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Supplemental Methods

Description of RaDaR

In total, 87 sites have recruited at least one patient to the RaDaR IgA nephropathy cohort, and 49 sites have recruited over 20 patients each. Mandatory data fields are required to be completed when a patient is recruited, and optional data fields are available to capture information about pathology reports, disease progressions, etc. In addition to these data, some patients have linkage to historical blood results and medication data supporting longitudinal analysis. Dialysis and transplant data from the UK Renal Registry (UKRR) was used to enrich the data recorded in RaDaR. Patients registered for RaDaR have given consent for their past, present, and future clinical data to be used for ongoing and future research into kidney diseases and related conditions.

To assess whether there is recruitment bias into RaDaR two methods were used. In the first, all patients with IgA nephropathy eligible for recruitment into RaDaR from two large renal centers were compared. No differences were observed in the ethnicity of recruited and non-recruited patients at each center (Chi-squared test; P=0.71, P=0.80 respectively). In the second, individuals in the RaDaR IgA nephropathy cohort who had reached kidney failure were compared with patients in the UKRR with a recorded primary renal disease of IgA nephropathy. The UKRR collects data on individuals receiving KRT from all renal centers in the UK. There was strong evidence that RaDaR IgA nephropathy patients with kidney failure were more likely to be White (85% vs. 79%, P<0.001) and less likely to be Asian (10% vs 15%, P<0.001) when compared with the UKRR dataset.

Calculation of Time-Averaged Proteinuria

The time-weighted averages for urinary protein-creatinine ratio (UPCR) used to define time-averaged proteinuria were calculated from the area under the curve of serial measurements

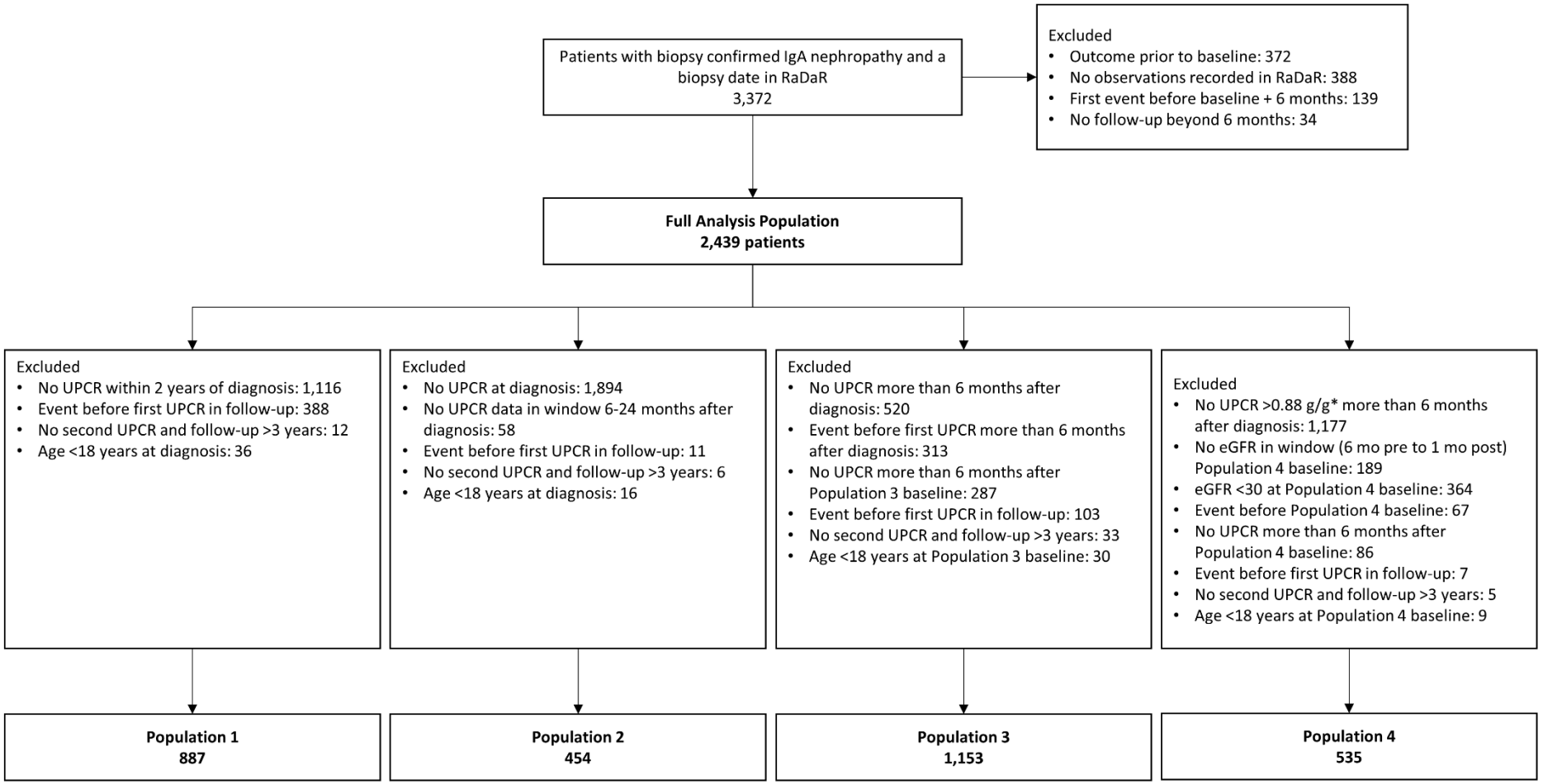
divided by the length of follow-up. In order to calculate time-averaged proteinuria across a window, it was necessary to extrapolate proteinuria prior to the first observation in the window and after the final observation in the window, a first observation carried back and last observation carried forward approach was applied to form a complete curve.

eGFR slope was calculated as an annualized value. From the beginning of the time-period for which the eGFR slope was being calculated, mean averages were calculated for all eGFR values falling in 0-3months, 3-6 months etc. up until the earliest of the end of the specified time-period, and all-cause mortality/kidney failure. These mean averages were used for calculating eGFR slope using linear mixed-models with random slope and intercept. As a sensitivity analysis, eGFR slopes were calculated excluding episodes of AKI. No significant differences in outcomes or associations were observed.

