

Table S1. Genotype, plus one or more other variables as predictors of incidence of ESRD (A), eGFR, 50% decline or ESRD (B), or htTKV, 50% increase (C)

Predictors		Genotypic group: HR (95% Confidence Interval)^				C-index	Model
A.	ESRD	PKD1-NT1	PKD1-NT2	PKD2	P		
	Genotype (unadjusted)	0.636 (0.461-0.877)	0.362 (0.256-0.512)	0.168 (0.107-0.265)	<0.001	0.655	
	Genotype + sex	0.633 (0.459-0.873)	0.349 (0.246-0.495)	0.152 (0.096-0.241)	<0.001	0.682	
	Genotype + baseline eGFR ¹ , 10 mL/min/1.73 m ²	0.847 (0.612-1.172)	0.567 (0.394-0.815)	0.306 (0.188-0.497)	<0.001	0.824	
	Genotype + baseline MIC	0.884 (0.612-1.276)	0.347 (0.214-0.562)	0.202 (0.115-0.356)	<0.001	0.780	
	Genotype + baseline BMI ¹ , 5 kg/m ²	0.628 (0.446-0.884)	0.352 (0.241-0.513)	0.158 (0.098-0.256)	<0.001	0.693	
	Genotype + sex + baseline eGFR + baseline BMI	0.857 (0.608-1.207)	0.515 (0.345-0.767)	0.267 (0.159-0.449)	<0.001	0.824	Table 3 Top
	Genotype + all others*	0.957 (0.653-1.402)	0.420 (0.252-0.699)	0.273 (0.150-0.497)	<0.001	0.845	Table 3 Bottom
B. eGFR, 50% decline or ESRD							
	Genotype (unadjusted)	0.678 (0.518-0.888)	0.373 (0.279-0.499)	0.247 (0.178-0.343)	<0.001	0.638	
	Genotype + sex	0.682 (0.521-0.893)	0.367 (0.274-0.492)	0.234 (0.168-0.325)	<0.001	0.656	
	Genotype + baseline eGFR ¹ , 10 mL/min/1.73 m ²	0.827 (0.631-1.085)	0.531 (0.394-0.715)	0.401 (0.284-0.565)	<0.001	0.736	
	Genotype + baseline MIC	0.850 (0.629-1.148)	0.450 (0.310-0.652)	0.326 (0.221-0.480)	<0.001	0.736	
	Genotype + baseline BMI ¹ , 5 kg/m ²	0.710 (0.536-0.940)	0.368 (0.269-0.503)	0.246 (0.175-0.346)	<0.001	0.668	
	Genotype + sex + baseline eGFR + baseline BMI	0.843 (0.636-1.118)	0.488 (0.355-0.673)	0.360 (0.252-0.514)	<0.001	0.732	Table 3 Top
	Genotype + all others*	0.947 (0.696-1.290)	0.500 (0.340-0.735)	0.381 (0.254-0.573)	<0.001	0.765	Table 3 Bottom
C. htTKV, 50% increase							
	Genotype (unadjusted)	0.981 (0.636-1.512)	0.852 (0.541-1.340)	0.668 (0.414-1.077)	0.40	0.532	
	Genotype + sex	0.968 (0.628-1.493)	0.749 (0.473-1.188)	0.598 (0.369-0.969)	0.17	0.589	
	Genotype + baseline eGFR ¹ , 10 mL/min/1.73 m ²	1.000 (0.646-1.550)	0.847 (0.533-1.346)	0.672 (0.409-1.103)	0.42	0.518	
	Genotype + baseline MIC	1.077 (0.696-1.665)	1.017 (0.641-1.615)	0.799 (0.489-1.305)	0.75	0.615	
	Genotype + baseline BMI ¹ , 5 kg/m ²	0.968 (0.623-1.505)	0.837 (0.531-1.319)	0.646 (0.400-1.045)	0.34	0.542	
	Genotype + sex + baseline eGFR + baseline BMI	0.988 (0.632-1.544)	0.743 (0.464-1.188)	0.575 (0.348-0.948)	0.12	0.580	Table 5 Top
	Genotype + all others*	1.048 (0.667-1.648)	0.863 (0.535-1.391)	0.615 (0.368-1.029)	0.26	0.636	Table 5 Bottom

Hazard ratios and p-values in bold denote statistical significance at the 0.05 level. Age scale used for all Cox regression models. *Sex, baseline eGFR, MIC, and baseline BMI; ^Referenced to PKD1-T; ¹Incremental unit associated with the outcome is indicated

Table S2. Baseline Mayo Imaging Class (MIC), plus one or more other variables as predictors of incidence of ESRD (A), or eGFR, 50% decline or ESRD (B).

