Supplementary table S2: Clinical characteristics and management implications of the 80 patients in whom pathogenic or likely pathogenic mutations in known monogenic kidney disease genes were identified on exome sequencing

Please refer to supplementary excel file

Supplementary Table S3. Variants of potential clinical relevance but of uncertain clinical significance

Please refer to supplementary excel file

ID, Age, Sex	Referral diagnosis	Presenting features, CKD stage, HPO term	Gene, ES diagnosis, OMIM No.	Mutation Description
P0072 Male	Brachio-oto-renal (BOR) syndrome	[HP:0012583] unilateral renal hypoplasia HP:0010721 Abnormal hair whorl [HP:0000365] hearing impairment	*EDN1* autosomal recessive auriculocondylar syndrome 615706	chr6:12290865 NM_001955.4(EDN1):c.3G>C NP_001946.3(EDN1):p. (Met1?) heterozygous missense variant paternal, VOUS
P05717 Female	SNRS	[HP:0000100] nephrotic syndrome biopsy: FSGS biopsy: FSGS	*PLCE1* autosomal recessive nephrotic syndrome, type 3 174050	chr10:96058261 NM_016341.3(PLCE1):c.5293G>T NP_057425.3(PLCE1):p.(Ala1765Ser) heterozygous missense variant unknown, VOUS
P1403 Female	aHUS	[HP:0001937] microangiopathic haemolytic anaemia proteinuria CKD 1	*CFH* autosomal dominant Hemolytic uremic syndrome, atypical 235400	chr1:196711152 NM_000186.3(CFH):c.3104G>A NP_000177.2(CFH):p.(Ser1035Asn) Heterozygous, unknown, VOUS

P143 **12** **Female**	CAKUT- syndromic	[HP:0002048] renal cortical atrophy (right) Mild brachydactyly [HP:0004322] short stature [HP:0000505] visual impairment [HP:0000010] recurrent urinary tract infections nephrolithiasis	*STXBP1* autosomal dominant STXBP1-related neurodevelopmental disorder	chr9:130423447 NM_003165.3(STXBP1):c.392C>T NP_003156.1(STXBP1):p.(Thr131Met) heterozygous missense variant unknown, VOUS
P145 **12** **Female**	SRNS	[HP:0000100] nephrotic syndrome	*FAT1* FAT1 related nephropathy	chr4:187557301T>C NM_005245.3(FAT1):c.4061A>G NP_005236.2(FAT1):p.(Glu1354Gly) Heterozygous missense variant unknown, VOUS
P022 **42** **Female**	Nephrolithiasis	[HP:0000093] proteinuria [HP:0000787] nephrolithiasis [HP:0002901] hypocalcemia	*SLC34A3* autosomal recessive Hypophosphatemic rickets with hypercalciuria 241530	chr9:140429059 NM_001177317.1(SLC34A3):c.1211G>C NP_001170788.1(SLC34A3):p.(Gly404Ala) homozygous missense variant unknown, VOUS
P037 **35** **Female**	Alport	[HP:0000790] hematuria [HP:0000093] proteinuria [HP:0000365] hearing impairment [HP:0100646] thyroiditis	*COL4A4* autosomal dominant Hematuria, familial benign 141200	chr2:227942777 NM_000092.4(COL4A4):c.1820C>T NP_000083.3(COL4A4):p.(Ala607Val) heterozygous missense variant unknown, VOUS

P104 **24** **Male**	SRNS	[HP:0000100] nephrotic syndrome [HP:0012586] bilateral renal atrophy biopsy: FSGS	*CLCN5* X-linked recessive Proteinuria, low molecular weight, with hypercalciuric nephrocalcinosis 308990	chrX:49834543 NM_001127899.3(CLCN5):c.173C>T NP_001121371.1(CLCN5):p.(Ser58Leu) hemizygous missense variant unknown, VOUS
P108 **50** **Female**	Buschke-Oloendorff syndrome/MPGN	[HP:0000790] hematuria biopsy:membranoproliferative glomerulonephritis [HP:0004319] hypoaldosteronism [HP:0010739] Osteopoikilosis	*LRP5* autosomal dominant Osteopetrosis 607634	chr11:68193587G>T NM_002335.2(LRP5):c.3569G>T NP_002326.2(LRP5):p.(Arg1190Leu) Heterozygous missense variant Unknown, VOUS
P133 **47** **Male**	Reflux nephropathy questioned	[HP:0000093] proteinuria	*ANLN* autosomal dominant focal segmental glomerulosclerosis 8 616032	chr7:36445877 NM_018685.4(ANLN):c.575C>G NP_061155.2(ANLN):p.(Ser192Trp) Heterozygous missense variant Unknown, VOUS
P136 **33** **Female**	aHUS	HP:0001878 hemolytic anaemia [HP:0000093] proteinuria biopsy: suggestive of haemolytic uraemic syndrome	*REN* autosomal dominant hyperuricemic nephropathy, familial juvenile 2 613092	chr1:204124235 NM_000537.3(REN):c.1130C>A NP_000528.1(REN):p.(Pro377His) Heterozygous missense variant Unknown, VOUS