Supplemental Table 1. Description of Populations 1–4

	Population 1	**Population 2**	**Population 3**	**Population 4**
Surrogate for	Incident population	Incident population	Prevalent population	Prevalent clinical trial population
Baseline date	Diagnosis	Diagnosis	First UPCR value more than 6 months after diagnosis	First UPCR value > 0.88 g/g*, more than 6 months after diagnosis
Inclusion criteria	1. UPCR value in first 2 years of follow-up 2. Additional UPCR value if follow-up > 3 years	1. UPCR value in first 2 years of follow-up 2. Additional UPCR value if follow-up > 3 years 3. UPCR value in window 6 months before baseline to 1 month after baseline	1. UPCR value at least 6 months after diagnosis 2. UPCR value at least 6 months after baseline 3. Additional UPCR value if follow-up > 3 years	1. UPCR value > 880 at least 6 months after diagnosis 2. eGFR > 30 at baseline 3. UPCR value at least 6 months after baseline 4. Additional UPCR value if follow-up > 3 years

Abbreviations: eGFR, estimated glomerular filtration rate; **UPCR**, urinary protein-creatinine ratio.
* 0.88 g/g = 100 mg/mmol (~1 g/day)

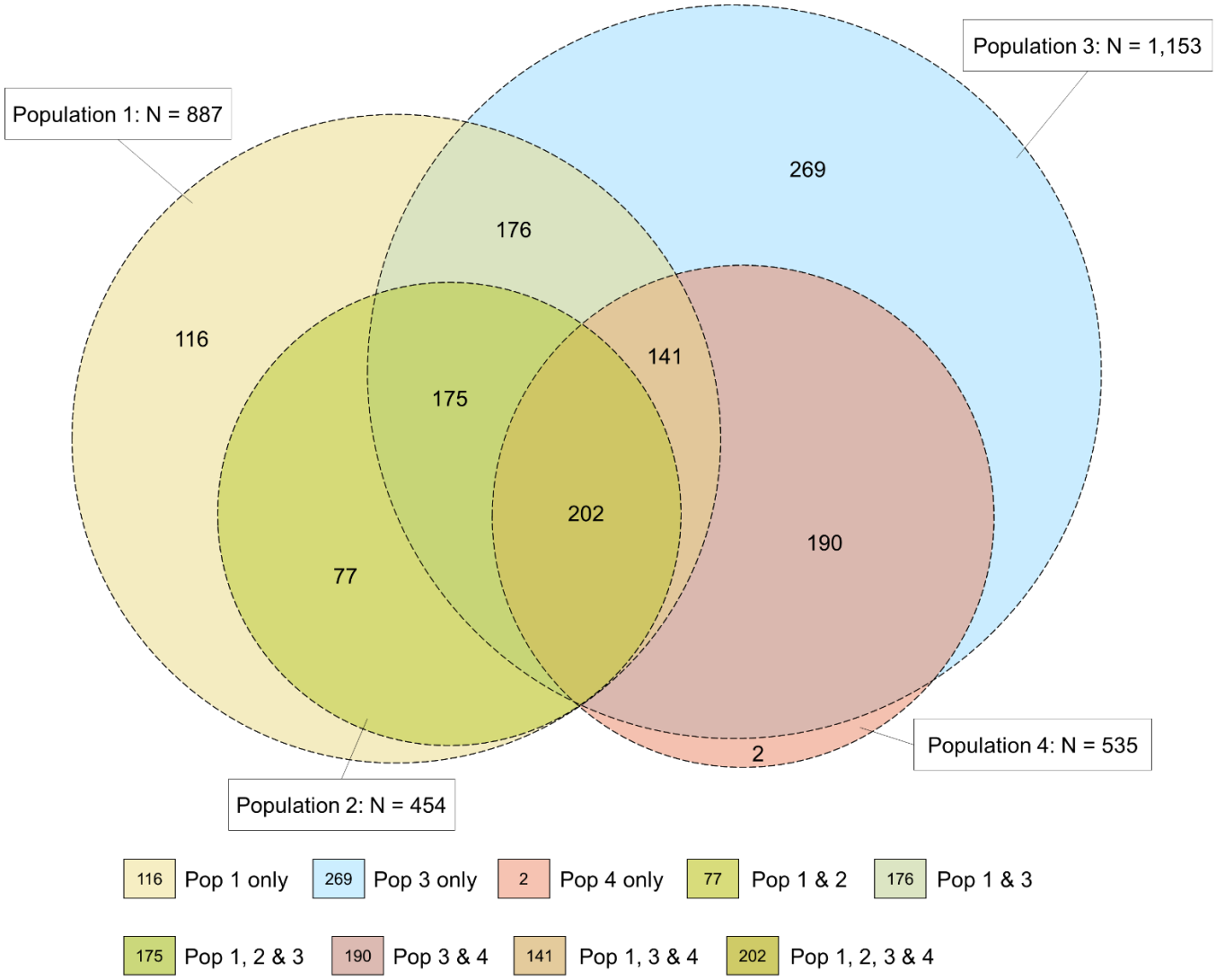


Supplemental Figure 1. Study population disposition

Abbreviations: eGFR, estimated glomerular filtration rate; **RaDaR**, Registry of Rare Kidney Diseases; **UPCR**, urinary protein-creatinine ratio.