Predictors		Mayo Imaging Class (MIC): HR (95% Confidence Interval)^					P	C-index	Model
A.	ESRD	MIC-1D	MIC-1C	MIC-1B	MIC-1A				
	MIC (unadjusted)	0.293 (0.193-0.445)	0.113 (0.072-0.178)	0.040 (0.023-0.070)	0.008 (0.002-0.027)	<0.001		0.734	
	MIC + genotype	0.266 (0.174-0.406)	0.117 (0.074-0.185)	0.037 (0.021-0.066)	0.007 (0.002-0.025)	<0.001		0.780	
	MIC + sex	0.290 (0.191-0.441)	0.111 (0.070-0.175)	0.039 (0.022-0.069)	0.007 (0.002-0.026)	<0.001		0.737	
	MIC + baseline eGFR ¹ , 10 mL/min/1.73 m ²	0.379 (0.244-0.591)	0.269 (0.165-0.439)	0.123 (0.067-0.227)	0.045 (0.012-0.161)	<0.001		0.833	
	MIC + baseline BMI ¹ , 5 kg/m ²	0.299 (0.193-0.463)	0.123 (0.077-0.197)	0.043 (0.024-0.076)	0.009 (0.003-0.032)	<0.001		0.755	
	MIC + sex + baseline eGFR + baseline BMI	0.308 (0.190-0.501)	0.216 (0.127-0.369)	0.092 (0.046-0.180)	0.033 (0.009-0.126)	<0.001		0.830	Table 3 Middle
	MIC + all others*	0.292 (0.178-0.479)	0.217 (0.127-0.374)	0.083 (0.041-0.168)	0.032 (0.008-0.127)	<0.001		0.845	Table 3 Bottom
B. eGFR, 50% decline or ESRD									
	MIC (unadjusted)	0.412 (0.291-0.583)	0.177 (0.123-0.255)	0.086 (0.056-0.131)	0.031 (0.015-0.063)	<0.001		0.705	
	MIC + genotype	0.394 (0.278-0.558)	0.189 (0.130-0.273)	0.089 (0.058-0.138)	0.035 (0.017-0.072)	<0.001		0.736	
	MIC + sex	0.406 (0.286-0.575)	0.173 (0.119-0.250)	0.082 (0.053-0.126)	0.029 (0.014-0.059)	<0.001		0.704	
	MIC + baseline eGFR ¹ , 10 mL/min/1.73 m ²	0.473 (0.332-0.675)	0.291 (0.197-0.428)	0.162 (0.103-0.255)	0.081 (0.038-0.173)	<0.001		0.752	
	MIC + baseline BMI ¹ , 5 kg/m ²	0.424 (0.295-0.608)	0.190 (0.130-0.278)	0.091 (0.059-0.140)	0.036 (0.018-0.075)	<0.001		0.716	
	MIC + sex + baseline eGFR + baseline BMI	0.432 (0.297-0.627)	0.265 (0.177-0.397)	0.136 (0.084-0.220)	0.070 (0.032-0.152)	<0.001		0.753	Table 3 Middle
	MIC + all others*	0.416 (0.286-0.606)	0.274 (0.182-0.411)	0.134 (0.082-0.219)	0.072 (0.032-0.160)	<0.001		0.765	Table 3 Bottom
C. htTKV, 50% increase									
	MIC (unadjusted)	0.542 (0.319-0.919)	0.387 (0.232-0.647)	0.316 (0.183-0.547)	0.153 (0.066-0.355)	<0.001		0.609	
	MIC + genotype	0.535 (0.315-0.909)	0.392 (0.233-0.657)	0.323 (0.185-0.563)	0.155 (0.066-0.363)	<0.001		0.615	
	MIC + sex	0.545 (0.321-0.926)	0.410 (0.245-0.685)	0.373 (0.214-0.652)	0.187 (0.080-0.438)	<0.001		0.628	
	MIC + baseline eGFR ¹ , 10 mL/min/1.73 m ²	0.499 (0.292-0.851)	0.343 (0.202-0.583)	0.271 (0.153-0.480)	0.123 (0.051-0.295)	<0.001		0.620	
	MIC + baseline BMI ¹ , 5 kg/m ²	0.561 (0.327-0.963)	0.409 (0.241-0.695)	0.331 (0.188-0.584)	0.168 (0.071-0.396)	<0.001		0.606	
	MIC + sex + baseline eGFR + baseline BMI	0.510 (0.295-0.881)	0.376 (0.218-0.648)	0.329 (0.181-0.597)	0.163 (0.066-0.400)	<0.001		0.632	Table 5 Middle
	MIC + all others*	0.488 (0.281-0.847)	0.377 (0.217-0.654)	0.344 (0.187-0.633)	0.166 (0.067-0.413)	<0.001		0.636	Table 5 Bottom