P18160 **Male**	Genetic FSGS	renal transplant	*FN1* Autosomal Dominant Glomerulopathy 601894	chr2:216236676 NM_212482.3(FN1):c.6670A>C NP_997647.1(FN1):p.(Ile2224Leu) Heterozygous missense variant Unknown, VOUS
P19864 **Male**	Primary hyperoxaluria	[HP:0000093] proteinuria biopsy:suggestive of calcium oxalate nephrolithiasis	*GLA* X-linked Fabry disease 301500	chrX:100658816 NM_000169.2(GLA):c.352C>T NP_000160.1(GLA):p.(Arg118Cys) Hemizygous missense variant Unknown, VOUS
P0030 **Female**	CAKUT	[HP:0005562] multiple renal cysts [HP:0000086] ectopic kidney (R)	*NPHP4* autosomal recessive Nephronophthisis 4 606966	chr1:6046228 NM_015102.3(NPHP4):c.122C>T NP_055917.1(NPHP4):p.(Pro41Leu) heterozygous missense variant unknown, VOUS
P01431 **Female**	Nephronophthisis	biopsy:suggestive of chronic tubulointerstitial nephritis	*UMOD* autosomal dominant Medullary cystic kidney disease 2 603860	chr16:20360508 NM_003361.3(UMOD):c.115G>C NP_003352.2(UMOD):p.(Ala39Pro) heterozygous missense variant unknown, VOUS

P149 11 Male	Alport	[HP:0000790] hematuria	*COL4A1* autosomal dominant COL4A1-related disease 611773	chr13:110817302 NM_001845.6(COL4A1)c.4057G>A NP_001836.3(COL4A1):p.(Asp1353Asn) heterozygous missense variant unknown, VOUS
P147 6 Female	Nephrocalcinosis	[HP:0000121] nephrocalcinosis [HP:0000407] sensorineural hearing impairment [HP:0005562] multiple renal cysts	*ADCY10* autosomal dominant Hypercalciuria, absorptive, susceptibility to 143870	chr1:167793897 NM_018417.5(ADCY10):c.9747T>C NP_060887.2(ADCY10):p.(Ile316Thr) heterozygous missense variant unknown, VOUS
P018 40 Female	FSGS	[HP:0000093] proteinuria	*CUBN* Autosomal Recessive Megaloblastic anemia-1, Finnish type 261100	chr10:17145204 NM_001081.3(CUBN):c.1450A>G NP_001072.2(CUBN):p.(Ser484Gly) heterozygous missense variant unknown, VOUS
P019 50 Male	FSGS	[HP:0000093] proteinuria biopsy: suggestive of FSGS	*COL4A1* autosomal dominant COL4A1-related disease 611773	chr13:110839607 NM_001845.4(COL4A1):c.1606G>A NP_001836.2(COL4A1):p.(Asp536Asn) heterozygous missense variant unknown, VOUS

P021 58 Male	ADTKD	[HP:0000790] hematuria bilateral small kidneys	*BICC1* autosomal dominant Renal dysplasia, cystic, susceptibility to 601331	chr10:6046815 NM_001080512.1(BICC1):c.520A>T NP_001073981.1(BICC1):p.(Asn174Tyr) heterozygous missense variant unknown, VOUS
P043 58 Female	FSGS	[HP:0000093] proteinuria biopsy: FSGS biopsy: FSGS	*MYO1E* autosomal recessive Glomerulosclerosis, focal segmental, 6 614131	chr15:59510161 NM_004998.3(MYO1E):c.1036G>C NP_004989.2(MYO1E):p.(Glu346Gln) heterozygous missense variant unknown, VOUS
P059 28 Female	ARPKD	[HP:0005562] multiple renal cysts	*PKHD1* autosomal recessive polycystic kidney disease 4, with or without hepatic disease 263200	chr6:51935804 NM_138694.3(PKHD1):c.667G>A NP_619639.3(PKHD1):p.(Gly223Ser) heterozygous missense variant unknown, LP
P060 36 Male	aHUS	[HP:0001878] hemolytic anaemia	*C3* autosomal dominant Hemolytic uremic syndrome, atypical, susceptibility to, 5 612925	chr19:6697742 NM_000064.2(C3):c.2504T>C NP_000055.2(C3):p.(Leu835Pro) heterozygous missense variant unknown, VOUS
P107 27 Male	FSGS	[HP:0000100] nephrotic syndrome	*FAT1* FAT1 related nephropathy	chr4:187630855 NM_005245.3(FAT1):c.127G>A NP_005236.2(FAT1):pm(Val43Met) heterozygous missense variant unknown, VOUS

P11154 Female	FSGS	bilateral small kidneys	*SLC3A1* cystinuria 220100	chr2:44547720 NM_000341.3(SLCVOUS1):c.2000T>C NP_000332.2(SLCVOUS1):p.(Phe667Ser) heterzygous missense variant unknown, VOUS
P11330 Female	Cystic Kidney Disease	[HP:0005562] multiple renal cysts	*PKD1* autosomal dominant Polycystic kidney disease 1 173900	chr16:2142549 NM_001009944.2(PKD1):c.11201A>G NP_001009944.2(PKD1):p.(Tyr3734Cys) heterozygous missense variant unknown, VOUS
P01215 Male	Unknown	[HP:0005562] multiple renal cysts [HP:0001256] Intellectual disability, mild [HP:0000508] ptosis [HP:0000316] hypertelorism [HP:0002808] kyphosis [HP:0100360] contractures upper limbs [HP:0001654] abnormality of heart valves	*FLNA* X-linked dominant Otopalatodigital syndrome types I and II; X-linked recessive Cardiac valvular dysplasia and Frontometaphyseal dysplasia 1, and FG syndrome 2	chrX:153585855 NM_001456.3(FLNA):c.4892C>T NP_001447.2(FLNA):p.(Pro1631Leu) hemizygous missense variant maternal, VOUS

