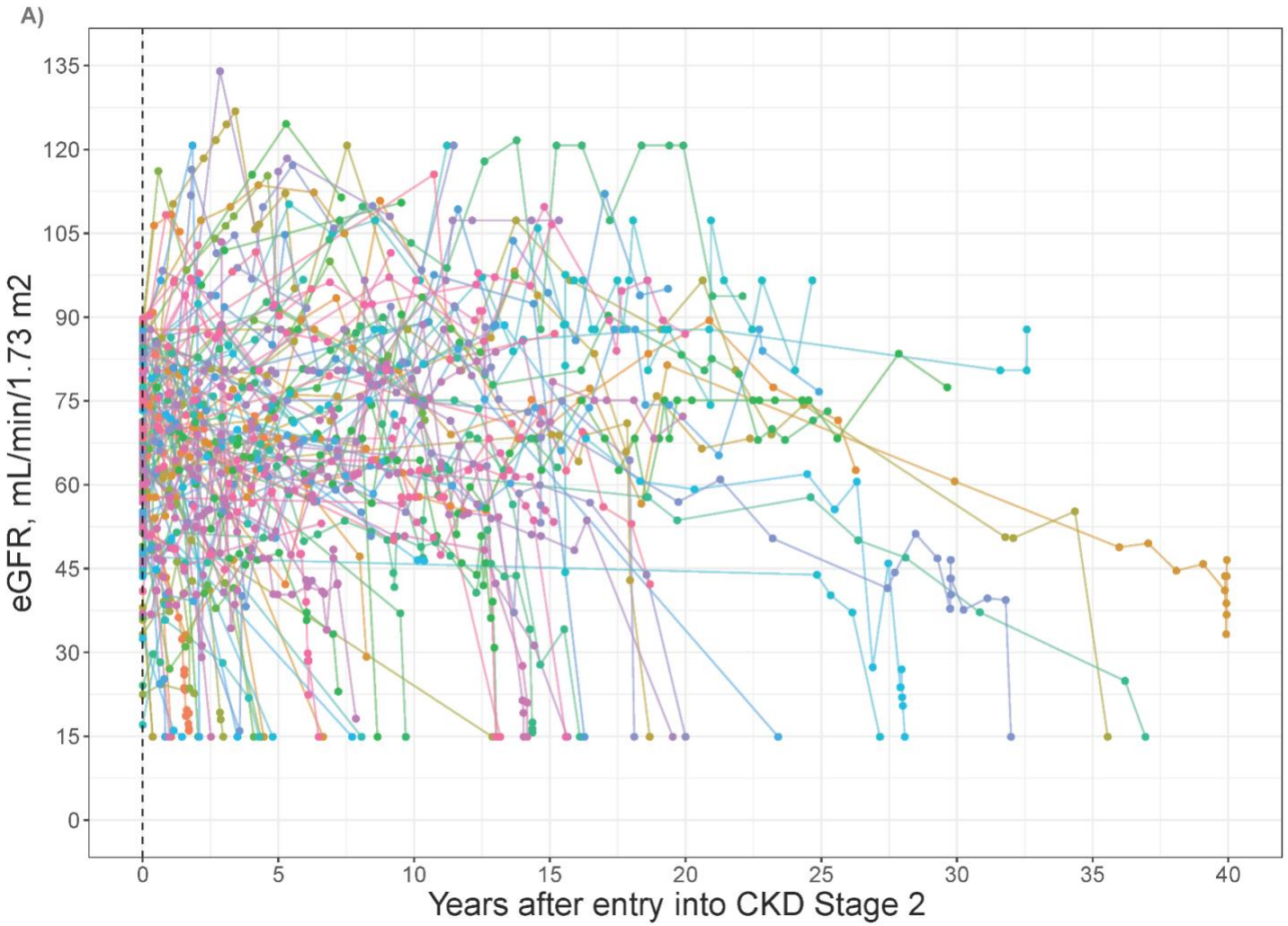
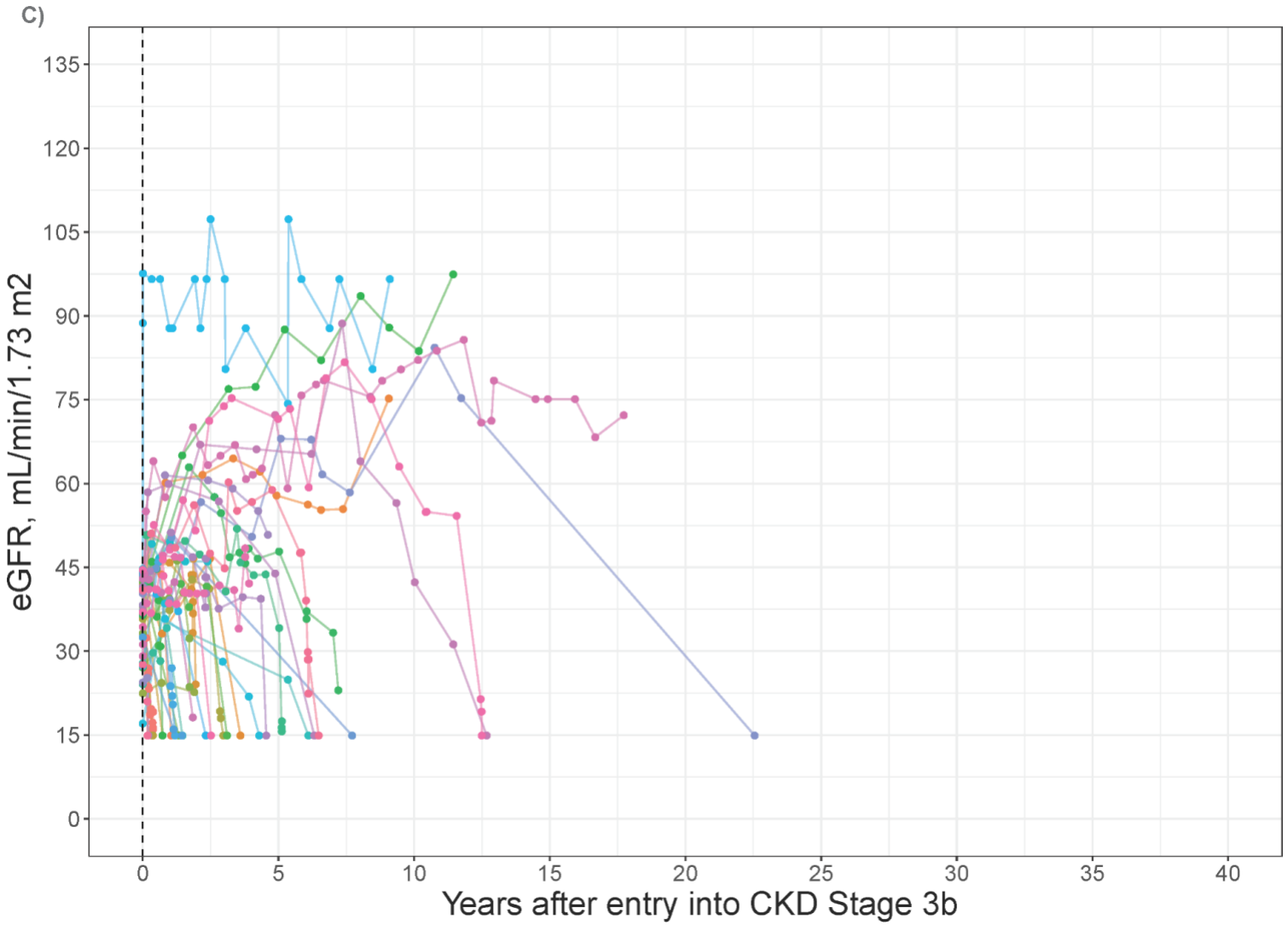
Figure S1: Individual patient trajectories of eGFR vs years after entry into CKD stage (A) 2, (B) 3a, (C) 3b, and (D) 4. Black dashed lined indicates time of entry into respective CKD stage.