Patient disposition for the Ful-Analysis Population and Populations 1–4.

* 0.88 g/g = 100 mg/mmol (~1 g/day).



Supplemental Figure 2. Venn diagram displaying the degree of overlap between proteinuria subpopulations

Supplemental Table 2. Univariable and multivariable analysis of 10-year survival and eGFR slope (Full-Analysis Population)

			Univariable analysis		Multivariable analysis	
	Variable	**Reference**	**HR**	**P > ChiSq**	**HR**	**P > ChiSq**
10-year survival						
Age (10-years)			1.18 (1.14, 1.23)	<.001	1.11 (1.06, 1.15)	<.001
Gender	Female	Male	0.74 (0.65, 0.85)	<.001	0.80 (0.70, 0.91)	0.001
Ethnicity	Asian	White	1.26 (1.04, 1.52)	0.02	1.36 (1.12, 1.64)	0.002
	Black	White	1.27 (0.79, 2.02)	0.32	1.18 (0.73, 1.88)	0.50
	Missing	White	1.01 (0.83, 1.22)	0.95	1.02 (0.84, 1.24)	0.86
	Mixed	White	0.88 (0.37, 2.13)	0.79	1.18 (0.49, 2.86)	0.71
	Other	White	0.89 (0.52, 1.50)	0.65	0.93 (0.54, 1.57)	0.78
BMI	Tertile 1	Tertile 2	0.88 (0.60, 1.28)	0.49		
	Tertile 3	Tertile 2	0.83 (0.57, 1.21)	0.33		
	Missing	Tertile 2	0.58 (0.44, 0.76)	<.001		
Systolic BP	Tertile 1	Tertile 2	0.54 (0.33, 0.90)	0.02		
	Tertile 3	Tertile 2	1.18 (0.77, 1.81)	0.45		
	Missing	Tertile 2	0.87 (0.63, 1.19)	0.38		
CKD stage	G2	G1	1.86 (1.08, 3.22)	0.03	1.77 (1.02, 3.05)	0.04
	G3a	G1	3.43 (2.01, 5.84)	<.001	3.08 (1.80, 5.26)	<.001
	G3b	G1	5.19 (3.15, 8.54)	<.001	4.22 (2.55, 6.99)	<.001
	G4+5	G1	9.74 (5.94, 15.99)	<.001	7.86 (4.75, 13.00)	<.001
	Missing	G1	3.05 (1.91, 4.86)	<.001	2.81 (1.76, 4.49)	<.001
eGFR slope						
Age (10 years)			0.45 (0.30, 0.61)	<.001	0.40 (0.20, 0.50)	<.001
Gender	Female	Male	0.22 (-0.29, 0.74)	0.40	0.60 (0.10, 1.10)	0.02
Ethnicity	Asian	White	-1.17 (-2.00, -0.35)	0.01	0.37 (0.21, 0.54)	0.004
	Black	White	-0.56 (-2.65, 1.54)	0.60	0.61 (0.09, 1.12)	0.38
	Missing	White	-0.49 (-1.28, 0.3)	0.22	-1.18 (-1.99, -0.38)	0.24
	Mixed	White	-0.04 (-3.26, 3.18)	0.98	-0.92 (-2.98, 1.14)	0.84
	Other	White	-0.07 (-1.88, 1.74)	0.94	-0.46 (-1.23, 0.31)	0.92

BMI	Tertile 1	Tertile 2	-1.13 (-2.59, 0.33)	0.13	0.32 (-2.84, 3.48)	
	Tertile 3	Tertile 2	-0.88 (-2.29, 0.54)	0.22	0.09 (-1.68, 1.86)	
	Missing	Tertile 2	0.39 (-0.67, 1.45)	0.47		
Systolic BP	Tertile 1	Tertile 2	-0.57 (-2.02, 0.88)	0.44		
	Tertile 3	Tertile 2	-0.21 (-1.70, 1.28)	0.78		
	Missing	Tertile 2	-0.50 (-1.59, 0.58)	0.36		
CKD stage	G2	G1	0.28 (-0.80, 1.35)	0.62		0.83
	G3a	G1	0.66 (-0.50, 1.82)	0.27		0.54
	G3b	G1	1.24 (0.18, 2.30)	0.02	0.12 (-0.95, 1.19)	0.19
	G4+5	G1	3.04 (1.84, 4.23)	<.001	0.36 (-0.80, 1.53)	<.001
	Missing	G1	1.67 (0.80, 2.55)	<.001	0.74 (-0.35, 1.83)	0.001

Abbreviations: BMI, body mass index; **BP**, blood pressure; **CKD**, chronic kidney disease; **eGFR**, estimated glomerular filtration rate; **HR**, hazard ratio.

Supplemental Table 3. Demographic and clinical characteristics at diagnosis and clinical outcomes during follow-up (Populations 1–4)

