Supplementary Information for

A Genome-Wide Association Study for Myopia and Refractive Error Identifies a Susceptibility Locus at 15q25

Figure 1. Ancestry of the TwinsUK Samples with respect to three HapMap Phase 2 Reference populations (CEU-Caucasian, YRI-African and CHB-Chinese).
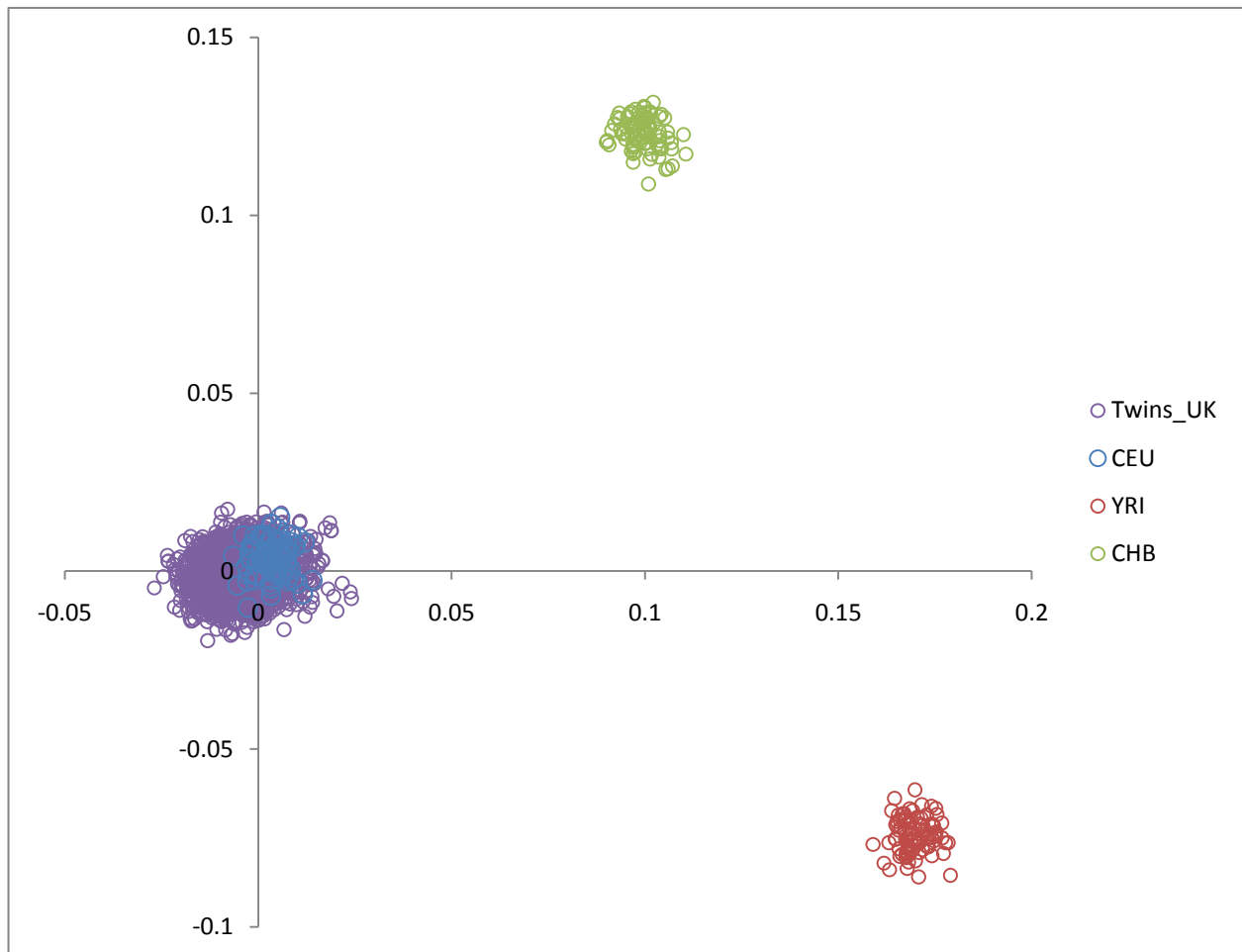
Figure 2. Quantile-Quantile for association between all SNPs analyzed and spherical equivalent in the main cohorts used in this study: (a) TwinsUK, (b) 1958 BC, (c)RS-I, (d) RS-II, (e) RS-III, (f) ERF.