B)
eGFR, mL/min/1.73 m2
135
120
105
90
75
60
45
30
15
0
0
5
10
15
20
25
30
35
40
Years after entry into CKD Stage 3a


C)
eGFR, mL/min/1.73 m2
135
120
105
90
75
60
45
30
15
0
0
5
10
15
20
25
30
35
40
Years after entry into CKD Stage 3b

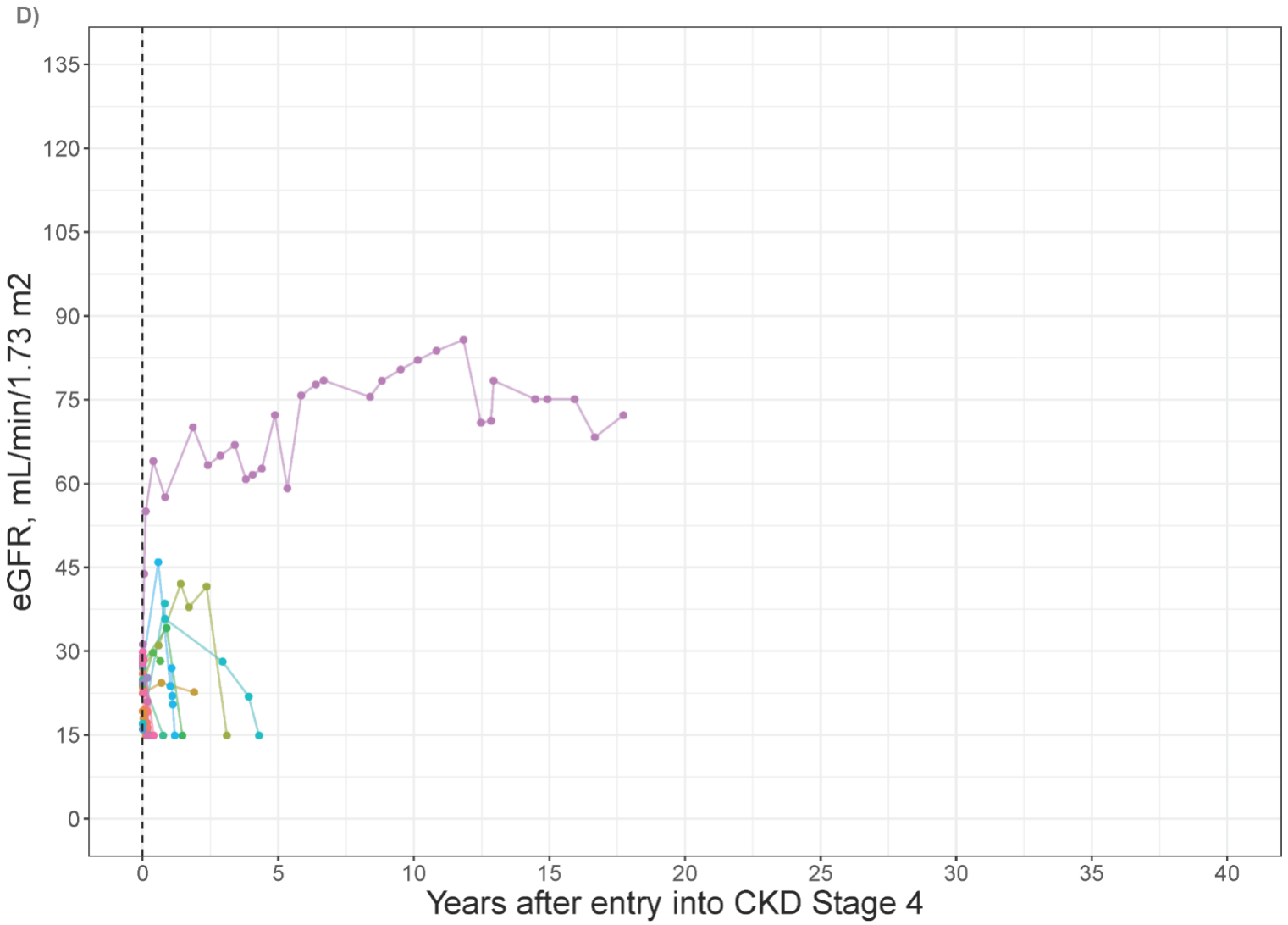

D)
eGFR, mL/min/1.73 m2
135
120
105
90
75
60
45
30
15
0
0
5
10
15
20
25
30
35
40
Years after entry into CKD Stage 4

Figure S2: Flowchart of patient entry into each CKD stage.