Category	Population 1		Population 2		Population 3		Population 4	
	n	%	n	%	N	%	n	%
Age at baseline	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
Mean, years (SD)	44 (15)		43 (15)		45 (14)		43 (13)	
Median, years (Q1, Q3)	42 (32, 54)		42 (32, 53)		44 (33, 55)		42 (32, 52)	
Gender	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
Female	287	32	151	33	362	31	183	34
Male	600	68	303	67	791	69	352	66
Ethnicity	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
Asian	104	12	60	13	124	11	62	12
Black	10	1	6	1	15	1	6	1
Mixed	4	0	3	1	6	1	2	0
Other	17	2	5	1	21	2	12	2
White	646	73	329	72	863	75	392	73
Not stated/missing	106	12	51	11	124	11	61	11
BMI at baseline	**242**	**27**	**160**	**35**	**165**	**14**	**88**	**16**
Mean, (SD)	29 (8.3)		28 (6.2)		29 (8.9)		29 (5.8)	
Median, (Q1, Q3)	28 (24.3, 31.2)		28 (24.3, 30.6)		27 (24.4, 30.8)		29 (24.5, 31.8)	
Systolic BP at baseline	**216**	**24**	**159**	**35**	**289**	**25**	**146**	**27**
Mean, mmHg (SD)	139 (19)		138 (20)		135 (17)		136 (15)	
Median, mmHg (Q1, Q3)	138 (126, 152)		138 (124, 152)		133 (123, 144)		135 (124, 148)	
UPCR* at baseline	**498**	**56**	**454**	**100**	**1,153**	**100**	**535**	**100**
Mean, g/g (SD)	2.39 (3.63)		2.44 (3.73)		1.21 (1.51)		1.98 (1.53)	
Median, g/g (Q1, Q3)	1.51 (0.64, 3.00)		1.54 (0.70, 3.13)		0.74 (0.25, 1.57)		1.49 (1.10, 2.20)	
Nephrotic range proteinuria (≥2.64 g/g)	150	17	137	30	1,023	89	99	19
eGFR at baseline	**551**	**62**	**376**	**83**	**920**	**80**	**535**	**100**
Mean, mL/min/1.73m^2 (SD)	57 (30)		59 (29)		57 (29)		61 (26)	
Median, mL/min/1.73m^2 (Q1, Q3)	50 (33, 78)		52 (34, 79)		50 (34, 77)		53 (40, 77)	
CKD stage	**551**	**62**	**376**	**83**	**920**	**80**	**535**	**100**
Stage 1	97	18	66	18	146	16	86	16
Stage 2	121	22	92	24	222	24	136	25
Stage 3	229	42	158	42	395	43	313	59
Stage 4	100	18	56	15	154	17	0	0
Stage 5	4	1	4	1	3	0	0	0
Time from biopsy to baseline	**-**	**-**	**-**	**-**	**1,153**	**100**	**535**	**100**
Mean, years (SD)	-		-		4.1 (6.2)		4.7 (6.5)	

Median, years (Q1, Q3)	-		-		1.3 (0.7, 5.1)		2.1 (0.8, 5.9)	
Length of follow-up	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
Mean, years (SD)	5.1 (3.3)		4.9 (3.2)		5.2 (3.6)		4.7 (3.2)	
Median, years (Q1, Q3)	4.5 (2.5, 6.8)		4.4 (2.4, 6.5)		4.4 (2.6, 7.0)		4.3 (2.5, 5.9)	
Kidney failure or death event	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
Yes	347	39	170	37	765	66	171	32
No	540	61	284	63	388	34	364	68
First event	**347**	**39**	**170**	**37**	**388**	**34**	**171**	**32**
Death	11	3	6	4	11	3	3	2
Dialysis	36	10	14	8	33	9	3	2
Transplant	14	4	8	5	16	4	5	3
eGFR <15	286	82	142	84	328	85	160	94
Time to first event	**347**	**39**	**170**	**37**	**388**	**34**	**171**	**32**
Mean, years (SD)	4.0 (3.1)		3.9 (2.9)		4.5 (3.3)		4.7 (3.2)	
Median, years (Q1, Q3)	3.1 (1.5, 5.6)		3.1 (1.6, 5.3)		3.8 (2.1, 5.9)		4.2 (2.6, 5.5)	
Age at first event	**347**	**39**	**170**	**37**	**388**	**34**	**171**	**32**
Mean, years (SD)	48 (15)		49 (14)		51 (14)		48 (13)	
Median, years (Q1, Q3)	47 (37, 58)		46 (38, 59)		51 (41, 61)		47 (37, 57)	
Survival rate, estimate (95% CI)	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
2.5-year	0.83 (0.80-0.85)		0.83 (0.79-0.86)		0.89 (0.87-0.90)		0.91 (0.89-0.94)	
5-year	0.69 (0.66-0.72)		0.69 (0.64-0.73)		0.72 (0.69-0.75)		0.71 (0.66-0.75)	
10-year	0.46 (0.41-0.51)		0.44 (0.36-0.51)		0.50 (0.45-0.54)		0.42 (0.34-0.50)	
15-year	0.27 (0.19-0.36)		0.22 (0.09-0.38)		0.31 (0.24-0.38)		0.25 (0.14-0.37)	
20-year	0.27 (0.19-0.36)		NE (NE-NE)		0.20 (0.12-0.30)		NE (NE-NE)	
Quartile survival estimate, year (95% CI)	**887**	**100**	**454**	**100**	**1,153**	**100**	**535**	**100**
75%	3.9 (3.4-4.5)		4.1 (3.2-4.8)		4.6 (4.2-5.0)		4.7 (4.3 ,5.0)	
50%	8.7 (7.5-10.2)		8.2 (7.4-10.1)		10.0 (8.6-12.1)		8.9 (7.5 ,10.9)	
25%	NE (13.5-NE)		14.8 (13.0-NE)		17.8 (14.6-NE)		14.6 (14.0-NE)	
eGFR slope, total	**837**	**94**	**422**	**93**	**1,042**	**90**	**501**	**94**
Mean, mL/min/1.73m^2/year (SD)	-3.8 (8.1)		-4.0 (7.0)		-3.6 (7.0)		-5.3 (7.3)	
Median, mL/min/1.73m^2/year (Q1, Q3)	-2.6 (-6.0, -0.4)		-2.8 (-6.5, -0.5)		-2.3 (-5.2, -0.5)		-3.7 (-7.2, -1.4)	

Abbreviations: BMI, body mass index; **BP**, blood pressure; **CI**, confidence interval; **CKD**, chronic kidney disease; **eGFR**, estimated glomerular filtration rate; **NE,** not estimable; **SD**, standard deviation; **UPCR**, urinary protein-creatinine ratio.
*0.0088 g/g = 1 mg/mmol