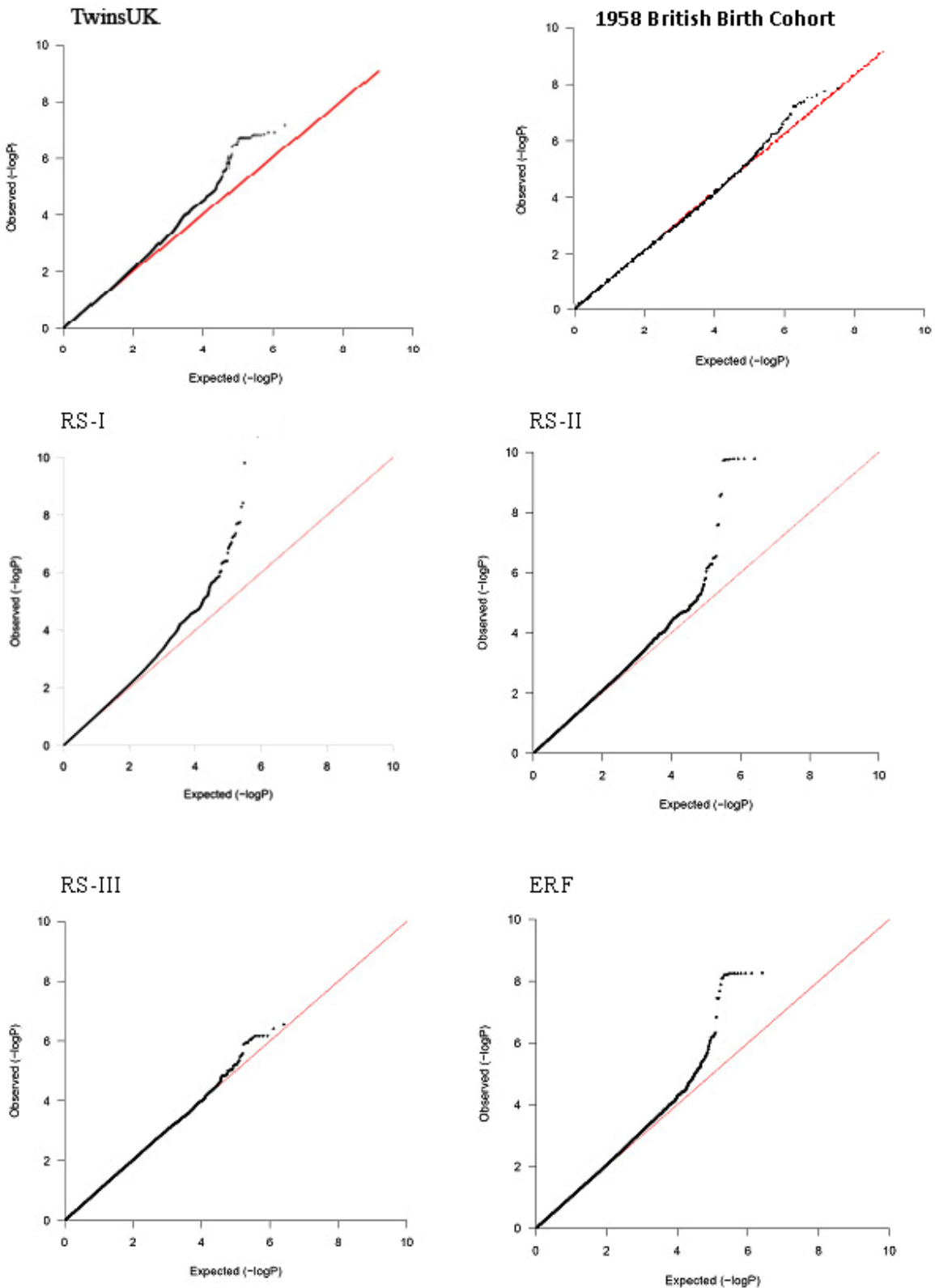
Figure 3. Linkage Disequilibrium calculated in terms of r^2. Black squares show perfect LD whereas clearer shades of grey show progressively fading LD.
