Genotype Name	Haplotypes G1 locus	G2 locus	Variant copy number	G1 copy number	G2 copy number	Number in cohort (% of total) *females/males*	Mean age (median, interquartile range)
G0/ G0	AT AT	TTATAA TTATAA	0	0	0	2,853 (38·2%) *1638/1215*	51·3 (50, 45-57)
G0/ G1	AT GG	TTATAA TTATAA	1	1	0	2,273 (30·5%) *1309/964*	52·2 (51, 46-58)
G0/ G2	AT AT	TTATAA 6 bp deletion	1	0	1	1,219 (16·3%) *701/518*	52·0 (51, 45-58)
G1/ G1	GG GG	TTATAA TTATAA	2	2	0	644 (8·6%) *379/265*	52·3 (51, 46-58)
G1/ G2	GG AT	TTATAA 6 bp deletion	2	1	1	320 (4·3%) *181/139*	52·0 (51, 45-58)
G2/ G2	AT AT	6 bp deletion 6 bp deletion	2	0	2	153 (2·1%) *100/53*	51·6 (50, 45-57)

Table 1: Haplotype frequencies at the *APOL1* G1 and G2 loci in the UK Biobank cohort (n = 7,462). Genotypes with G1 and G2 on the same haplotype are theoretically possible but have not been observed.

Analysis model	Genotype/grouping	Comparator	Level 2 codes: P<0·05 and FDR<20%
Genotype	G0/G1	G0/G0	0
Genotype	G0/G2	G0/G0	**1**
Genotype	G1/G1	G0/G0	0
Genotype	G1/G2	G0/G0	**26**
Genotype	G2/G2	G0/G0	0
G1 dominant	1xG1 (G0/G1, G1/G2)	0xG1 (G0/G0, G0/G2, G2/G2)	0
G1 recessive	2xG1 (G1/G1)	0xG1 (G0/G0, G0/G2, G2/G2)	0
G2 dominant	1xG2 (G0/G2, G1/G2)	0xG2 (G0/G0, G0/G1, G1/G1)	0
G2 recessive	2xG2 (G2/G2)	0xG2 (G0/G0, G0/G1, G1/G1)	0
Risk allele dominant	1 variant (G0/G1, G0/G2)	0 variants (G0/G0)	0
Risk allele recessive	2 variants (G1/G1, G1/G2, G2/G2)	0 variants (G0/G0)	0
G1 additive	G1 count	0 variants (G0/G0)	0
G2 additive	G2 count	0 variants (G0/G0)	0
Risk allele additive	Risk allele count	0 variants (G0/G0)	0

Table 2: Models of association considered in the phenome-wide screen, and number of potential associations identified by each model. Dominant models were where one risk allele was sufficient to produce phenotype, recessive models where two risk alleles were required to produce phenotype, and additive models where risk of phenotype was proportional to the number of variant alleles present.

Genotype	n (total)	n (hospitalisation) (%)	Odds ratio	P	n (death) (%)	Odds ratio	P
G0/G0	2,853	666 (23·3%)	1·0 (ref)		10 (0·4%)	1·0 (ref)	
G0/G1	2,273	517 (22·7%)	0·9 (0·8-1·1)	0·35	10 (0·4%)	1·0 (0·4-2·5)	0·95
G0/G2	1,219	269 (22·1%)	0·9 (0·8-1·1)	0·27	5 (0·4%)	1·0 (0·3-2·8)	0·94
G1/G1	644	148 (23·0%)	0·9 (0·7-1·1)	0·37	1 (0·2%)	0·5 (0·5-2·2)	0·39
G1/G2	320	**101 (31·6%)**	**1·4 (1·1-1·9)**	**0·007**	1 (0·3%)	0·9 (0·1-4·0)	0·91
G2/G2	153	33 (21·6%)	0·9 (0·6-1·3)	0·55	0 (0·0%)	0·8 (0·0-6·4)	0·88

Table 3: Association of risk of hospitalisation and death as a result of a (non-COVID-19) infectious disease (defined as ICD-9 and ICD-10 codes A00-B99, J00-J06, J09-J18, and J20-J22) with *APOL1* genotypes compared to G0/G0, adjusted for age, sex, Townsend deprivation index, and genetic principal components 1-4. P values < 0·05 are shown in bold. The G1/G2 genotype was associated with hospitalisation as a result of a (non-COVID-19) infectious disease.