Supplemental Table 4. Clinical outcomes in proteinuria analysis Population 1

Proteinuria Analysis Population 1									
Time-averaged proteinuria* duration		**Total**				**0-24 months**			
Time-averaged proteinuria category	**Overall**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**
Survival rate, estimate (95% CI)									
	n = 887	**n = 215**	**n = 175**	**n = 251**	**n = 246**	**n = 247**	**n = 168**	**n = 230**	**n = 242**
5-year	0.69 (0.66-0.72)	0.88 (0.82-0.92)	0.88 (0.81-0.92)	0.70 (0.64-0.76)	0.40 (0.33-0.46)	0.89 (0.83-0.92)	0.83 (0.76-0.89)	0.68 (0.60-0.74)	0.41 (0.34-0.47)
15-year	0.27 (0.19-0.36)	0.57 (0.36-0.73)	0.33 (0.09-0.61)	0.14 (0.04-0.31)	0.10 (0.03-0.21)	0.52 (0.36-0.66)	NE (NE-NE)	0.09 (0.02-0.23)	0.21 (0.14-0.30)
Quartile time-to-event, year (95% CI)									
75%	3.9 (3.4-4.5)	10.1 (7.2-12.8)	7.9 (5.7-11.2)	4.1 (3.4-5.2)	1.5 (1.4-1.8)	8.2 (6.2-10.2)	6.3 (5.1-7.6)	3.8 (2.8-4.9)	1.5 (1.3-1.8)
50%	8.7 (7.5-10.2)	NE (NE-NE)	13.0 (11.2-NE)	7.5 (6.3-9.7)	3.7 (3.2-4.5)	NE (NE-NE)	13.5 (7.9-NE)	7.2 (6.2-9.7)	3.9 (3.2-4.5)
25%	15.2 (13.5-NE)	NE (NE-NE)	NE (NE-NE)	13.0 (10.3-NE)	6.8 (5.9-8.4)	NE (NE-NE)	NE (NE-NE)	12.3 (10.2-15.0)	8.4 (6.0-NE)
eGFR slope, 0-24 months (mL/min/1.73m^2/year)									
	n = 887	**n = 215**	**n = 175**	**n = 251**	**n = 246**	**n = 247**	**n = 168**	**n = 230**	**n = 242**
Mean (SD)	-2.5 (10.9)	1.5 (10.8)	-0.2 (7.9)	-2.2 (9.2)	-8.5 (11.9)	1.2 (10.8)	-1.1 (6.6)	-2.0 (10.2)	-8.1 (12.0)
Median (IQR)	-2.6 (-7.4, 1.5)	0.0 (-2.9, 4.3)	-1.6 (-5.1, 2.3)	-2.7 (-6.5, 0.8)	-7.9 (-12.8, -2.7)	-0.1 (-4.0, 4.3)	-1.6 (-4.7, 1.8)	-2.9 (-6.4, 0.7)	-7.5 (-12.4, -2.1)

Abbreviations: CI, confidence interval; **eGFR**, estimated glomerular filtration rate; **IQR**, interquartile range; **SD**, standard deviation.
* 0.44 g/g = 50 mg/mmol (~0.5 g/day); 0.88 g/g = 100 mg/mmol (~1 g/day); 1.76 g/g = 200 mg/mmol (~2 g/day)

Supplemental Table 5. Clinical outcomes in Proteinuria Analysis Populations 2 and 3