P056 **19** **Female**	Unknown	[HP:0000003] multicystic kidney dysplasia [HP:0000121] nephrocalcinosis [HP:0002650] scoliosis [HP:0002091] restrictive lung disease [HP:0003701] proximal muscle weakness [HP:0002917] hypomagnesemia [HP:0003159] hyperoxaluria	*MED13L* autosomal dominant Mental retardation and distinctive facial features with or without cardiac defects 616789 *GJB2* autosomal dominant Mental retardation and distinctive facial features with or without cardiac defects 616789	chr12:116409906 NM_015335.4(MED13L):c.5867A>T NP_056150.1(MED13L):p.(Gln1956Leu) heterozygous missense variant unknown, VOUS chr13:20763650 NM_004004.5(GJB2):c.71G>A NP_003995.2(GJB2):p.(tryp24Ter) heterozygous missense variant unknown, P
P112 **24** **Male**	SRNS	[HP:0000089] hyperechogenic kidneys [HP:0000100] nephrotic syndrome biopsy: FSGS	*INF2* autosomal dominant glomerulosclerosis, focal segmental, 5 613237 *CLCNKB* autosomal recessive Bartter syndrome, type 3 607364	chr14:105169723 NM_022489.3(INF2):c.599T>G NP_071934.3(INF2):p.(Val200Gly) Heterozygous missense variant Unknown, VOUS chr1:16378296 NM_000085.4(CLCNKB):c.1389delA NP_000076.2(CLCNKB):p.(Tyr466Metfs*13) Heterozygous nonsense variant Unknown, P chr1:16373036 NM_000085.4(CLCNKB):c.236A>G NP_000076.2(CLCNKB):p.(Gln79Arg) Heterozygous missense variant Unknown, VOUS

P080 10 Male	Cystic Kidney Disease-syndromic	[HP:0005562] multiple renal cysts [HP:0006136] Bilateral postaxial polydactyly [HP:0002342] intellectual disability, moderate [HP:0000365] hearing impairment [HP:0001541] ascites [HP:0004383] hypoplastic left heart [HP:0004469] chronic bronchitis	*PKHD1* autosomal recessive polycystic kidney disease 4, with or without hepatic disease 263200 *CUL7* autosomal recessive polycystic kidney disease 4, with or without hepatic disease 263200 *SDCCAG8* autosomal recessive Bardet-Biedl syndrome. 615993	chr6:51889738 NM_138694.3(PKHD1):c.4870C>T NP_619639.3(PKHD1):p.(Arg1624Trp) Heterozygous missense variant unknown, P chr6:43011367 NM_014780.4(CUL7):c.3173-3_3174delTAGAT Heterozygous deletion variant unknown, LP chr1:243542101 NM_006642.4(SDCCAG8):c.1552A>G, NP_006633.1(SDCCAG8):p.(Arg518Gly) Heterozygous missense variant unknown, VOUS
P154 9 Female	Alport	[HP:0000790] hematuria [HP:0000093] proteinuria US consistent with nutcracker syndrome	*FAT1* FAT1 related nephropathy	chr4:187540085 NM_005245.4(FAT1):c.7655A>G NP_005236.2(FAT1):p.(Glu2552Gly) Heterozygous missense variant unknown, VOUS chr4:187630099 NM_005245.4(FAT1):c.883G>A NP_005236.2(FAT1):p.(Val295Met Heterozygous missense variant unknown, VOUS

P033 20 Female	Unknown	[HP:0000089] hyperechogenic kidneys	*COL4A1* autosomal dominant COL4A1-related disease 611773 *MYH9* autosomal dominant MYH9 realted disease 155100	chr13:110804732 NM_001845.4(COL4A1):c.4877C>G NP_001836.2(COL4A1):p.(Ala1626Gly) Heterozygous missense variant Unknown, VOUS chr22:36690158 NM_002473.4(MYH9):c.3817G>A NP_002464.1(MYH9):p.(Asp1273Asn) Heterozygous missense variant Unknown, VOUS
P011 43 Male	Familial nephritis	[HP:0000822] hypertension [HP:0000365] hearing impairment	*UMOD* autosomal dominant Medullary cystic kidney disease 2 603860 *MYH9* autosomal dominant Medullary cystic kidney disease 2 603860	chr16:20360360 NM_003361.3(UMOD):c.263G>A NP_003352.2(UMOD):p.(Gly88Asp) heterozygous missense variant unknown, VOUS chr22:36688151 NM_002473.4(MYH9):c.4225G>A NP_002464.1(MYH9):p.(Asp1409Asn) heterozygous missense variant unknown, VOUS
P116 14 Female	Alport	[HP:0000100] nephrotic syndrome biopsy: suggestive of minimal change disease	*CFHR5* autosomal dominant Nephropathy due to CFHR5 deficiency 614809 *INF2* autosomal dominant Nephropathy due to CFHR5 deficiency 614809	chr1:196973872G>A NM_030787.3(CFHR5):c.1412G>A NP_110414.1(CFHR5):p.(Gly471Glu) heterozygous missense variant unknown, VOUS chr14:105180740G>C NM_022489.3(INF2):c.3241G>C NP_071934.3(INF2):p.(Asp1081His) heterozygous missense variant unknown, VOUS

