 55.93)	39.33 (29.70 - 56.80)	37.15 (28.07 - 43.44)	40.56 (31.10 - 51.17)	43.29 (26.07 - 59.10)	42.25 (28.20 - 55.84)	42.10 (29.36 - 51.63)	46.92 (31.21 - 58.77)
Received kidney transplant, n (%)	129 (55%)	10 (71%)	15 (17%)	4 (40%)	103 (59%)	320 (81%)	12 (80%)	36 (88%)	278 (81%)	1244 (85%)	151 (87%)	95 (88%)	1001 (84%)
Family history of kidney disease, n (%)	648 (34%)	32 (60%)	61 (50%)	28 (28%)	532 (32%)	331 (30%)	18 (46%)	22 (32%)	294 (29%)	937 (34%)	179 (64%)	51 (39%)	711 (31%)
Missing	41 (2%)	0 (0%)	0 (0%)	1 (1%)	40 (2%)	NA	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
esCR at biopsy, ml/min/1.73m2 median (IQR)	83.33 (53.69 - 110.60)	79.55 (52.90 - 114.51)	62.81 (37.35 - 85.95)	91.57 (55.00 - 115.01)	85.17 (55.00 - 111.78)	48.16 (25.52 - 89.31)	37.25 (20.59 - 91.68)	37.13 (24.44 - 63.16)	52.49 (26.64 - 90.91)	27.24 (10.11 - 70.10)	29.86 (11.68 - 84.11)	11.86 (5.90 - 50.28)	29.15 (10.32 - 69.96)
Missing	286 (15%)	5 (9%)	17 (14%)	10 (10%)	256 (16%)	764 (70%)	13 (33%)	38 (58%)	713 (72%)	895 (33%)	21 (8%)	26 (20%)	849 (37%)
UPCR at biopsy, g/g median (IQR)	3.39 (1.10 - 7.27)	4.45 (2.07 - 8.32)	3.54 (1.63 - 7.74)	3.07 (1.09 - 5.83)	3.54 (1.63 - 7.74)	NA	NA	NA	NA	NA	NA	NA	NA
UPCR >= 3 g/g at biopsy, n (%)	769 (40%)	24 (45%)	51 (42%)	42 (42%)	658 (40%)	NA	NA	NA	NA	NA	NA	NA	NA
Missing	465 (24%)	12 (23%)	33 (27%)	21 (21%)	401 (24%)	NA	NA	NA	NA	NA	NA	NA	NA
UACR >= 3 g/g, n (%)	NA	NA	NA	NA	NA	0.74 (0.01 - 1.23)	1.23 (0.66 - 2.51)	1.18 (0.49 - 1.42)	0.55 (0.01 - 1.23)	0.13 (0.01 - 0.55)	0.07 (0.01 - 0.37)	0.34 (0.07 - 0.96)	0.14 (0.01 - 0.63)
Missing	NA	NA	NA	NA	NA	35 (3%)	4 (10%)	3 (5%)	28 (3%)	48 (2%)	5 (2%)	3 (2%)	40 (2%)
Self-described race and ethnicity						834 (74%)	16 (41%)	46 (70%)	752 (76%)	1051 (39%)	20 (7%)	31 (24%)	1001 (43%)
Asian, n (%)	164 (9%)	2 (4%)	0 (0%)	12 (12%)	150 (9%)	171 (16%)	4 (10%)	0 (0%)	167 (17%)	223 (8%)	17 (6%)	1 (1%)	205 (9%)
Black/African American, n (%)	282 (15%)	4 (8%)	106 (87%)	19 (19%)	106 (87%)	112 (10%)	4 (10%)	45 (66%)	66 (7%)	436 (16%)	29 (10%)	95 (93%)	217 (14%)
Native American, n (%)	13 (1%)	1 (2%)	1 (1%)	0 (0%)	11 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0(0%))	0 (0%)	0 (0%)	5 (0(2%))
Pacific Islander, n (%)	6 (0(3%))	1 (2%)	3 (2%)	0 (0%)	3 (0(2%))	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA	NA	NA	NA
Multiracial, n (%)	52 (3%)	1 (2%)	5 (4%)	2 (2%)	44 (3%)	2 (0(2%))	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown, n (%)	64 (3%)	6 (11%)	2 (2%)	2 (2%)	55 (3%)	51 (5%)	1 (3%)	4 (6%)	61 (6%)	314 (12%)	31 (11%)	9 (7%)	280 (12%)