Hazard ratios and p-values in bold denote statistical significance at the 0.05 level. Age scale used for all Cox regression models. *Genotype, sex, baseline eGFR, and baseline BMI; ^Referenced to MIC-1E; ¹Incremental unit associated with the outcome is indicated

Table S3. Comparison of baseline characteristics of the Analysis and Validation cohorts

Baseline Characteristic	Analysis Cohort (N=1079)	Validation Cohort (N=832)	P
Sex			<0.001
F	655 (60.7%)	424 (51.0%)	
M	424 (39.3%)	408 (49.0%)	
MSG group			0.002
PKD1-T	549 (50.9%)	465 (55.9%)	
PKD1-NT1	166 (15.4%)	145 (17.4%)	
PKD1-NT2	190 (17.6%)	96 (11.5%)	
PKD2	174 (16.1%)	126 (15.1%)	
PKD class			<0.001
Total	646	490	
1A	72 (11.1%)	21 (4.3%)	
1B	156 (24.1%)	110 (22.4%)	
1C	198 (30.7%)	174 (35.5%)	
1D	140 (21.7%)	116 (23.7%)	
1E	80 (12.4%)	69 (14.1%)	
1st eGFR measure			
eGFR			<0.001
N	890	832	
Mean (SD)	62.9 (30.6)	75.2 (27.7)	
Median (Q1, Q3)	63.9 (38.2, 85.1)	73.6 (52.8, 96.1)	
Age			<0.001
Mean (SD)	43.2 (12.7)	40.4 (10.9)	
Median (Q1, Q3)	43.4 (35.1, 51.6)	40.8 (33.9, 47.6)	
1st htTKV measure			
htTKV			<0.001
N	645	490	
Mean (SD)	929.4 (814.6)	674.7 (385.3)	
Median (Q1, Q3)	659.1 (405.8, 1172.9)	575.0 (393.1, 833.5)	
Age			<0.001
Mean (SD)	43.0 (12.6)	35.0 (8.7)	
Median (Q1, Q3)	42.9 (34.7, 51.4)	35.9 (29.3, 42.4)	

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

Table S4. Coefficients for the polynomial model predicting eGFR with genotypic group (A) or Mayo Imaging Class (B)

Variable	Coefficient	SE	P
A. Genotypic group			
Intercept	160.6239315	4.2588961	<0.001
Age, per decade	-24.6487871	1.8861001	<0.001
Age ² , per decade	-0.1732553	0.2161428	0.42
Genotype group			
PKD1-T	Ref	Ref	Ref
PKD1-NT1	47.7918701	10.8334966	<0.001
PKD1-NT2	-30.1620433	11.0033402	0.006
PKD2	-24.7224933	10.9069183	0.023
Age, per decade x MSG			
Age x PKD1-NT1	-10.3718604	4.7394907	0.029
Age x PKD1-NT2	20.6923914	4.7265815	<0.001
Age x PKD2	13.5738101	4.6540383	0.004
Age², per decade x MSG			
Age ² x PKD1-NT1	0.5121629	0.5234171	0.33
Age ² x PKD1-NT2	-1.8256422	0.5093658	<0.001
Age ² x PKD2	-0.2822898	0.5007487	0.57
B. Mayo Imaging Class			
Intercept	201.146894	8.9594595	<0.001
Age, per decade	-52.679874	4.6918594	<0.001
Age ² , per decade	2.696095	0.6285822	<0.001
Mayo Imaging Class			
1E	Ref	Ref	Ref
1D	-36.540071	12.5179146	0.003
1C	-57.221993	11.1151132	<0.001
1B	-125.138605	11.8245850	<0.001
1A	-123.159168	17.6086370	<0.001
Age, per decade x MIC			
Age x 1D	32.724901	6.2527185	<0.001
Age x 1C	41.580611	5.5006436	<0.001
Age x 1B	68.282861	5.7055145	<0.001
Age x 1A	68.990081	7.9274478	<0.001
Age², per decade x MIC			
Age ² x 1D	-4.173090	0.7968613	<0.001
Age ² x 1C	-4.272955	0.7025311	<0.001
Age ² x 1B	-6.078826	0.7160393	<0.001
Age ² x 1A	-5.694613	0.9199329	<0.001

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

Table S5. Paired differences between observed and predicted eGFR, by genotypic group (A) or Mayo Imaging Class (B) at different ages using a polynomial model