P0532 **Female**	Cystic Kidney Disease	[HP:0005562] multiple renal cysts [HP:0001903] anemia	*PRKCSH* autosomal dominant polycystic liver disease 174050 *SLIT2* autosomal dominant polycystic liver disease 174050	chr19:11560096 NM_002743.2(PRKCSH):c.1456G>A NP_002734.2(PRKCSH):p.(Gly486Arg) Heterozygous missense variant paternal, VOUS chr4:20535203 NM_004787.3(SLIT2):c.1697G>A NP_004778.1(SLIT2):p.(Ser566Asn) Heterozygous missense variant unknown, VOUS
P16337 **Female**	SRNS	[HP:0000100] nephrotic syndrome	*LAMA5* autosomal dominant LAMA5-related FSGS *INF2* autosomal dominant FSGS,5 613237	chr20:60887790 NM_005560.5(LAMA5):c.9125G>A (NP_005551.3(LAMA5):p.(Arg3042His) Heterozygous missense variant Unknown, VOUS chr14:105169767 NM_022489.3(INF2):c.643A>C NP_071934.3(INF2):p.(Thr215Pro) Heterozygous missense variant Unknown, VOUS
P01017 **Female**	Cystic Kidney Disease	bilateral small kidneys [HP:0001513] obesity [HP:0000833] glucose intolerance	*TTC21B* autosomal dominant and recessive Nephronophthisis 613820 *CSPP1* autosomal dominant and recessive Nephronophthisis 613820	chr2:166740416 NM_024753.4(TTC21B):c.3572T>C NP_079029.3(TTC21B):p.(Ile1191Thr) Heterozygous missense variant Unknown, VOUS chr8:68049694 NM_024790.6(CSPP1):c.1816C>T NP_079066.5(CSPP1):p.(Arg606Trp) Heterozygous missense variant Unknown, VOUS

P168 60 Female	Familial Meditarranean fever, FSGS	[HP:0000790] hematuria [HP:0000093] proteinuria [HP:0001955] unexplained fevers	*MEFV* autosomal recessive familial Mediterranean fever 249100	chr16:3304567 NM_000243.2(MEFV):c.501G>C NP_000234.1(MEFV):p.(Glu167Asp) Heterozygous missense variant Unknown, LP chr16:3297166 NM_000243.2(MEFV):c.1437C>G NP_000234.1(MEFV):p.(Phe479Leu) Heterozygous missense variant Unknown, VOUS chr16:3304380 NM_000243.2(MEFV):c.688G>A NP_000234.1(MEFV):p.(Glu230Lys Heterozygous missense variant Unknown, VOUS
P039 16 Male	Alport	[HP:0000790] hematuria	*COL4A3* autosomal dominant Alport syndrome 3 104200 *DHCR7* autosomal recessive Smith-Lemli-Opitz syndrome 270400	chr2:228155601 NM_000091.4(COL4A3):c.3209C>A NP_000082.2(COL4A3):p.(Thr1070Lys) heterozygous missense variant unknown, VOUS chr11:71146886 NM_001360.2(DHCR7):c.964-1G>C, heterozygous splice site variant unknown, P
P058 54 Male	FSGS	[HP:0000093] proteinuria [HP:0012586] bilateral renal atrophy	*PKHD1* autosomal recessive polycystic kidney disease 4, with or without hepatic disease 263200	chr6:51923153 NM_138694.3(PKHD1):c.1480C>T NP_619639.3(PKHD1):p.(Arg494*) heterozygous nonsense variant unknown, P

P18020 **Female**	MCKD	[HP:0005562] multiple renal cysts [HP:0000089] hyperechogenic kidneys [HP:0000093] proteinuria biopsy:features of medullary cystic kidney disease	*PKHD1* autosomal recessive polycystic kidney disease 4, with or without hepatic disease 263200	chr6:51923256_51923257delinsG NM_138694.3(PKHD1):c.1376fdelinsG NP_619639.3(PKHD1):p.(His459Argfs*3) heterozygous nonsense variant unknown, LP chr6:51915018 NM_138694.3(PKHD1):c.2216C>T NP_619639.3(PKHD1):p.(Pro739Leu) heterozygous unknown, VOUS
P06247 **Female**	FSGS	[HP:0000093] proteinuria	*CUBN* Autosomal Recessive Megaloblastic anemia-1, Finnish type 261100 *FAT1* FAT1 related nephropathy	chr10:16948208 NM_001081.3(CUBN):c.7906C>T NP_001072.2(CUBN):p.(Arg26236*) heterozygous nonsense variant unknown, LP chr4:187519198 NM_005245.3(FAT1):c.12185T>G NP_005236.2(FAT1):p.(Leu4062Arg) heterozygous missense variant unknown, VOUS
P08342 **Male**	MCKD	bilateral small kidneys	*NPHS2* autosomal recessive Nephrotic syndrome, type 2 600995	chr1:179521755 NM_014625.3(NPHS2):c.855_856del NP_055440.1(NPHS2):p.(Arg286Thrfs*17) heterozygous nonsense variant unknown, P chr1:179526214 NM_014625.3(NPHS2):c.686G>A NP_055440.1(NPHS2):p.(Arg229Gln) heterozygous missense variant unknown, VOUS