White, n (%)	1332 (70%)	38 (72%)	5 (4%)	65 (65%)	1225 (74%)	743 (68%)	30 (77%)	31 (28%)	697 (70%)	1694 (62%)	202 (72%)	25 (19%)	1468 (63%)
Self-described race and ethnicity													
Hispanic or Latinx, n (%)	237 (12%)	12 (23%)	14 (11%)	12 (12%)	201 (12%)	197 (18%)	9 (23%)	24 (35%)	169 (17%)	687 (25%)	53 (19%)	35 (27%)	600 (26%)
Missing	3 (0%)	0 (0%)	1 (1%)	0 (0%)	2 (0(1%))	12 (1%)	1 (3%)	2 (3%)	10 (1%)	26 (1%)	5 (2%)	2 (2%)	21 (1%)
Hypertension at biopsy, n (%)	756 (40%)	25 (47%)	53 (44%)	49 (49%)	659 (39%)	383 (35%)	15 (38%)	34 (50%)	336 (34%)	1024 (38%)	111 (40%)	61 (47%)	855 (37%)
Diabetes Mellitus at biopsy, n (%)	18 (1%)	0 (0%)	0 (0%)	1 (1%)	17 (1%)	109 (10%)	3 (8%)	13 (19%)	93 (9%)	384 (14%)	20 (7%)	26 (20%)	338 (15%)
Immunosuppression use at biopsy, n (%)	608 (32%)	9 (17%)	32 (26%)	34 (34%)	536 (32%)	165 (15%)	1 (3%)	1 (1%)	163 (16%)	54 (2%)	0 (0%)	2 (2%)	52 (2%)
Missing	314 (16%)	12 (23%)	19 (16%)	13 (13%)	272 (16%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
RAAS inhibitor use at enrollment, n (%)	1498 (78%)	44 (83%)	103 (84%)	77 (77%)	1286 (78%)	241 (22%)	0 (0%)	3 (4%)	238 (24%)	60 (2%)	1 (0(4%))	1 (1%)	58 (3%)
GN Diagnosis													
MCD, n (%)	421 (22%)	11 (21%)	12 (10%)	24 (24%)	375 (23%)	84 (8%)	0 (0%)	2 (3%)	82 (8%)	NA	NA	NA	NA
FSGS, n (%)	488 (26%)	33 (62%)	90 (74%)	26 (26%)	349 (21%)	289 (26%)	35 (90%)	56 (82%)	204 (20%)	NA	NA	NA	NA
MN, n (%)	462 (24%)	2 (4%)	12 (10%)	23 (23%)	426 (26%)	176 (16%)	0 (0%)	4 (6%)	172 (17%)	NA	NA	NA	NA
IgAN, n (%)	542 (28%)	7 (13%)	8 (7%)	27 (27%)	501 (30%)	549 (50%)	4 (10%)	6 (9%)	539 (54%)	NA	NA	NA	NA
Non-GN Diagnosis													
Diabetic Kidney Disease, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	328 (12%)	8 (3%)	17 (13%)	303 (13%)
Congenital or Mendelian, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	693 (26%)	133 (48%)	11 (8%)	551 (24%)
Glomerular, non-CureGN diagnosis, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	724 (27%)	68 (24%)	23 (18%)	633 (27%)
Hypertension-associated kidney disease, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	244 (9%)	6 (2%)	32 (25%)	206 (9%)
Tubulointerstitial kidney disease, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	76 (3%)	9 (3%)	2 (2%)	65 (3%)
CKD of unknown etiology, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	422 (16%)	44 (16%)	34 (26%)	347 (15%)
Other, n (%)	NA	NA	NA	NA	NA	NA	NA	NA	NA	229 (8%)	11 (4%)	11 (8%)	208 (9%)