Proteinuria Analysis Population 2											
Baseline UPCR*		**<0.88 g/g**					**≥0.88 g/g**				
Total Time-averaged proteinuria category	**Overall**	**Combined**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**	**Combined**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**
	n = 454	**n = 138**	**n = 70**	**n = 34**	**n = 20**	**n = 14**	**n = 316**	**n = 39**	**n = 61**	**n = 96**	**n = 120**
%		Reference	50.7%	24.6%	14.5%	10.1%	Reference	12.3%	19.3%	30.4%	38.0%
Survival rate, estimate (95% CI)											
5-year	0.69 (0.64-0.73)	0.88 (0.81-0.93)	0.92 (0.80-0.97)	0.97 (0.81-1.00)	0.81 (0.51-0.94)	0.64 (0.34-0.83)	0.61 (0.55-0.67)	0.87 (0.71-0.94)	0.82 (0.69-0.90)	0.63 (0.52-0.73)	0.40 (0.30-0.49)
10-year	0.44 (0.36-0.51)	0.61 (0.45-0.74)	0.74 (0.48-0.89)	0.90 (0.60-0.98)	0.40 (0.08-0.72)	0.13 (0.01-0.42)	0.37 (0.29-0.45)	0.80 (0.59-0.91)	0.70 (0.51-0.83)	0.29 (0.13-0.47)	0.14 (0.06-0.25)
15-year	0.22 (0.09-0.38)	0.42 (0.22-0.61)	0.25 (0.01-0.65)	NE (NE- NE)	NE (NE-NE)	NE (NE-NE)	NE (NE-NE)	NE (NE-NE)	NE (NE-NE)	NE (NE-NE)	NE (NE-NE)
Quartile time-to-event, year (95% CI)											
75%	4.1 (3.2-4.8)	7.2 (6.1-8.7)	7.7 (6.2-12.0)	10.2 (6.8-NE)	5.2 (1.5-8.7)	3.4 (1.2-5.2)	3.0 (2.3-3.9)	10.2 (2.30-NE)	7.7 (4.3-13.0)	3.8 (2.3-4.7)	1.7 (1.4-2.2)
50%	8.2 (7.4-10.1)	10.2 (8.7-NE)	10.1 (7.7-NE)	NE (NE-NE)	8.7 (5.2-NE)	5.2 (1.5-8.7)	7.2 (5.8-8.2)	NE (NE-NE)	13.0 (12.8-NE)	7.1 (5.2-9.7)	3.9 (2.7-4.9)
25%	14.8 (13.0-NE)	NE (NE-NE)	12.0 (10.1-NE)	NE (NE-NE)	NE (NE-NE)	8.7 (5.16-NE)	13.5 (12.8-NE)	NE (NE-NE)	NE (NE-NE)	13.5 (8.7-NE)	7.2 (5.8-NE)
Kidney failure risk (10-year), HR (95% Wald CL)											
Unadjusted	N/A	Reference	Reference	0.47 (0.10-2.28)	2.99 (1.00-8.91)	6.75 (2.56-17.77)	2.75 (1.79-4.21)	Reference	1.06 (0.40-2.83)	3.00 (1.28-7.09)	6.06 (2.64-13.90)
Adjusted	N/A	Reference	Reference	0.62 (0.11-3.40)	3.40 (1.00-11.58)	13.08 (3.86-44.30)	2.65 (1.72-4.09)	Reference	0.89 (0.33-2.41)	2.74 (1.15-6.51)	7.06 (3.05-16.31)
eGFR slope, 6-30 months (mL/min/1.73m^2/year)											
	n = 398	**n = 122**	**n = 63**	**n = 29**	**n = 18**	**n = 12**	**n = 276**	**n = 36**	**n = 53**	**n = 87**	**n = 100**
Mean (SD)	-2.8 (10.0)	0.4 (11.4)	1.5 (13.8)	0.9 (8.5)	-2.6 (7.8)	-1.9 (7.7)	-4.3 (9.0)	1.2 (7.7)	-0.2 (8.1)	-3.3 (6.3)	-9.2 (9.5)
Median (IQR)	-2.4 (-7.7,1.7)	-0.9 (-4.7, 4.4)	0.4 (-4.3, 4.6)	-0.3 (-2.8, 5.5)	-3.8 (-5.4, 2.7)	-1.9 (-5.8, 3.6)	-3.2 (-8.8, 0.7)	0.9 (-2.3, 5.2)	-1.6 (-4.2, 2.7)	-2.6 (-6.3, 0.6)	-8.8 (-14.7, -3.1)
eGFR slope, total (mL/min/1.73m^2/year)											
	n = 422	**n = 128**	**n = 67**	**n = 30**	**n = 19**	**n = 12**	**n = 294**	**n = 38**	**n = 59**	**n = 92**	**n = 105**

Mean (SD)	-4.0 (7.0)	-1.5 (5.8)	0.1 (6.0)	-1.3 (3.5)	-3.8 (4.2)	-7.6 (7.3)	-5.1 (7.2)	-0.6 (6.0)	-1.2 (4.2)	-4.4 (5.0)	-9.7 (7.9)
Median (IQR)	-2.8 (-6.5, -0.5)	-1.5 (-3.7, 0.4)	-0.5 (-2.4, 1.8)	-1.7 (-3.0, -0.8)	-3.3 (-5.1, -1.9)	-6.0 (-9.6, -3.2)	-3.4 (-8.0, -0.8)	-0.2 (-1.6, 1.3)	-1.2 (-2.8, 0.1)	-3.7 (-6.3, -1.3)	-8.9 (-13.4, -4.0)
Proteinuria Analysis Population 3											
Baseline UPCR*		**<0.88 g/g**					**≥0.88 g/g**				
Total Time-averaged proteinuria category	**Overall**	**Combined**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**	**Combined**	**<0.44 g/g**	**0.44 to <0.88 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**
	n = 1,153	**n = 638**	**n = 302**	**n = 150**	**n = 141**	**n = 45**	**n = 515**	**n = 16**	**n = 77**	**n = 210**	**n = 212**
%		Reference	47.3%	23.5%	22.1%	7.1%	Reference	3.1%	15.0%	40.8%	41.2%
Quartile time-to-event, year (95% CI)											
75%	4.6 (4.2-5.0)	6.8 (6.2-7.9)	NE (NE-NE)	12.2 (7.1-13.9)	5.0 (4.1-5.9)	4.1 (2.5-4.8)	3.18 (2.9-3.5)	9.3 (9.3-NE)	6.9 (3.3-9.0)	4.4 (3.7-4.8)	2.1 (1.6-2.4)
50%	10.0 (8.6-12.1)	13.9 (12.2-15.4)	NE (NE-NE)	14.0 (12.3-NE)	8.2 (6.4-10.6)	5.4 (4.7-7.5)	6.4 (5.3-7.5)	NE (NE-NE)	14.0 (7.5-NE)	8.1 (6.4-9.8)	3.9 (3.2-4.4)
25%	17.8 (14.6-NE)	NE (NE-NE)	NE (NE-NE)	15.3 (14.0-NE)	12.8 (12.0-NE)	14.6 (6.7-NE)	14.0 (11.1-16.7)	NE (NE-NE)	NE (NE-NE)	12.1 (10.0-16.7)	7.5 (5.8-14.1)
kidney failure risk (10-year), HR (95% Wald CL)											
Unadjusted	N/A	Reference	Reference	1.00 (0.56-1.81)	3.61 (2.34-5.56)	5.90 (3.49-9.97)	2.84 (2.29-3.52)	Reference	3.55 (0.48-26.54)	6.01 (0.84-43.06)	14.10 (1.98-100.6)
Adjusted	N/A	Reference	Reference	0.88 (0.49-1.60)	3.13 (2.01-4.88)	4.61 (2.69-7.90)	2.80 (2.25-3.49)	Reference	5.19 (0.69-39.05)	8.44 (1.17-61.00)	29.53 (4.09-213.2)
eGFR slope, 6-30 months (mL/min/1.73m^2/year)											
	n = 921	**n = 507**	**n = 243**	**n = 117**	**n = 115**	**n = 32**	**n = 414**	**n = 14**	**n = 63**	**n = 174**	**n = 163**
Mean (SD)	-3.2 (9.4)	-1.4 (9.4)	0.0 (8.8)	-1.6 (7.6)	-2.8 (11.2)	-6.3 (10.7)	-5.5 (9.0)	-1.3 (4.5)	-2.5 (4.9)	-3.3 (7.4)	-9.4 (10.5)
Median (IQR)	-2.4 (-6.9, 0.7)	-1.2 (-4.6, 1.8)	-0.4 (-3.1, 2.8)	-1.2 (-5.1, 1.5)	-3.1 (7.2, 0.1)	-5.3 (-8.2, -2.6)	-3.9 (-8.5, -0.6)	-1.4 (-3.3, 0.3)	-2.7 (-5.0, 0.6)	-2.7 (-6.5, 0.0)	-7.3 (-13.4, -2.8)
eGFR slope, total (mL/min/1.73m^2/year), mean (SD)											
	n = 1042	**n = 588**	**n = 281**	**n = 135**	**n = 132**	**n = 40**	**n = 454**	**n = 15**	**n = 71**	**n = 189**	**n = 179**
Mean (SD)	-3.6 (7.0)	-1.9 (6.0)	-0.5 (3.7)	-1.8 (3.3)	-3.2 (8.9)	-7.9 (9.4)	-5.8 (7.6)	-0.7 (3.1)	-1.9 (3.4)	-4.0 (4.8)	-9.7 (9.6)
Median (IQR)	-2.3 (-5.2, -0.5)	-1.4 (-3.6, -0.1)	-0.5 (-1.7, 0.8)	-1.7 (-3.4, -0.5)	-3.1 (-5.4, -1.5)	-5.3 (-8.2, -2.6)	-3.9 (-7.4, -1.6)	-1.2 (-2.2, -0.3)	-1.8 (-2.9, -0.3)	-3.1 (-5.4, -1.4)	-6.8 (-13.2, -4.0)