Age	15-29		30-39		40-49		50-65	
Predicted parameter	N	Diff (SE)	N	Diff (SE)	N	Diff (SE)	N	Diff (SE)
A. Genotypic Group – Analysis Cohort								
PKD1-T	466	-20.0 (1.4)	1082	-10.4 (0.9)	1704	-0.7 (0.7)	1801	14.4 (0.5)
PKD1-NT1	124	-37.6 (2.7)	177	-13.4 (2.3)	565	-3.1 (1.2)	679	26.1 (1.0)
PKD1-NT2	96	-10.7 (1.6)	158	-6.7 (1.4)	649	0.1 (1.2)	731	-2.1 (1.0)
PKD2	38	4.1 (1.6)	270	-8.8 (1.3)	523	3.0 (1.0)	747	-5.7 (0.9)
B. Validation Cohort								
PKD1-T	-		-		-		-	
PKD1-NT1	627	4.3 (0.9)	1224	3.9 (0.7)	1899	9.7 (0.5)	1290	21.7 (0.5)
PKD1-NT2	105	-27.4 (2.8)	447	-11.1 (1.1)	567	3.4 (1.0)	469	15.2 (0.8)
PKD1-NT2	61	-7.1 (3.6)	228	-10.9 (1.7)	451	-1.9 (1.1)	308	-0.2 (1.2)
PKD2	100	4.5 (1.5)	164	6.0 (1.3)	546	4.8 (0.8)	613	-7.0 (0.7)
C. Mayo Imaging Class - Analysis Cohort								
1E	-		-		-		-	
1D	237	-24.4 (2.1)	343	-7.3(1.5)	323	9.9 (1.2)	323	31.0 (1.8)
1C	76	-11.1 (2.1)	322	-4.5 (1.5)	724	-6.7 (0.7)	543	12.5 (0.6)
1B	138	-9.8 (1.3)	571	-6.3 (0.8)	776	-7.1 (0.8)	1175	3.3 (0.6)
1A	117	7.2 (1.7)	170	3.3 (1.5)	772	5.2 (0.7)	996	-1.2 (0.7)
1A	23	8.0 (2.3)	58	-5.1 (2.0)	294	3.3 (0.9)	366	-7.1 (1.1)
D. Validation Cohort								
1E	-		-		-		-	
1D	337	9.1 (1.4)	376	14.7 (1.2)	64	6.9 (1.5)	NA	NA
1C	223	4.1 (1.1)	461	4.1 (0.8)	470	16.4 (1.0)	77	36.4 (2.0)
1B	187	0.7 (1.6)	571	3.9 (0.7)	1018	8.2 (0.6)	311	13.2 (1.0)
1A	103	14.4 (1.4)	307	11.1 (0.7)	701	6.8 (0.6)	236	0.9 (1.4)
1A	13	9.7 (2.4)	42	2.1 (2.4)	97	1.2 (1.8)	41	-3.1 (3.6)

*Diff = observed eGFR – predicted GFR, ml/min/1.73 m²; positive (+) means underestimated; N = number of eGFR values

Table S6. Coefficients for the polynomial model predicting ln(htTKV) with genotypic group (A) or MIC (B)

Variable	Coefficient	SE	P
A. Genotypic group			
Intercept	4.3908010	0.0999775	<0.001
Age, per decade	0.7326714	0.0426548	<0.001
Age ² , per decade	-0.0334462	0.0050854	<0.001
Genotype group			
PKD1-T	Ref	Ref	Ref
PKD1-NT1	-0.2446446	0.1425766	0.09
PKD1-NT2	-1.1675105	0.1443438	<0.001
PKD2	-0.8779331	0.1493932	<0.001
Age, per decade x MSG			
Age x PKD1-NT1	-0.0194629	0.0264681	0.46
Age x PKD1-NT2	0.1158409	0.0256690	<0.001
Age x PKD2	0.0219117	0.0258811	0.40
B. Mayo Imaging Class			
Intercept	4.8226725	0.2036496	<0.001
Age, per decade	0.9235524	0.1165965	<0.001
Age ² , per decade	-0.0446766	0.0164286	0.007
Mayo Imaging Class			
1E	Ref	Ref	Ref
1D	-0.1448802	0.2883640	0.62
1C	-0.4981851	0.2500150	0.046
1B	-0.2548785	0.2521335	0.31
1A	0.3040507	0.3279877	0.35
Age, per decade x MIC			
Age x 1D	-0.2776101	0.1541878	0.072
Age x 1C	-0.2980688	0.1350656	0.027
Age x 1B	-0.6243045	0.1342649	<0.001
Age x 1A	-0.9644288	0.1608954	<0.001
Age², per decade x MIC			
Age ² x 1D	0.0305061	0.0204864	0.14
Age ² x 1C	0.0237030	0.0182011	0.19
Age ² x 1B	0.0522998	0.0180153	0.004
Age ² x 1A	0.0687169	0.0203127	<0.001