Supplementary Table 5. Predictors of monogenic kidney disorders and high-risk *APOL1* genotypes across all three cohorts.

	Adjusted OR Monogenic HR (95% CI), P	Adjusted OR <i>APOL1</i> HR (95% CI), P
<b>CureGN (n = 1913)</b>		
Family History	2.80 (1.57 - 4.98), $4.61 \times 10^{-4}$	1.51 (0.91 - 2.49), 0.11
Age at biopsy	1.00 (0.999 0 1.00), 0.79	1.00 (0.999 0 1.001), 0.86
Pathology Diagnosis		
MCD	Ref	Ref
FSGS	2.78 (1.35 - 5.74), $5.61 \times 10^{-3}$	8.86 (4.29 - 18.29), $4.19 \times 10^{-9}$
MN	0.18 (0.04 - 0.84), 0.029	0.88 (0.33 - 2.30), 0.79
IgAN	0.45 (0.17 - 1.18), 0.10	1.67 (0.59 - 4.73), 0.33
Race		
White	Ref	Ref
Asian	0.42 (0.10 - 1.80), 0.24	-
Black/African American	0.28 (0.10 - 0.81), 0.019	167 (64 - 432), $3.49 \times 10^{-25}$
Native American	1.46 (0.17 - 12.81), 0.73	11.9 (1.18 - 119), 0.036
Pacific Islander	4.80 (0.46 - 50.57), 0.19	364 (46 - 2892), $2.70 \times 10^{-8}$
Multiracial	0.51 (0.07 - 3.89), 0.51	28.5 (7.50 - 109), $9.62 \times 10^{-7}$
Unknown	2.37 (0.74 - 7.60), 0.15	3.37 (0.56 - 20.3), 0.18
Ethnicity		
Not Hispanic/Latinx	Ref	Ref
Hispanic/Latinx	1.10 (0.46 - 2.62), 0.83	2.46 (1.01 - 5.95), 0.047
<b>Columbia-GN (n = 1098)</b>		
Family History	1.69 (0.85 - 3.37), 0.14	0.91 (0.46 - 1.79), 0.78
Age at biopsy	1.00 (1.00 - 1.00), 0.84	1.00 (1.00 - 1.00), 0.98
Pathology Diagnosis		
MCD	Ref	Ref
FSGS	-	5.27 (1.15 - 24.23), 0.033
MN	-	0.56 (0.09 - 3.54), 0.54
IgAN	-	0.42 (0.07 - 2.34), 0.32
Race		
White	Ref	Ref
Asian	1.32 (0.41 - 4.25), 0.64	-
Black/African American	0.67 (0.21 - 2.10), 0.49	28.88 (13.31 - 62.66), $<2 \times 10^{-16}$
Multiracial	0 (0 - 0), 1.00	-
Unknown	0.34 (0.04 - 2.73), 0.31	1.36 (0.40 - 4.64), 0.62
Ethnicity		
Not Hispanic/Latinx	Ref	Ref
Hispanic/Latinx	1.31 (0.56 - 3.07), 0.53	6.03 (2.66 - 13.69), $1.70 \times 10^{-5}$
<b>Columbia-CKD (n = 2716)</b>		
Family History	3.59 (2.73 - 4.71), $<2 \times 10^{-16}$	1.28 (0.86 - 1.90), 0.23
Kidney Diagnosis		
Diabetic kidney disease	Ref	Ref
Congenital or Mendelian	6.97 (3.34 - 14.58), $2.43 \times 10^{-7}$	0.45 (0.20 - 1.01), 0.052
Glomerular	3.81 (1.80 - 8.09), $4.89 \times 10^{-4}$	0.80 (0.41 - 1.58), 0.53
Hypertension	1.02 (0.34 - 2.99), 0.98	2.14 (1.11 - 4.14), 0.024
Tubulointerstitial	3.91 (1.43 - 10.68), $7.77 \times 10^{-3}$	0.72 (0.15 - 3.40), 0.68
CKD of unknown cause	3.64 (1.67 - 7.93), $1.17 \times 10^{-3}$	1.99 (1.04 - 3.80), 0.038
Other	1.52 (0.57 - 4.05), 0.40	1.21 (0.53 - 2.77), 0.66
Race		
White	Ref	Ref
Asian	0.69 (0.40 - 1.20), 0.19	0.32 (0.04 - 2.40), 0.27
Black/African American	0.75 (0.48 - 1.17)	16.92 (10.57 - 27.09), $<2 \times 10^{-16}$
Multiracial	-	-
Native American	-	-
Unknown	0.75 (0.46 - 1.24), 0.26	1.26 (0.55 - 2.86), 0.58
Ethnicity		
Not Hispanic/Latinx	Ref	Ref
Hispanic/Latinx	0.72 (0.50 - 1.04), 0.08	1.83 (1.13 - 2.96), 0.014

Supplementary Table 6. Matching adjusted and complete case including UACR and eGFR cox proportional hazard models of kidney failure risk in the Columbia cohorts.