Abbreviations: CI, confidence interval; **eGFR**, estimated glomerular filtration rate; **HR**, hazard ratio; **IQR**, interquartile range; **SD**, standard deviation; **UPCR**, urinary protein-creatinine ratio.
* 0.44 g/g = 50 mg/mmol (~0/5 g/day); 0.88 g/g = 100 mg/mmol (~1 g/day); 1.76 g/g = 200 mg/mmol (~2 g/day)

Supplemental Table 6. Clinical outcomes in Proteinuria Analysis Population 4

Proteinuria Analysis Population 4									
Time-averaged proteinuria* duration		**6-12 months**				**6-24 months**			
Time-averaged proteinuria category	**Overall**	**Combined**	**<0.44 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**	**Combined**	**<0.44 g/g**	**0.88 to <1.76 g/g**	**≥1.76 g/g**
Survival rate, estimate (95% CI)									
	n = 535	**n = 410**	**n = 125**	**n = 158**	**n = 127**	**n = 509**	**n = 152**	**n = 200**	**n = 157**
2.5-year	0.91 (0.89-0.94)	0.90 (0.86-0.93)	0.97 (0.92-0.99)	0.93 (0.87-0.96)	0.79 (0.70-0.85)	0.91 (0.88-0.93)	0.98 (0.94-1.00)	0.94 (0.90-0.97)	0.81 (0.73-0.86)
Quartile time-to-event, year (95% CI)									
75%	4.7 (4.3-5.0)	4.5 (4.0-5.0)	6.0 (4.7-7.9)	4.9 (4.4-6.9)	2.9 (2.3-3.2)	4.6 (4.2-5.0)	6.9 (5.3-10.9)	4.7 (4.2-5.4)	2.9 (2.3-3.5)
50%	8.9 (7.5-10.9)	8.0 (7.2-9.4)	10.9 (7.5-NE)	8.9 (7.4-11.8)	5.1 (3.9-5.9)	8.3 (7.4-10.9)	14.6 (8.9-NE)	9.4 (6.0-14.1)	5.3 (4.5-7.6)
25%	14.6 (14.0-NE)	14.6 (10.9-NE)	14.6 (10.9-NE)	NE (11.3-NE)	8.3 (7.2-NE)	NE (14.0-NE)	NE (14.6-NE)	NE (14.0-NE)	8.4 (8.0-NE)

Abbreviations: CI, confidence interval.
* 0.44 g/g = 50 mg/mmol (~0/5 g/day); 0.88 g/g = 100 mg/mmol (~1 g/day); 1.76 g/g = 200 mg/mmol (~2 g/day)

Supplemental Table 7. Univariable and multivariable analysis of 10-year survival and eGFR slope (Populations 1–4)