P095 32 Female	Podocytopathy	[HP:0000093] proteinuria biopsy: suggestive of thin basement membrane disease	*FAT1* FAT1 related nephropathy *FN1* Autosomal Dominant Glomerulopathy 601894	chr4:187510197 NM_005245.3(FAT1):c.13316delC NP_005236.2(FAT1):p.(Pro4439Glnfs*48) Heterozygous nonsense variant Unknown, VOUS chr2:216269303 NM_212482.1(FN1):c.3062G>A NP_997647.1(FN1):p.(Arg1021Gln) Heterozygous missense variant Unknown, VOUS
P079 9 Male	CAKUT- syndromic	[HP:0000122] unilateral renal agenesis [HP:0000110] renal dysplasia [HP:0005111] dilatation of the ascending aorta [HP:0010442] polydactyly [HP:0002808] kyphosis [HP:0001476] delayed closure of the anterior fontanelle	*TTC21B* autosomal recessive short-rib thoracic dysplasia 4 with or without polydactyly 613819 *MED12* autosomal recessive short-rib thoracic dysplasia 4 with or without polydactyly 613819 *TBX18* autosomal dominant congenital anomalies of kidney and urinary tract 2 143400	chr2:166764256 NM_024753.5(TTC21B):c.2500C>T NP_079029.3(TTC21B):p.(Gln834*) Heterozygous Unknown, P chrX:70361764 NM_005120.3(MED12):c.6440A>G NP_005111.2(MED12):p.(Gln2147Arg) hemizygous missense variant Unknown, VOUS chr6:85466472 NM_001080508.3(TBX18):c.715G>A NP_001073977.1(TBX18):p.(Val239Ile) Heterozygous missense variant Unknown, VOUS

P069 **18** **Female**	Nephronophthisis	[HP:0000093] proteinuria [HP:0000556] retinal dystrophy biopsy: non specific changes	*CEP290* autosomal recessive Bardet-Biedl syndrome 14 615991 *CEP250* Cone-rod dystrophy and hearing loss 2 618358	chr12:88514913_88514914del NM_025114.3(CEP290):c.1219_1220del NP_079390.3(CEP290):p.(Met407Glufs*14) heterozygous nonsense variant unknown, P chr20:34092055 NM_007186.5(CEP250):c.5858G>A NP_009117.2(CEP250_i001):p.(Arg1953Gln) heterozygous missense variant unknown, VOUS chr20:34096837 NM_007186.5(CEP250):c.6972G>C NP_009117.2(CEP250):p.(Glu2324Asp) heterozygous missense variant unknown, VOUS
P124 **15** **Female**	ADPKD	[HP:0005562] multiple renal cysts [HP:0000105] enlarged kidneys	*PKD2* autosomal dominant Polycystic kidney disease 2. 613095	chr4:88940729 NM_000297.4(PKD2):c.709+6T>G heterozygous unknown, VOUS
P202 **8** **Male**	Cystic kidney disease	[HP:0005562] multiple renal cysts [HP:0000790] hematuria	*HNF1B* autosomal dominant Renal cysts and diabetes syndrome 137920	chr17:36047399 NM_000458.4(HNF1B):c.1654-4G>A heterozygous splice site variant unknown, VOUS

P05156 **Male**	Renal Cysts and Diabetes	[HP:0005562] multiple renal cysts [HP:0000105] enlarged kidneys	*PKD1* autosomal dominant Polycystic kidney disease 1 173900 *MUC1* Medullary cystic kidney disease 1 174000	chr16:2156087 NM_001009944.2(PKD1):c.7703+5G>T heterozygous splice site variant unknown, VOUS chr16:2140926 NM_0011009944.2(PKD1):c.11962C>T NP_001009944.2(PKD1):p.(Arg3988Cys) heterozygous missense variant unknown, VOUS chr1:155162053 NM_001204286.1(MUC1):c.107C>T NP_001191215.1(MUC1):p.(Ala36Val) heterozygous missense variant unknown, VOUS
P15964 **Male**	Unknown	[HP:0000093] proteinuria	*COL4A3* autosomal dominant Alport syndrome 3 104200 *ACTN4* Glomerulosclerosis, focal segmental, 1 603278	chr2:228149062 NM_000091.4(COL4A3):c.2881+1G>A heterozygous splice site variant unknown, VOUS chr19:39216428 NM_004924.6(ACTN4):c.2075A>G NP_004915.2(ACTN4):p.(Gln692Arg) heterozygous missense variant unknown, VOUS