Columbia-GN	HR for Kidney Failure Matching Adjusted (n = 1098)			HR for Kidney Failure Fully Adjusted, Complete Case (n=274)		
	HR	(95%CI)	P	HR	(95%CI)	P
Monogenic Glomerular Disorder	1.84	(1.05 to 3.23)	3.32E-01	1.30	(0.52 to 3.23)	5.75E-01
<i>APOL1</i> high-risk genotype	1.72	(1.10 to 2.70)	1.80E-02	1.00	(0.41 to 2.46)	9.98E-01
Pathology Diagnosis:						
FSGS	8.21	(3.29 to 20.49)	6.39E-06	7.60	(0.96 to 59.93)	5.43E-01
MN	3.84	(1.49 to 9.90)	5.43E-03	2.55	(0.31 to 21.06)	3.85E-01
IgAN	10.00	(4.06 to 24.62)	5.43E-07	3.97	(0.50 to 31.78)	1.94E-01
Female Sex	0.98	(0.79 to 1.21)	8.30E-01	0.82	(0.52 to 1.28)	3.86E-01
Hypertension at biopsy	1.23	(0.99 to 1.52)	5.90E-02	1.55	(0.94 to 2.55)	8.91E-02
Diabetes at biopsy	0.90	(0.60 to 1.33)	5.90E-02	1.19	(0.55 to 2.58)	6.65E-01
RAAS inhibitor use at enrollment	0.75	(0.56 to 1.00)	5.20E-02	0.87	(0.48 to 1.59)	6.60E-01
Age at biopsy (Day)	1.00003	(1.00 to 1.00)	5.66E-04	0.9999	(0.9999 to 1.00)	1.24E-05
Immunosuppressive use at biopsy	3.33	(2.50 to 4.44)	<2E-16	0.87	(0.93 to 3.24)	8.15E-02
eGFR at biopsy	NA	NA	NA	0.95	(0.94 to 0.96)	<2E-16
UPCR at biopsy	NA	NA	NA	1	(0.9999 to 1.0002)	6.12E-01
Genetic Ancestry Cluster						
cluster1	1.34	(0.95 to 1.87)	9.28E-02	1.34	(0.63 to 2.85)	4.53E-01
cluster2	1.12	(0.75 to 1.68)	5.72E-01	1.11	(0.41 to 3.03)	8.41E-01
cluster3	1.28	(0.86 to 1.89)	2.17E-01	2.66	(1.07 to 6.64)	3.58E-02
cluster4	1.15	(0.76 to 1.75)	5.13E-01	0.69	(0.25 to 1.87)	4.67E-01
cluster5	1.89	(1.16 to 3.09)	1.06E-02	2.04	(0.70 to 5.97)	1.91E-01
cluster6	0.98	(0.65 to 1.48)	9.28E-01	1.67	(0.70 to 3.95)	2.46E-01
cluster7	1.41	(0.80 to 2.49)	2.38E-01	1.3	(0.38 to 4.42)	6.72E-01
cluster8	1.69	(1.10 to 2.61)	1.75E-02	4.15	(1.55 to 11.10)	4.55E-03
cluster9	2.06	(1.26 to 3.36)	4.00E-03	1.04	(0.37 to 2.96)	9.42E-01
cluster10	-	-	-	-	-	-
Columbia-CKD						
	HR	(95%CI)	P	HR	(95%CI)	P
Monogenic Glomerular Disorder	1.59	(1.35 to 1.87)	2.06E-08	1.51	(1.27 to 1.80)	4.10E-06
<i>APOL1</i> high-risk genotype	1.74	(1.39 to 2.18)	1.01E-06	1.48	(1.15 to 1.91)	2.51E-03
Female Sex	0.87	(0.79 to 0.97)	1.30E-02	1.07	(0.95 to 1.21)	2.65E-01
Hypertension at biopsy	0.88	(0.78 to 0.98)	2.10E-02	0.81	(0.71 to 0.93)	2.27E-03
Diabetes at biopsy	0.75	(0.65 to 0.87)	1.52E-04	0.85	(0.71 to 1.01)	7.14E-02
RAAS inhibitor use at enrollment	0.45	(0.28 to 0.74)	1.56E-03	0.32	(0.15 to 0.68)	2.84E-03
Immunosuppressive use	0.91	(0.56 to 1.49)	7.20E-01	1.45	(0.77 to 2.71)	2.49E-01
eGFR at biopsy	NA	NA	NA	0.99	(0.99 to 0.99)	<2E-16
UPCR at biopsy	NA	NA	NA	1.0001	(1.00 to 1.00)	1.55E-05
Genetic Ancestry Cluster						
cluster1	1.33	(1.12 to 1.57)	1.04E-03	1.22	(1.00 to 1.49)	4.58E-02
cluster2	0.6	(0.49 to 0.73)	6.14E-07	0.59	(0.46 to 0.75)	1.35E-05
cluster3	1.07	(0.87 to 1.32)	5.00E-01	0.93	(0.73 to 1.19)	5.54E-01
cluster4	0.87	(0.71 to 1.08)	2.07E-01	0.81	(0.63 to 1.04)	9.75E-02
cluster5	1.32	(1.07 to 1.62)	9.93E-03	1.01	(0.79 to 1.28)	9.52E-01
cluster6	1.12	(0.86 to 1.47)	3.93E-01	1.03	(0.77 to 1.39)	8.35E-01
cluster7	1.28	(1.01 to 1.62)	4.51E-02	1.05	(0.79 to 1.34)	7.56E-01
cluster8	1.24	(0.92 to 1.68)	1.61E-01	1.01	(0.70 to 1.46)	9.57E-01
cluster9	1.88	(1.41 to 2.51)	1.96E-05	1.69	(1.21 to 2.37)	2.25E-03
cluster10	0.97	(0.48 to 1.98)	9.40E-01	0.999	(0.49 to 2.04)	9.97E-01