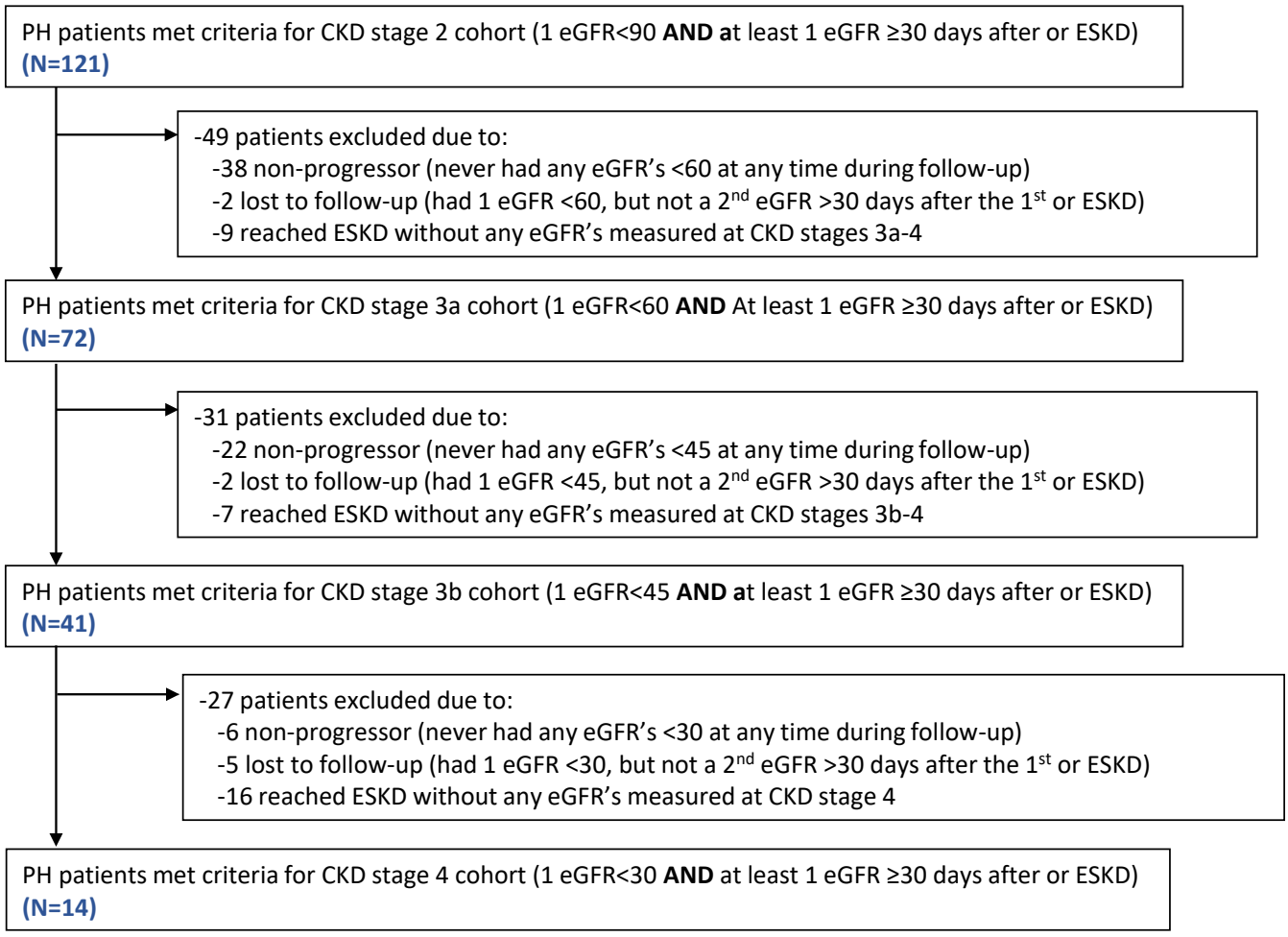


Table S1: eGFR annual rates of percent change during follow-up

	Annual percent change (%/year)				
	Mean (SD)	**Median [IQR]**	**Beta Coefficient* (SE)**	**P**	**P-trend**
CKD Stage					**<0.001**
2 (<90)	-4.1 (32)	-1.8 [-7.4, 1.3]	Ref	Ref	
3a (<60)	-7.9 (42)	-3.3 [-16, 1.1]	-0.038 (0.018)	**0.04**	
3b (<45)	-28 (34)**	-13 [-43, -5.2]	-0.13 (0.034)	**<0.001**	
4 (<30)	-39 (41)**	-33 [-80, -8.6]	-0.23 (0.076)	**0.001**	