P110 33 Female	Minimal Change Disease	[HP:0000790] hematuria [HP:0000093] proteinuria biopsy: suggestive of minimal change disease	*LAMA5* autosomal recessive LAMA5-associated nephrotic syndrome *FN1* Glomerulopathy with fibronectin deposits 2 601894	chr20:60890080 NM_005560.4(LAMA5):c.8047+4C>T heterozygous splice site variant unknown, VOUS NM_005560.4(LAMA5):c.149VOUS>T NP_005551.3(LAMA5):p/(Ala498Val) heterozygous missense variant unknown, VOUS chr2:216252994 NM_212482.2(FN1):c.4283G>A NP_997647.1(FN1):p.(Ser1428Asn) heterozygous missense variant unknown, VOUS
P031 36 Female	Hereditary nephritis	[HP:0000093] proteinuria biopsy: features consistent with MCD	*HNF1B*	chr17:36091705_36091707dup NM_000458.4(HNF1B):c.924_926dupATT NP_000449.1(HNF1B):p.(Ala308_Phe309insLeu) Heterozygous insertion variant Unknown, VOUS

Supplementary Table S4. Multivariable logistic regression analysis of baseline clinical factors of patients

	Odds Ratio	95% Confidence Interval	P value
Age category			
< 1 year	9.06	2.90-28.26	
1-17 years	2.75	1.21-6.24	
18-30 years	0.53	0.20-1.44	
>30 years	(ref)		<0.001
Family history	2.43	1.21-4.84	0.01
Female sex	1.74	0.93-3.25	0.08
Extra-renal manifestations	0.77	0.37-1.60	0.48
Parental consanguinity	1.04	0.27-4.00	0.96

Age category: age at first presentation to nephrology
Family history: at least 1 first or second degree relative with renal disease
ref: reference group
Parental consanguinity: self-reported

Supplementary table S5: Additional positive diagnoses through the renal genetics clinic which did not count towards the diagnostic yield of whole exome sequencing for kidney disease.

ID, Age, Sex	Referral diagnosis	Presenting features, CKD stage, HPO term	ES result	Gene, Genetic diagnosis, OMIM No.	Mutation description	Clinical Course
P1224 Female	Nephrotic syndrome - syndromic	[HP:0000100] nephrotic syndrome [HP:0000089] hyperechogenic kidneys [HP:0000268] scaphocephaly [HP:0002863] myelodysplasia [HP:0004322] short stature [HP:0000405] conductive hearing impairment 1	Mendeliome analysed, diagnostic but does not explain renal phenotype	*SAMD9* AD Mirage Syndrome 617053	chr7:92732907 NM_017654.3(SAMD9):c.2504G>C NP_060124.2(SAMD9):p.(Cys835Ser) heterozygous missense variant, de novo, LP chr7:92731354 NM_017654.3(SAMD9):c.4057A>G NP_060124.2(SAMD9):p.(Lys1353Glu) heterozygous missense variant, de novo, VOUS	No result for kidney disease, but explains bone marrow failure - for recruitment to separate functional research for genomic cause of kidney disease
P13239 Male	Nephrocalcinosis, interstital nephritis	[HP:0000093] proteinuria biopsy: consistent with tubulointerstitial nephritis secondary to mushroom poisoning	no diagnosis on ES but pathogenic change in CMA found	*CLCN5* XLR Dent Disease Complex 300009	arr[hg19]Xp11.23p11.22(49,799,998-49,862,832)x0 CNV	CMA and ES ordered concurrently. No changes to current management, maternal aunt advised to have testing as has grand children.

		3				
P0641 Male	Nephronophthisis	renal hypoplasia [HP:0005562] multiple renal cysts [HP:0000089] hyperechogenic kidneys [HP:0000093] proteinuria [HP:0002240] hepatomegaly [HP:0001903] anaemia [HP:0002904] hyperbilirubinemia	CMA result showed HNF1B, given extra renal manifestations that were still unexplained by renal diagnosis, Mendeliome analyzed.	*UGT1A1* AR crigler-najjar syndrome 218800 *HNF1B* AD Renal cysts and diabetes syndrome 137920	chr2:234681059 NM_000463.2(UGT1A1):c.1456T>G NP_000454.1(UGT1A1):p.(Tyr486Asp) homozygous missense variant, unknown, P arr[GRCh37] 17q12(34841209_36352447)x1 CNV	Surveillance for diabetes, segregation in parents recommended. Parents and sibling referred for renal ultrasound.
		1				
P09824 Male	FSGS versus Alports	[HP:0000093] proteinuria [HP:0001249] intellectual disability [HP:0001513] obesity [HP:0000256] macrocephaly	CMA initially performed, explaining extra-renal features, ES subsequently performed; non diagnostic	1611.2 microdeletion syndrome	arr[GRCh37] 16p11.2(28455418_29186561)x1,16p11.2(29652488_30332561)x1 CNV	Explains other features but not renal phenotype, no changes to current management
		3a				