Supplementary Table 7. Risk of kidney failure within specific glomerular subgroups of CureGN and Columbia-GN, including unadjusted, and fully adjusted Cox proportional hazard models based on monogenic glomerular disorders and *APOL1* kidney risk genotype.

	<b>Unadjusted HR HR (95% CI), P</b>	<b>Full Adjusted HR HR (95% CI), P</b>
<b>CureGN (n = 1913)</b>		
MCD (n = 421)		
Monogenic Disorder	3.54 (0.76 - 16.56), 0.10	4.47 (0.76 - 26.37), 0.08
<i>APOL1</i> high-risk genotype	2.94 (0.63 - 13.79), 0.16	1.29 (0.12 - 13.91), 0.81
FSGS (n = 490)		
Monogenic Disorder	1.23 (0.59 - 2.56), 0.57	1.81 (0.83 - 3.94), 0.13
<i>APOL1</i> high-risk genotype	2.12 (1.39 - 3.25), $6.72 \times 10^{-4}$	1.32 (0.69 - 2.55), 0.40
MN (n = 462)		
Monogenic Disorder	NA	NA
<i>APOL1</i> high-risk genotype	11.20 (4.46 - 28.15), $7.79 \times 10^{-6}$	12.78 (2.51 - 65.18), $6.22 \times 10^{-7}$
IgAN (n = 542)		
Monogenic Disorder	5.96 (2.13 - 16.67), $9.36 \times 10^{-4}$	4.84 (1.27 - 18.56), 0.022
<i>APOL1</i> high-risk genotype	2.25 (0.54 - 9.41), 0.26	0.51 (0.09 - 2.91), 0.44
<b>Columbia-GN (n = 1098)</b>		
MCD (n = 84)		
Monogenic Disorder	NA	NA
<i>APOL1</i> high-risk genotype	5.98 (0.66 - 54.17), 0.11	NA
FSGS (n = 289)		
Monogenic Disorder	1.45 (0.84 - 2.49), 0.18	1.89 (1.02 - 3.49), 0.043
<i>APOL1</i> high-risk genotype	1.57 (1.04 - 2.36), 0.032	1.38 (0.77 - 2.49), 0.28
MN (n = 176)		
Monogenic Disorder	NA	NA
<i>APOL1</i> high-risk genotype	3.52 (0.83 - 14.82), 0.087	2.23 (0.26 - 19.27), 0.40
IgAN (n = 549)		
Monogenic Disorder	NA	NA
<i>APOL1</i> high-risk genotype	8.35 (3.39 - 20.58), $4.01 \times 10^{-6}$	7.31 (2.53 - 21.15), $2.42 \times 10^{-4}$

Supplementary Table 8. Risk of not achieving complete remission within the CureGN cohort based on monogenic kidney disorder and *APOL1* kidney risk genotype. Adjusted for age at biopsy, sex, primary diagnosis, *APOL1* kidney risk genotype, hypertension, diabetes, eGFR, UPCR, use of immunosuppression at time of biopsy, genetic ancestry cluster, and use of RAAS inhibitor at enrollment.