Description	Variable	Reference	Population 1				Population 2				Population 3				Population 4			
			Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
			HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq	HR	P > ChiSq
10-year survival																		
Age			1.01	0.11	0.99	0.12	1.01	0.10	0.99	0.24	1.01	0.001	1.00	0.27	1.00	0.80	0.97	<.001
Gender	Female	Male	0.66	0.001	0.66	0.002	0.56	0.004	0.57	0.01	0.67	0.002	0.70	0.01	0.51	0.00	0.48	<.001
Ethnicity	Asian	White	1.49	0.01	1.58	0.01	1.33	0.20	1.41	0.13	1.02	0.92	0.94	0.73	0.79	0.37	1.01	0.98
	Black	White	2.88	0.01	1.86	0.14	2.47	0.12	1.86	0.30	1.22	0.66	1.14	0.78	0.92	0.91	1.17	0.83
	Missing	White	1.10	0.60	1.07	0.69	1.15	0.59	1.13	0.63	0.77	0.15	0.77	0.16	0.61	0.07	0.60	0.07
	Mixed	White	1.85	0.39	1.18	0.82	1.07	0.94	0.61	0.63	0.39	0.34	0.48	0.46	1.09	0.94	0.80	0.83
	Other	White	0.46	0.18	0.52	0.26	0.71	0.73	0.47	0.45	0.43	0.14	0.44	0.15	0.69	0.60	0.47	0.30
UPCR	≥0.88 g/g	<0.88 g/g	2.40	<.001	2.19	<.001	2.75	<.001	2.65	<.001	2.84	<.001	2.80	<.001	N/A	N/A	N/A	N/A
	Missing	<0.88 g/g	1.71	0.01	1.37	0.118	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CKD stage	G2	G1	1.63	0.21	1.57	0.25	1.51	0.33	1.38	0.45	1.76	0.11	1.59	0.19	1.37	0.37	1.84	0.09
	G3a	G1	3.51	<.001	3.46	<.001	3.05	0.01	2.64	0.02	2.95	0.02	2.67	0.01	2.34	0.01	3.85	<.001
	G3b	G1	5.26	<.001	5.02	<.001	4.11	<.001	3.78	0.001	5.98	<.001	5.33	<.001	4.56	<.001	8.64	<.001
	G4+5	G1	8.87	<.001	8.58	<.001	6.32	<.001	5.51	<.001	12.30	<.001	12.46	<.001	N/A	N/A	N/A	N/A
	Missing	G1	4.23	<.001	4.64	<.001	4.31	<.001	4.14	<.001	4.56	<.001	4.32	<.001	N/A	N/A	N/A	N/A
eGFR slope																		
Age			0.72	<.001	0.61	<.001	0.76	<.001	0.63	0.002	0.73	<.001	0.68	<.001	0.98	<.001	1.06	<.001
Gender	Female	Male	0.17	0.69	0.95	0.02	-0.16	0.79	0.81	0.18	-0.15	0.63	0.36	0.22	0.78	0.13	1.45	0.01
Ethnicity	Asian	White	-1.71	0.01	-1.35	0.03	-1.22	0.15	-0.74	0.37	-0.62	0.19	-0.14	0.76	0.18	0.82	0.02	0.97
	Black	White	-0.97	0.67	-0.19	0.93	-1.77	0.53	-1.35	0.62	-1.17	0.37	-0.53	0.66	-0.94	0.67	-1.18	0.58
	Missing	White	-0.89	0.14	-0.89	0.13	-1.19	0.18	-1.05	0.23	-0.31	0.51	-0.16	0.70	-0.28	0.71	0.04	0.96
	Mixed	White	-0.68	0.84	0.30	0.93	0.62	0.87	1.95	0.60	1.21	0.49	1.78	0.27	1.33	0.71	1.09	0.75
	Other	White	-1.88	0.17	-1.49	0.26	-1.00	0.72	-0.96	0.73	-0.02	0.98	-0.04	0.97	1.70	0.39	1.79	0.35
BMI	Tertile 1	Tertile 2	-1.61	0.08	N/A	N/A	-1.30	0.24	N/A	N/A	-0.11	0.90	N/A	N/A	-1.10	0.45	N/A	N/A

	Tertile 3	Tertile 2	-1.04	0.24	N/A	N/A	-1.40	0.21	N/A	N/A	0.06	0.94	N/A	N/A	-1.11	0.46	N/A	N/A
	Missing	18 - <24	0.40	0.55	N/A	N/A	-0.33	0.69	N/A	N/A	0.12	0.86	N/A	N/A	0.25	0.81	N/A	N/A
Systolic BP	Tertile 1	Tertile 2	-0.77	0.40	N/A	N/A	-0.92	0.41	N/A	N/A	1.38	0.04	N/A	N/A	-0.81	0.47	N/A	N/A
	Tertile 3	Tertile 2	-0.63	0.50	N/A	N/A	0.03	0.98	N/A	N/A	-0.25	0.71	N/A	N/A	-1.65	0.14	N/A	N/A
	Missing	Tertile 2	-0.96	0.16	N/A	N/A	-0.80	0.36	N/A	N/A	0.09	0.87	N/A	N/A	-0.43	0.61	N/A	N/A
UPCR	≥0.88 g/g	<0.88 g/g	-2.60	<.001	-2.82	<.001	0.00	<.001	-2.61	<.001	-2.95	<.001	-2.82	<.001	N/A	N/A	N/A	N/A
	Missing	<0.88 g/g	-1.17	0.026	-1.52	0.01	-2.34	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CKD stage	G2	G1	0.45	0.54	0.44	0.54	1.10	0.22	1.15	0.19	-0.35	0.49	-0.62	0.20	-0.24	0.75	-0.81	0.30
	G3a	G1	0.74	0.36	0.50	0.53	1.61	0.11	1.55	0.12	-0.54	0.32	-1.01	0.06	0.22	0.78	-1.23	0.13
	G3b	G1	1.14	0.12	0.60	0.43	2.06	0.02	1.55	0.11	0.25	0.61	-0.51	0.32	1.25	0.09	-0.49	0.55
	G4+5	G1	3.13	<.001	2.55	0.00	3.45	0.00	3.19	0.00	1.34	0.02	0.06	0.91	N/A	N/A	N/A	N/A
	Missing	G1	1.28	0.05	0.71	0.31	2.13	0.03	1.63	0.10	-0.09	0.86	-0.71	0.15	N/A	N/A	N/A	N/A

Abbreviations: BMI, body mass index; **BP**, blood pressure; **CKD**, chronic kidney disease; **eGFR**, estimated glomerular filtration rate; **HR**, hazard ratio; **N/A**, not applicable; **UPCR**, urinary protein-creatinine ratio.