*Beta coefficient represents the estimated percent change in eGFR slope (%/year) for each subsequent CKD stage, relative to CKD stage 2. Results were calculated using Generalized Estimating Equations (GEE) with compound symmetric working correlation to account for patients contributing multiple observations to the data.
**Significantly different from 0 at the 0.05 alpha level.
P-values in bold denote statistical significance at the 0.05 alpha level.

Table S2: Univariate associations between eGFR percentage change and factors at entry into CKD stage

	Patient characteristic	N	Estimate*	Lower 95% CI	Upper 95% CI	P
Stage 2 (eGFR<90)	Male, n(%)	121	0.047	-0.07	0.16	0.4
	Age at PH dx (per 10 years)	121	-0.03	-0.06	0.01	0.2
	Difference b/t Symptom Onset and PH dx (years)	106	-0.003	-0.01	0.002	0.3
	Age at 1st entry into CKD stage (per decade)	121	-0.04	-0.08	-0.01	**0.02**
	eGFR at 1st entry into CKD stage (per 10 mL/min/1.73 m2)	121	0.01	-0.02	0.05	0.5
	Nephrocalcinosis, n(%)	121	0.08	-0.03	0.21	0.2
	Plasma oxalate† (per 1 umol/L)	28	0.01	-0.007	0.03	0.3
	BSA adjusted urine oxalate†(per 0.1 mmol/1.73 m2/24 h)	80	-0.003	-0.01	0.002	0.3
Stage 3a (eGFR<60)	Male, n(%)	72	0.15	-0.04	0.34	0.1
	Age at PH dx (per 10 years)	72	-0.02	-0.09	0.04	0.4
	Difference b/t Symptom Onset and PH dx (years)	66	-0.002	-0.01	0.01	0.7
	Age at 1st entry into CKD stage (per decade)	72	-0.05	-0.11	0.003	0.07
	eGFR at 1st entry into CKD stage (per 10 mL/min/1.73 m2)	72	0.04	-0.06	0.15	0.4
	Nephrocalcinosis, n(%)	72	0.10	-0.09	0.29	0.3
	Plasma oxalate† (per 1 umol/L)	20	0.02	-0.001	0.05	0.07
	BSA adjusted urine oxalate† (per 0.1 mmol/1.73 m2/24 h)	47	-0.004	-0.01	0.005	0.4
Stage 3b (eGFR<45)	Male, n(%)	41	0.04	-0.17	0.25	0.7
	Age at PH dx (per 10 years)	41	-0.002	-0.07	0.06	0.9
	Difference b/t Symptom Onset and PH dx (years)	36	0.003	-0.01	0.01	0.5
	Age at 1st entry into CKD stage (per decade)	41	-0.02	-0.08	0.03	0.4
	eGFR at 1st entry into CKD stage (per 10 mL/min/1.73 m2)	41	-0.02	-0.16	0.13	0.8
	Nephrocalcinosis, n(%)	41	0.06	-0.16	0.27	0.6
	Plasma oxalate† (per 1 umol/L)	18	-0.004	-0.02	0.01	0.7
	BSA adjusted urine oxalate† (per 0.1 mmol/1.73 m2/24 h)	29	-0.01	-0.02	-0.001	**0.04**
Stage 4 (eGFR<30)	Male, n(%)	14	-0.01	-0.47	0.46	0.9
	Age at PH dx (per 10 years)	14	0.077	-0.07	0.22	0.3
	Difference b/t Symptom Onset and PH dx (years)	13	0.02	-0.001	0.04	0.09
	Age at 1st entry into CKD stage (per decade)	14	0.02	-0.10	0.14	0.8
	eGFR at 1st entry into CKD stage (per 10 mL/min/1.73 m2)	14	-0.09	-0.63	0.45	0.8
	Nephrocalcinosis, n(%)	14	-0.50	-0.84	-0.16	**0.01**
	Plasma oxalate† (per 1 umol/L)	8	-0.01	-0.03	0.01	0.4
	BSA adjusted urine oxalate† (per 0.1 mmol/1.73 m2/24 h)	11	-0.02	-0.04	0.002	0.1

Models are fit separately for different CKD stages.