	Unadjusted OR OR (95%CI) P	Adjusted OR OR (95%CI) P
Monogenic Glomerular Disorder	4.72 (2.49 - 8.92), $1.89 \times 10^{-6}$	5.25 (2.56 - 10.77), $6.31 \times 10^{-6}$
High-risk <i>APOL1</i> Genotypes	2.76 (1.85 - 4.11), $6.41 \times 10^{-7}$	1.36 (0.79 - 2.31), 0.27

## Supplementary Table 9. Imputed dataset and complete case sensitivity analysis across the models within CureGN

CureGN	HR for Kidney Failure			HR for Kidney Failure			HR for Kidney Failure			HR for Kidney Failure			HR for Kidney Failure			HR for Kidney Failure		
	Minimally Adjusted, Imputed (n=1913)			Minimally Adjusted, Complete Case (n=1913)			Matching Adjusted, Imputed (n=1913)			Matching Adjusted, Complete Case (n=1599)			Fully Adjusted, Imputed (n=1913)			Fully Adjusted, Complete Case (n=1116)		
	HR	(95%CI)	P	HR	(95%CI)	P	HR	(95%CI)	P	HR	(95%CI)	P	HR	(95%CI)	P	HR	(95%CI)	P
Monogenic Glomerular Disorder	2.01	(1.15 to 3.51)	1.45E-02	2.01	(1.15 to 3.5)	1.38E-02	2.21	(1.25 to 3.91)	6.42E-03	2.36	(1.25 to 4.44)	8.01E-03	2.44	(1.38 to 4.34)	2.42E-03	3.36	(1.63 to 6.92)	1.01E-03
APOL1 high-risk genotype	2.72	(1.87 to 3.95)	2.97E-07	2.72	(1.88 to 3.94)	1.26E-07	1.43	(0.87 to 2.33)	1.58E-01	1.51	(0.9 to 2.53)	1.23E-01	1.28	(0.79 to 2.09)	3.12E-01	1.48	(0.76 to 2.86)	2.47E-01
Pathology Diagnosis:																		
FSGS	3.40	(2.12 to 5.46)	6.73E-07	3.40	(2.13 to 5.44)	3.14E-07	2.94	(1.81 to 4.78)	1.97E-05	2.67	(1.61 to 4.40)	1.26E-04	2.23	(1.36 to 3.65)	1.51E-03	1.93	(1.03 to 3.64)	4.05E-02
MN	1.19	(0.68 to 2.08)	5.40E-01	1.19	(0.68 to 2.07)	5.39E-01	1.03	(0.58 to 1.83)	9.25E-01	1.03	(0.57 to 1.87)	9.25E-01	1.10	(0.62 to 1.95)	7.55E-01	1.01	(0.47 to 2.14)	9.87E-01
IgAN	2.29	(1.43 to 3.68)	6.85E-04	2.29	(1.43 to 3.67)	5.74E-04	2.26	(1.37 to 3.73)	1.47E-03	2.30	(1.37 to 3.86)	1.55E-03	1.58	(0.95 to 2.63)	7.91E-02	1.71	(0.89 to 3.27)	1.04E-01
Female Sex	0.75	(0.58 to 0.98)	3.48E-02	0.75	(0.58 to 0.98)	3.37E-02	0.73	(0.56 to 0.96)	2.35E-02	0.75	(0.56 to 1.00)	5.34E-02	0.73	(0.56 to 0.96)	2.41E-02	0.73	(0.51 to 1.05)	8.67E-02
Hypertension at biopsy							1.79	(1.34 to 2.4)	1.01E-04	1.64	(1.20 to 2.24)	1.93E-03	1.47	(1.10 to 1.96)	6.65E-03	1.57	(1.06 to 2.30)	2.30E-02
Diabetes at biopsy							0.39	(0.05 to 2.83)	3.49E-01	0.43	(0.06 to 3.08)	3.98E-01	0.33	(0.05 to 2.42)	2.74E-01	0.42	(0.06 to 3.10)	3.95E-01
RAAS inhibitor use at enrollment							1.67	(1.11 to 2.52)	1.51E-02	1.77	(1.04 to 3.01)	3.48E-02	1.77	(1.17 to 2.66)	6.85E-03	1.96	(1.04 to 3.67)	3.67E-02