Genotype	n (total)	n (hospitalisation) (%)	Odds ratio	P	n (death) (%)	Odds ratio	P
G0/G0	2,853	54 (1·9%)	1·0 (ref)		14 (0·5%)	1·0 (ref)	
G0/G1	2,273	49 (2·2%)	1·1 (0·7-1·6)	0·72	12 (0·5%)	1·3 (0·6-2·9)	0·54
G0/G2	1,219	23 (1·9%)	1·0 (0·6-1·6)	0·87	5 (0·4%)	1·0 (0·3-2·6)	0·99

G1/G1	644	11 (1·7%)	0·8 (0·4-1·6)	0·58	2 (0·3%)	0·9 (0·2-3·3)	0·93
G1/G2	320	**15 (4·7%)**	**2·3 (1·2-4·1)**	**0·01**	**8 (2·5%)**	**6·6 (2·5-16·7)**	**0·0003**
G2/G2	153	2 (1·3%)	0·8 (0·2-2·4)	0·74	1 (0·7%)	2·4 (0·3-10·1)	0·38

Table 4: Association of risk of hospitalisation and death as a result of COVID-19 (defined as ICD-10 code U071) with *APOL1* genotypes compared to G0/G0, adjusted for age, sex, Townsend deprivation index, and genetic principal components 1-4. P values < 0·05 are shown in bold. The G1/G2 genotype was associated with hospitalisation and death as a result of a COVID-19.

Genotype	n (total)	uACR > 3 mg/mmol **or** eGFR < 60 mL/min/1·73m^2		uACR > 3 mg/mmol		eGFR < 60 mL/min/1·73m^2	
		Odds ratio (95% CI)	p	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
0 variants	2,853	1·0 (ref)		1·0 (ref)		1·0 (ref)	
1 variant	3,492	1·1 (0·9-1·3)	0·52	1·1 (0·9-1·4)	0·18	0·9 (0·7-1·3)	0·69
2 variants	1,117	**1·4 (1·1-1·8)**	**0·002**	**1·5 (1·2-2·0)**	**0·001**	1·4 (1·0-2·0)	0·05

Table 5: Association of risk indicators of chronic kidney disease with number of *APOL1* risk variants, compared to 0 variants, adjusted for age, sex, body mass index, diabetes, hypertension, Townsend deprivation index, and genetic principal components 1-4. Genotypes with p values < 0·05 are shown in bold. Carriage of two APOL1 risk variants was associated with having chronic kidney disease risk indicators, consistent with previous studies(2). The numbers and percentages are shown in Supplementary Table 7.

Genotype	n (total)	uACR > 3 mg/mmol **or** eGFR < 60 mL/min/1·73m^2		uACR > 3 mg/mmol		eGFR < 60 mL/min/1·73m^2	
		Odds ratio (95% CI)	p	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
G0/G0	2,853	1·0 (ref)		1·0 (ref)		1·0 (ref)	
G0/G1	2,273	1·0 (0·8-1·3)	0·75	1·1 (0·9-1·4)	0·24	0·9 (0·6-1·2)	0·52
G0/G2	1,219	1·1 (0·9-1·4)	0·37	1·1 (0·9-1·5)	0·28	1·0 (0·7-1·5)	0·86
G1/G1	644	**1·4 (1·1-1·9)**	**0·01**	**1·6 (1·2-2·1)**	**0·003**	1·2 (0·8-1·9)	0·37
G1/G2	320	**1·6 (1·1-2·2)**	**0·01**	**1·7 (1·1-2·5)**	**0·01**	1·5 (0·9-2·6)	0·15
G2/G2	153	1·2 (0·7-2·0)	0·52	1·0 (0·5-1·8)	0·96	**2·3 (1·1-4·4)**	**0·02**

Table 6: Association of risk indicators of chronic kidney disease with *APOL1* genotypes compared to G0/G0, adjusted for age, sex, body mass index, diabetes, hypertension, Townsend deprivation index, and genetic principal components 1-4. Genotypes with p values < 0·05 are shown in bold. The numbers of affected participants with each genotype and percentages are shown in Supplementary Table 8.