*Estimate: Change in annual percent rate of change of eGFR (%/year) per 1 unit increase in patient characteristic

†Lab values at baseline were defined as occurring between 1 year prior to and up to 1 week after entry into CKD stage

P-values in bold denote statistical significance at the 0.05 alpha level.

Table S3: Coefficients from linear mixed models for plasma oxalate vs eGFR

Predictor	Coefficient	SE	P
Outcome: ln(Plasma Oxalate)*			
Intercept	6.755	0.450	**<0.001**
Ln(eGFR)	-1.237	0.108	**<0.001**

*Fitted equation: ln(POX) ~ ln(eGFR), with random intercepts per subject
P-values in bold denote statistical significance at the 0.05 alpha level.

Table S4: eGFR annual rates of change during follow-up, by G170R mutation status

	N	N eGFR	N follow-up eGFR per patient, Median [IQR]	Annual rate of change (ml/min/1.73m^2/year)				
				Mean (SD)	Median [IQR]	Beta Coefficient* (SE)	P	P-trend
Homozygous G170R mutation								
CKD Stage								NE
2 (<90)	11	118	10 [7, 14]	1.3 (1.9)	1.3 [0.1, 2.2]	Ref	Ref	
3a (<60)	1	16	16 []	3.0 ()	3.0 []	NE	NE	
3b (<45)	0	-	-	-	-	-	-	
4 (<30)	0	-	-	-	-	-	-	
Heterozygous G170R mutation								
CKD Stage								0.4
2 (<90)	50	492	8 [4, 13]	-3.1 (10.8)	-1.3 [-3.7, 1.0]	Ref	Ref	
3a (<60)	29	336	10 [7, 15]	-6.6 (22.4)	-1.4 [-4.4, 1.2]	-3.6 (3.7)	0.3	
3b (<45)	16	143	8 [3, 13]	-11.8 (27.7)	-3.1 [-6.9, -0.2]	-4.9 (5.3)	0.4	
4 (<30)	5	20	3 [3, 6]	-11.1 (11.9)	-7.5 [-13.3, -2.4]	-2.8 (3.9)	0.5	
No G170R mutation								
CKD Stage								**0.002**
2 (<90)	60	629	8 [4, 14]	-2.3 (17.2)	-1.0 [-3.2, 0.7]	Ref	Ref	
3a (<60)	42	415	6 [3, 13]	-4.6 (20.9)	-1.5 [-6.6, 0.2]	-1.7 (0.9)	0.07	
3b (<45)	25	218	6 [3, 11]	-16.5 (22.6)	-5.2 [-24.3, -1.8]	-7.6 (2.7)	**0.005**	
4 (<30)	9	73	3 [3, 8]	-19.6 (23.5)	-11.7 [-34.5, -0.1]	-14.3 (5.4)	**0.008**	

NE=Not estimable due to small sample size.

*Beta coefficient represents the estimated change in eGFR slope (ml/min/1.73m2/year) for each subsequent CKD stage, relative to CKD stage 2. Results were calculated using Generalized Estimating Equations (GEE) with compound symmetric working correlation to account for patients contributing multiple observations to the data.

P-values in bold denote statistical significance at the 0.05 alpha level.

Table S5: Predicted Pox and rate of change across different CKD stages using a linear mixed model framework

Predicted Plasma Oxalate		
eGFR	**Estimate (95% CI)*, umol/L**	**Slope****
15	30.47 (22.14, 41.68)	-2.48
30	12.88 (10.54, 15.64)	-0.53
45	7.77 (6.7, 9.03)	-0.21
60	5.44 (4.82, 6.3)	-0.11
75	4.13 (3.6, 4.82)	-0.07
90	3.29 (2.8, 3.9)	-0.05

*95% CI for the mean predicted value at a given eGFR estimated using bootstrapping method

**Slope represents the estimated average change in Pox for every 1-unit increase in eGFR (units= (µmol/L)/ (ml/min/1.73m^2)) , and was calculated by taking the derivative of the equation at different levels of eGFR.