Age at biopsy (Mo)	1.00	(1.00 to 1.00)	2.01E-02	1.00	(1.00 to 1.00)	1.92E-02	1.00	(1.00 to 1.00)	5.89E-01	1.00	(1.00 to 1.00)	5.63E-01	1.00	(1.00 to 1.00)	1.58E-03	1.00	(1.00 to 1.00)	3.24E-02
Immunosuppressive use at biopsy							1.07	(0.78 to 1.47)	6.69E-01	1.16	(0.84 to 1.6)	3.71E-01	1.09	(0.79 to 1.49)	6.03E-01	1.26	(0.84 to 1.89)	2.66E-01
eGFR at biopsy												0.98	(0.97 to 0.98)	6.41E-15	0.98	(0.97 to 0.99)	6.11E-10	
UPCR at biopsy												1.03	(1.01 to 1.05)	4.26E-04	1.03	(1.01 to 1.06)	2.44E-03	
Genetic Ancestry Cluster																		
cluster2							1.13	(0.67 to 1.92)	6.41E-01	1.22	(0.69 to 2.17)	4.99E-01	1.30	(0.76 to 2.21)	3.40E-01	1.58	(0.78 to 3.18)	2.00E-01
cluster3							2.95	(1.7 to 5.11)	1.44E-04	3.30	(1.82 to 5.97)	7.87E-05	2.74	(1.58 to 4.77)	4.11E-04	3.47	(1.62 to 7.43)	1.36E-03
cluster4							1.71	(1.02 to 2.86)	4.26E-02	1.84	(1.03 to 3.26)	3.79E-02	1.83	(1.08 to 3.07)	2.37E-02	2.01	(0.97 to 4.18)	6.11E-02
cluster5							1.32	(0.76 to 2.3)	3.19E-01	1.38	(0.75 to 2.55)	3.02E-01	1.33	(0.76 to 2.34)	3.11E-01	1.44	(0.66 to 3.11)	3.60E-01
cluster6							1.83	(1.01 to 3.33)	4.75E-02	1.78	(0.91 to 3.46)	9.11E-02	1.94	(1.05 to 3.57)	3.32E-02	2.20	(0.97 to 4.96)	5.83E-02
cluster7							1.43	(0.74 to 2.77)	2.87E-01	1.68	(0.83 to 3.40)	1.45E-01	1.32	(0.68 to 2.58)	4.12E-01	1.29	(0.47 to 3.50)	6.21E-01
cluster8							1.60	(0.78 to 3.26)	1.97E-01	1.74	(0.81 to 3.71)	1.55E-01	2.03	(0.99 to 4.19)	5.38E-02	2.72	(1.15 to 6.42)	2.27E-02
cluster9							1.50	(0.65 to 3.49)	3.43E-01	1.81	(0.77 to 4.27)	1.76E-01	1.97	(0.83 to 4.64)	1.21E-01	1.92	(0.54 to 6.78)	3.12E-01
cluster10							2.97	(1.01 to 8.67)	4.69E-02	1.67	(0.39 to 7.22)	4.93E-01	3.08	(1.01 to 9.39)	4.77E-02	3.08	(0.65 to 14.66)	1.58E-01

Supplementary Table 10. Personal and family histories of ACMG V3.1 Secondary Findings associated conditions in CureGN subjects with ACMG secondary findings. Associations evaluated using logistic regression. American College of Medical Genetics (ACMG)

ACGM SF Category	Personal History of Complication			Family History of Complication		
		n (%)	P		n (%)	P
Cancer	0/21	0%	0.99	7/21	33%	0.98
<i>BRCA1/2</i> in females	0/5	0%	0.99	2/5	40%	0.75
Cardiovascular						
Aortopathy	0/6	0%	0.99	NA	NA	NA
Arrhythmia	3/18	17%	0.100	NA	NA	NA
Cardiomyopathy	0/23	0%	0.98	NA	NA	NA
Hypercholesterolemia	0/20	0%	0.98	9/20	45%	0.15
<i>HNF1A</i> and DM	0/5	0%	0.98	1/5	20%	0.60

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