Genotype	n (total)	n (end stage kidney disease) (%)	Odds ratio	P
G0/G0	2,853	23 (0·8%)		
G0/G1	2,273	18 (0·8%)	0·9 (0·5-1·8)	0·84
G0/G2	1,219	10 (0·8%)	1·1 (0·5-2·2)	0·91
G1/G1	644	9 (1·4%)	1·5 (0·7-3·3)	0·33
G1/G2	320	**10 (3·1%)**	**3·3 (1·5-7·2)**	**0·005**
G2/G2	153	1 (0·7%)	1·3 (0·1-5·2)	0·78

Table 7: Association of risk of end stage kidney disease with *APOL1* genotypes compared to G0/G0, adjusted for age, sex, body mass index, diabetes, hypertension, Townsend deprivation index, and genetic principal components 1-4. P values < 0·05 are shown in bold.

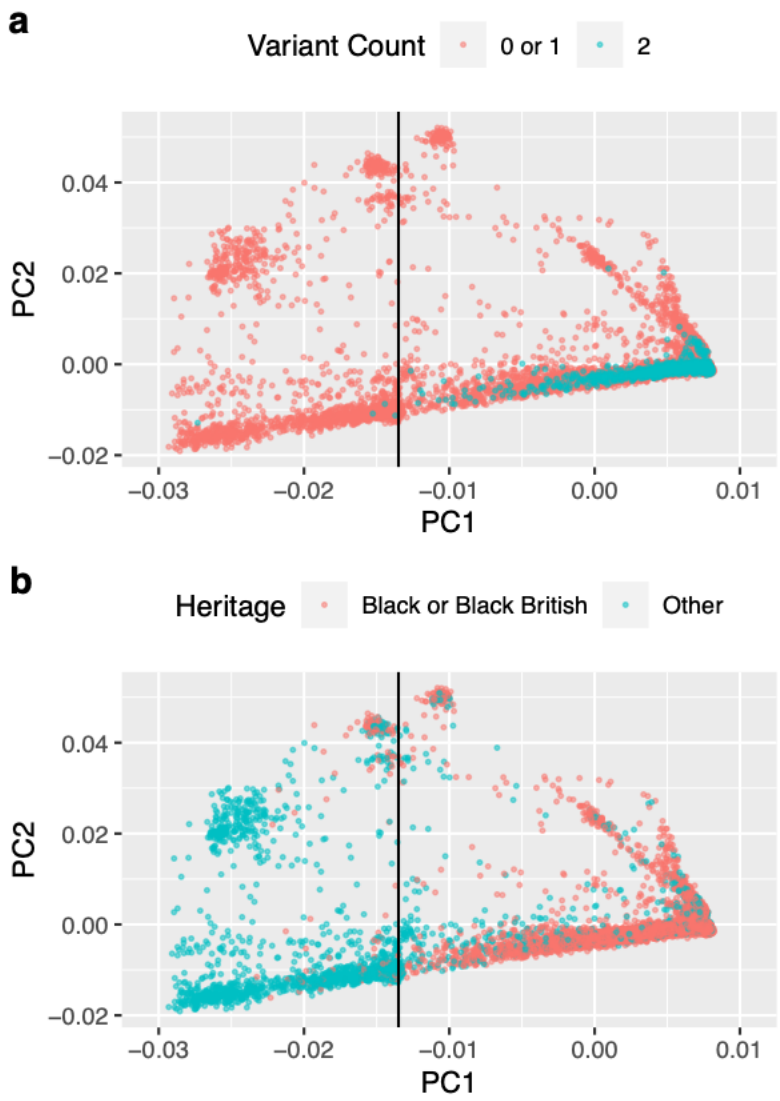

Figure 1: PCA plots of principal components calculated from Affymetrix genotype data from the 10,179 participants that had UK Biobank PC1 > 100 and PC2 > 0. (a) Participants were classified by whether they have a two-risk-variant *APOL1* genotype. (b) Participants were classified by their self-declared ethnicity: Black or Black British participants have UK Biobank ethnicity codes 4001, 4002, or 4003. The vertical line indicates the cut off used to select participants. Everyone to the right of the line was included.