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

Table S7. Paired differences between observed and predicted htTKV, by genotypic group (A) or Mayo Imaging Class (B) at different ages using a polynomial model

Age	15-29		30-39		40-49		50-65	
Predicted parameter	N	Diff (SE)	N	Diff (SE)	N	Diff (SE)	N	Diff (SE)
A. Genotypic Group – Analysis Cohort								
PKD1-T	183	197 (34)	350	249 (37)	395	145 (48)	253	-418 (49)
PKD1-NT1	42	454 (116)	67	362 (86)	172	107 (57)	131	-227 (102)
PKD1-NT2	22	302 (65)	74	307 (37)	137	168 (73)	118	-148 (61)
PKD2	9	202 (34)	55	100 (31)	171	182 (51)	149	188 (62)
B. Validation Cohort								
PKD1-T	309	271 (19)	427	291 (33)	396	-136 (29)	84	-532 (49)
PKD1-NT1	55	388 (71)	178	297 (34)	161	123 (42)	21	-240 (110)
PKD1-NT2	32	481 (60)	80	334 (50)	123	282 (55)	20	-10 (133)
PKD2	49	177 (21)	70	86 (21)	172	105 (25)	54	143 (80)
C. Mayo Imaging Class - Analysis Cohort								
1E	77	213 (76)	92	-50 (92)	76	51 (115)	12	-573 (103)
1D	46	54 (11)	149	65 (18)	190	3 (29)	84	-209 (50)
1C	65	77 (6)	192	68 (13)	273	-18 (18)	231	-58 (24)
1B	53	64 (9)	91	56 (7)	237	32 (9)	209	-17 (19)
1A	15	19 (8)	22	13 (5)	99	3 (5)	115	23 (12)
D. Validation Cohort								
1E	167	6 (29)	156	-90 (45)	20	-105 (196)	NA	NA
1D	117	96 (13)	191	97 (16)	171	18 (26)	19	-306 (58)
1C	93	127 (16)	243	50 (8)	362	-3 (12)	75	-80 (45)
1B	59	80 (4)	137	68 (7)	250	37 (6)	72	24 (20)
1A	9	27 (5)	28	50 (5)	49	56 (9)	13	23 (24)

Diff = observed htTKV – predicted htTKV, ml/m; positive (+) means underestimated; N = number of htTKV values

Figure S1

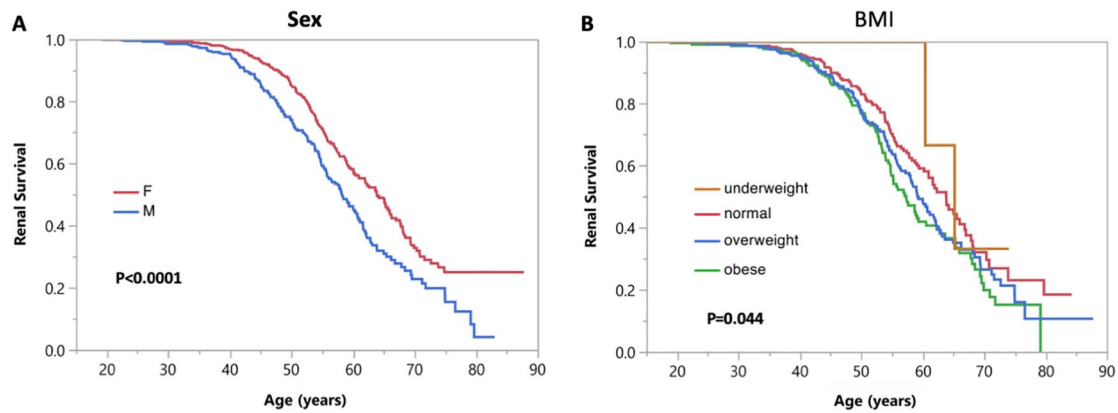


Figure S1. Unadjusted Kaplan-Meier renal survival analysis from birth (data shown from 15y) analyzing: Sex (A), and BMI (B), with P values shown. The median age at ESKD is: 63.9y and 58.2y for females and males, respectively (A, $n=1079$; $P < 0.0001$); and 65.1y, 64.2y, 62.2y and 60.6y, for BMI <20 , 20-24.9, 25-29.9, >30 , respectively (B, $n=741$, $P=0.043$);