P146 12 Male	Cystic kidney disease	[HP:0005562] multiple renal cysts [HP:0002904] hyperbilirubinemia 1	diagnostic but does not explain renal phenotype	*SLC4A1* AD hereditary spherocytosis, type 4 612653	chr17:42336894 NM_000342.4(SLC4A1):c.665delC NP_000333.1(SLC4A1):p.(Pro222Argfs*9) heterozygous nonsense variant, unknown, P	no changes to current management, father with similar symptoms referred for testing

Supplementary table S6: Results of patients in whom rapid ES was performed

ID, Age, Sex	Referral Diagnosis	Presenting features, HPO term, CKD stage	Reason for Rapid ES	ES result	Gene, ES diagnosis, OMIM No.	Mutation description	Clinical Course
P123 1m Male	Ciliopathy	[HP:0000089] hyperechogenic kidneys [HP:0005562] multiple renal cysts 3	need for early diagnosis to determine frequency of review/surveillance and prognosis	diagnostic	*PKD1* AD Polycystic kidney disease 1 173900	chr16:2140752G>A NM_001009944.2(PKD1):c.12061C>T NP_001009944.2(PKD1):p.(Arg4021*) heterozygous missense variant, de novo, P chr16:2164551G>A NM_001009944.2(PKD1):c.2473C>T NP_001009944.2(PKD1):p.(Arg825Trp) heterozygous missense variant, paternal, VOUS	changed diagnosis; surveillance for extra renal involvement including yearly liver scans no longer required, testing of parents revealed de novo mutation, implications for them and patients sibling
P169 14 Male	Steroid resistant nephrotic syndrome	[HP:0000100] nephrotic syndrome [HP:0000717] autism biopsy consistent with FSGS 1	avoidance of renal biopsy and diagnostic trial of immunosuppression	diagnostic	*COL4A4* AD COL4A4 nephropathy 141200	chr2:227985827 NM_000092.4(COL4A4):c.230G>C NP_000083.3(COL4A4):p.(Gly77Ala) heterozygous missense variant, LP	changed diagnosis; opthalmology and audiology surveillance, additional diagnosis to SRNS and partial phenotype match, testing of parents and genetic counselling for sister prior to commencing family in future. In remission with cyclosporin
P187 7 Male	Dents Disease versus Alport	[HP:0000790] hematuria [HP:0000093] proteinuria [HP:0012408] medullary nephrocalcinosis [HP:0000717] autism	avoidance of biopsy- some features of Alport but severe proteinruia out of keeping	diagnostic	*CLCN5* XLR Dent disease 300009	chrX:49851299dupC NM_000084.4(CLCN5):c.1119dupC NP_000075.1(CLCN5):p.(Asn374Glnfs*2) hemizygous nonsense variant, P	clarified suspected diagnosis; biopsy cancelled, optham and audiology surveillance ceased

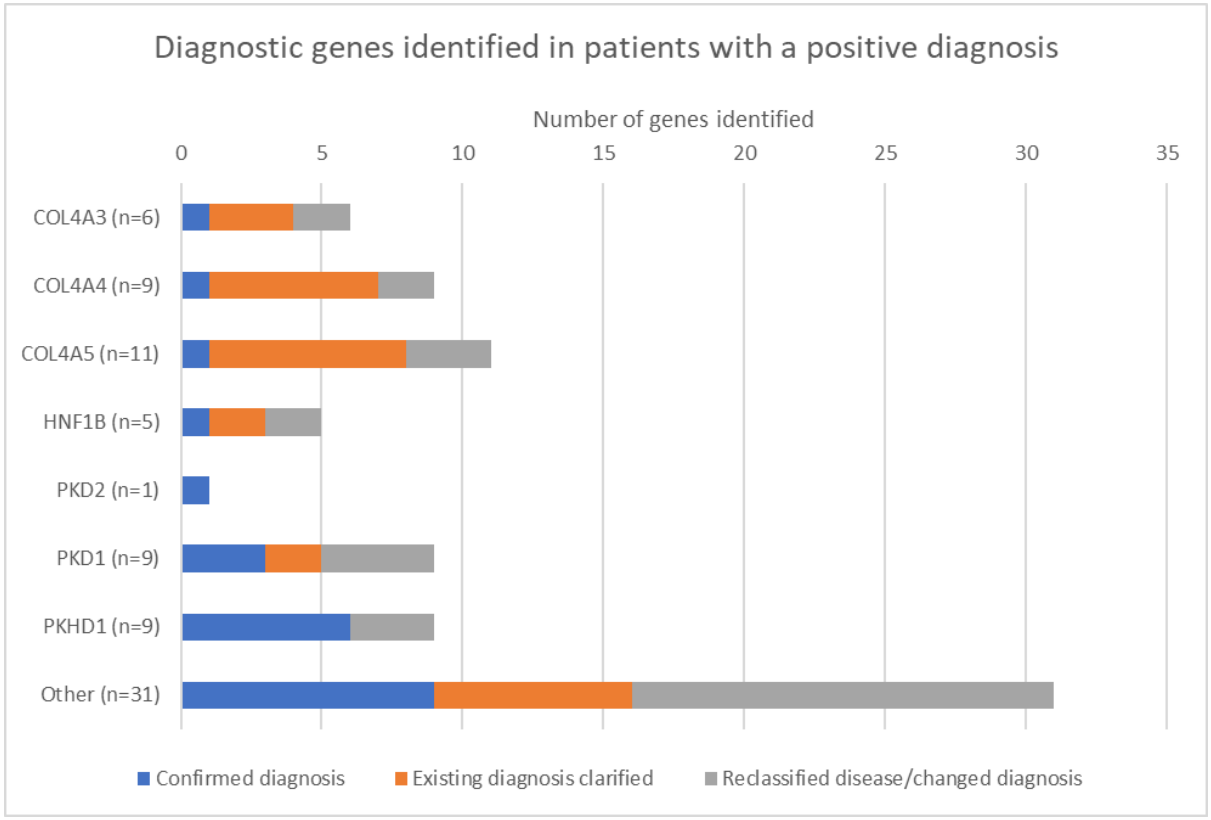
		2					
P11820 Female	ciliopathy-Senior Loken Syndrome	[HP:0000093] proteinuria [HP:0000089] hyperechogenic kidneys [HP:0001394] cirrhosis [HP:0000556] bilateral retinol dystrophy [HP:0004322] short stature biopsy: advanced chronic renal parenchymal damage 5	to faciliate transplant planning in context of hyperacute graft loss due to thrombosis in graft, to exclude genetic cause of thrombosis and faciliate donation from father	diagnostic	*IFT172* AR Short-rib thoracic dysplasia 10 with or without polydactyly 615630 *BBS9* AR Bardet-Biedl syndrome 9 615986	chr2:27667370 NM_015662.1(IFT172):c.5179T>C NP_056477.1(IFT172):p.(Cys1727Arg) heterozygous missense variant, maternal, P chr2:27695196 NM_015662.1(IFT172):c.1445T>G NP_056477.1(IFT172):p.(Val482Gly) heterozygous missense variant, paternal, LP chr7:33192414 NM_015662.1(IFT172):c.1445T>G NP_056477.1(IFT172)p.(Val482Gly) heterozygous missense variant, LP	changed diagnosis; reassurance before live donation from parent, no genetic cause of thrombosis in previous transplant identified, underwent living transplant