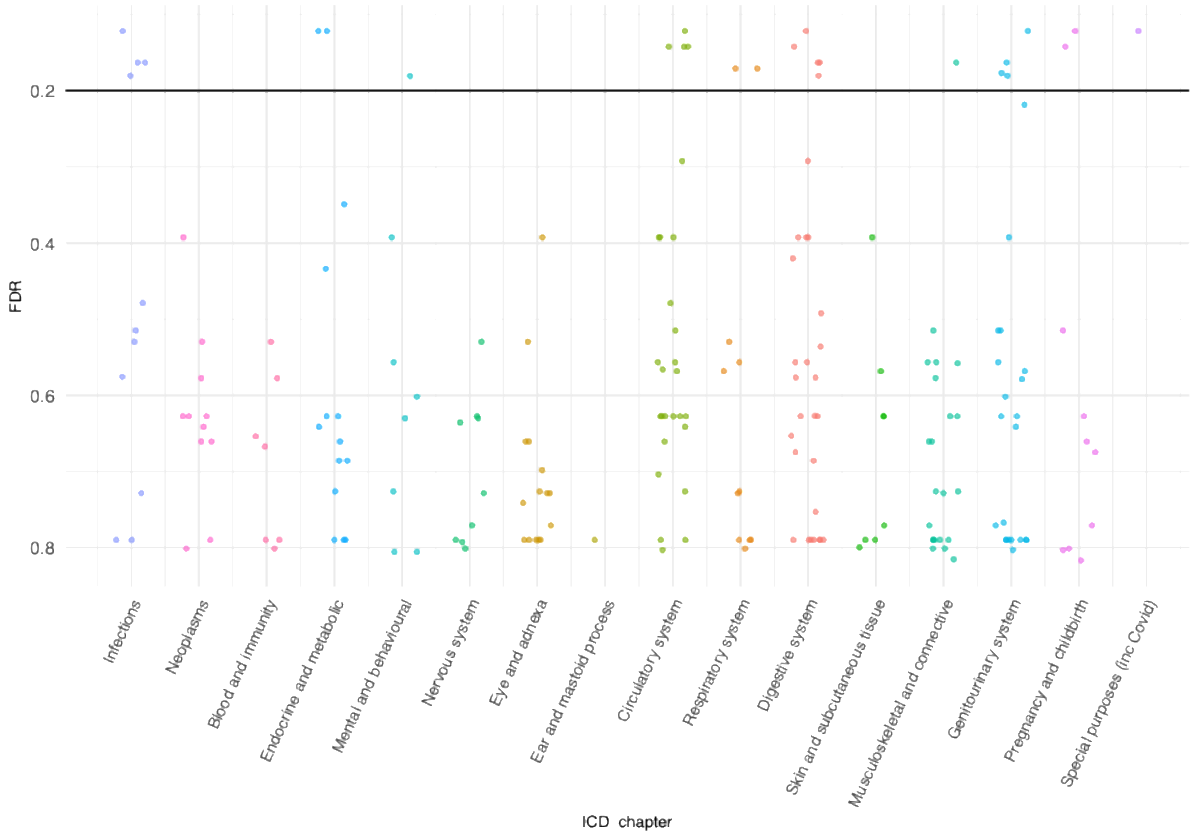

Figure 2: False discovery rate values for association between Level 2 ICD-10 codes and *APOL1* G1/G2 genotype. Horizontal line indicates the threshold that was used for the false discovery rate (20%) for a potentially significant association. Colouring is used to demarcate ICD chapters. Codes which were recorded for at least 50 cohort members were tested. The number of codes tested in each chapter is shown in Supplementary Table 4.