P1224 Female	Nephrotic syndrome - syndromic	[HP:0000100] nephrotic syndrome [HP:0000089] hyperechogenic kidneys [HP:0000268] scaphocephaly [HP:0002863] myelodysplasia [HP:0004322] short stature [HP:0000405] conductive hearing impairment 1	avoidance of renal biopsy and diagnostic trial of immunosuppression	diagnostic but not for kidney disease	*SAMD9* AD Mirage Syndrome 617053	chr7:92732907 NM_017654.3(SAMD9):c.2504G>C NP_060124.2(SAMD9):p.(Cys835Ser) heterozygous missense variant, de novo, LP chr7:92731354 NM_017654.3(SAMD9):c.4057A>G NP_060124.2(SAMD9):p.(Lys1353Glu) heterozygous missense variant, de novo, VOUS	No result for kidney disease, but explains bone marrow failure - recruitment to separate functional research for genomic cause of kidney disease
P19943 Female	thin basement membrane disease versus Alport	[HP:0000093] proteinuria [HP:0000822] hypertension biopsy consistent with TBMD 3a	to facilitate transplant planning: brother would commence dialysis soon and sister was only potential donor for consideration	non diagnostic	N/A	N/A	gene discovery research pathway underway, sister diagnosed with renal disease following renal genetics clinic
P14512 Female	Steroid resistant nephrotic syndrome	[HP:0000100] nephrotic syndrome 1	avoidance of renal biopsy and diagnostic trial of immunosuppression	non diagnostic-VOUS identified	*FAT1* FAT1 related nephropathy	chr4:187557301T>C NM_005245.3(FAT1):c.4061A>G NP_005236.2(FAT1):p.(Glu1354Gly) Heterozygous missense variant unknown, 3B	avoided biopsy as anti-PLA2R antibodies returned soon after, managed as primary membranous nephropathy
P0651 Male	Steroid resistant nephrotic syndrome	[HP:0000100] nephrotic syndrome [HP:0000790] hematuria renal biopsy consistent with FSGS	differential diagnosis of SRNS - avoidance of renal biopsy and diagnostic trial of immunosuppression	non-diagnostic	N/A	N/A	renal biopsy consistent with FSGS, partial response to tacrolimus; treated as immunological FSGS

		1					
P17355 Male	Alport	[HP:0000365] hearing impairment [HP:0001256] intellectual disability, mild [HP:0001650] aortic valvular stenosis [HP:0000790] hematuria [HP:0000093] proteinuria [HP:0000089] hyperechogenic kidneys	rapid progression of CKD and difficult to biopsy in context of warfarinisation for mechanical heart valve	non-diagnostic	N/A	N/A	No change to management, no renal biopsy due to high risk
		4					

AD, Autosomal Dominant; AR, Autosomal Recessive; FSGS, Focal segmental glomerulosclerosis; N/A, Not applicable; PLA2R, Phospholipase-A2-receptor; ES, Exome sequencing.

Supplementary Figure 1. Diagnostic genes identified



Supplemental Figure 2: Multivariable Logistic Regression analysis of baseline factors associated with a positive diagnosis. Estimates shown include adjusted odds ratios with 95% confidence intervals.