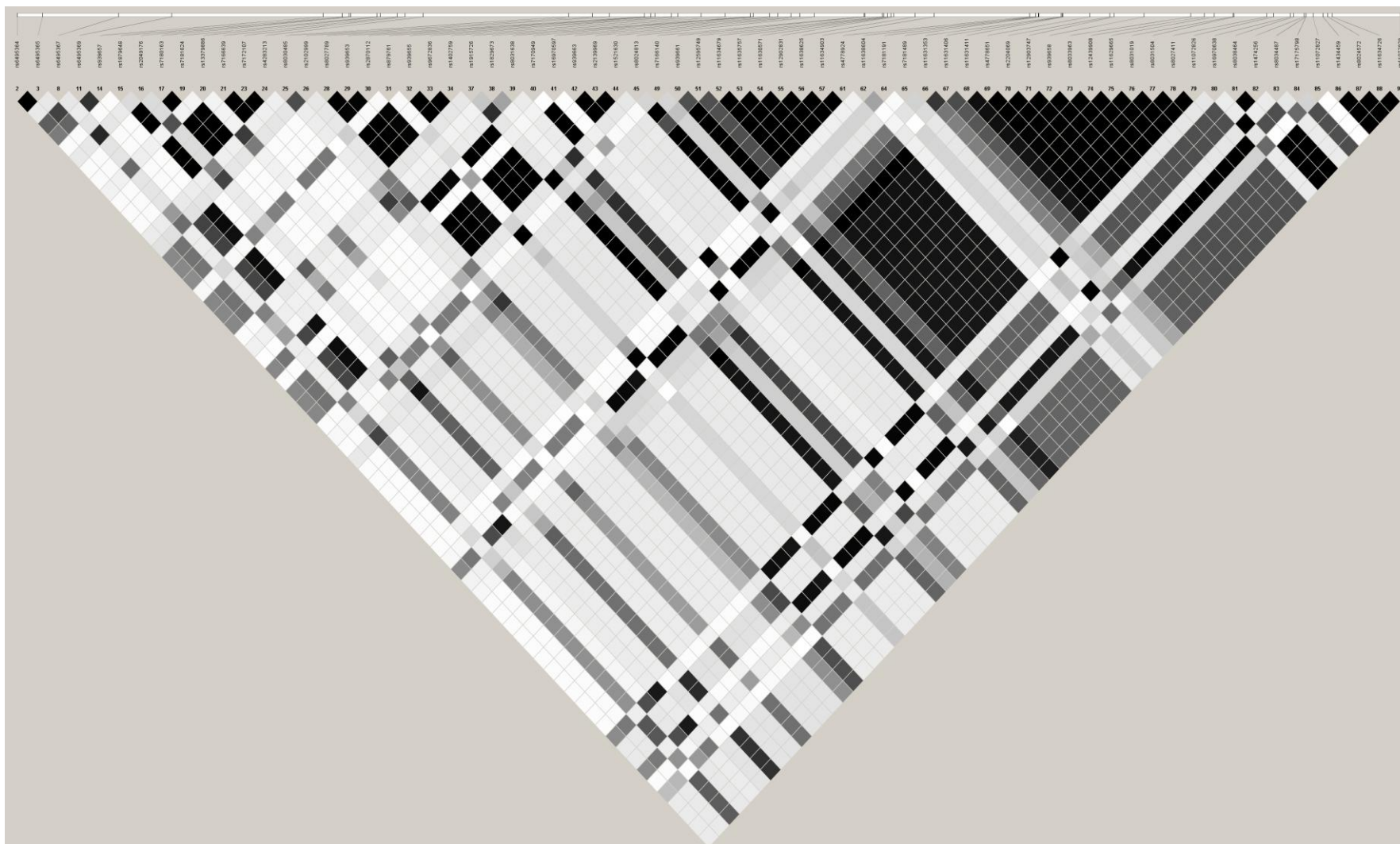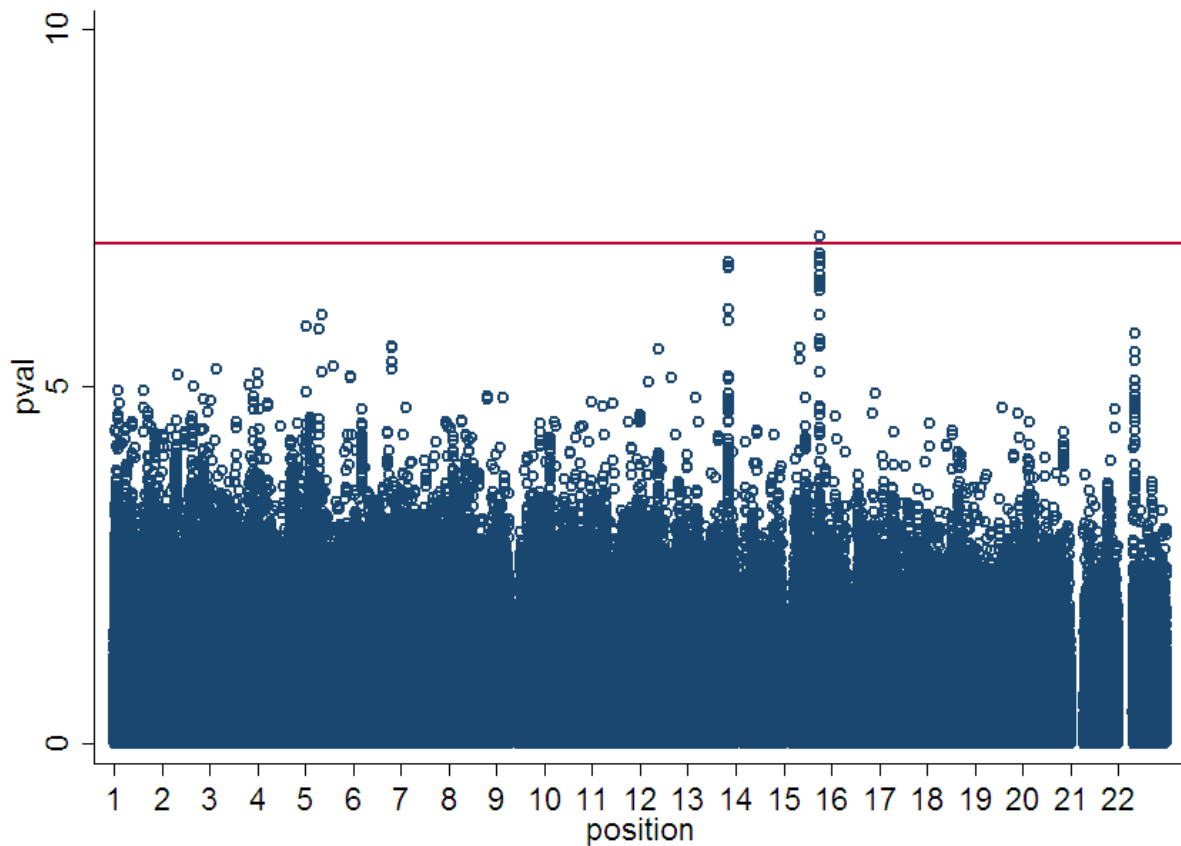
Figure 4. Plot of Association observed Genome-wide (a) and on Chromosome 15 (b) in the TwinsUK Cohort. . The red line denotes p=e-07 level of association significance. On chromosome 15, the main peak, pointed at by red arrows corresponds to the SNPs near the RASGRF1 gene. The second locus (blue arrow) corresponds to the SNPs nearer the GJD2 gene.
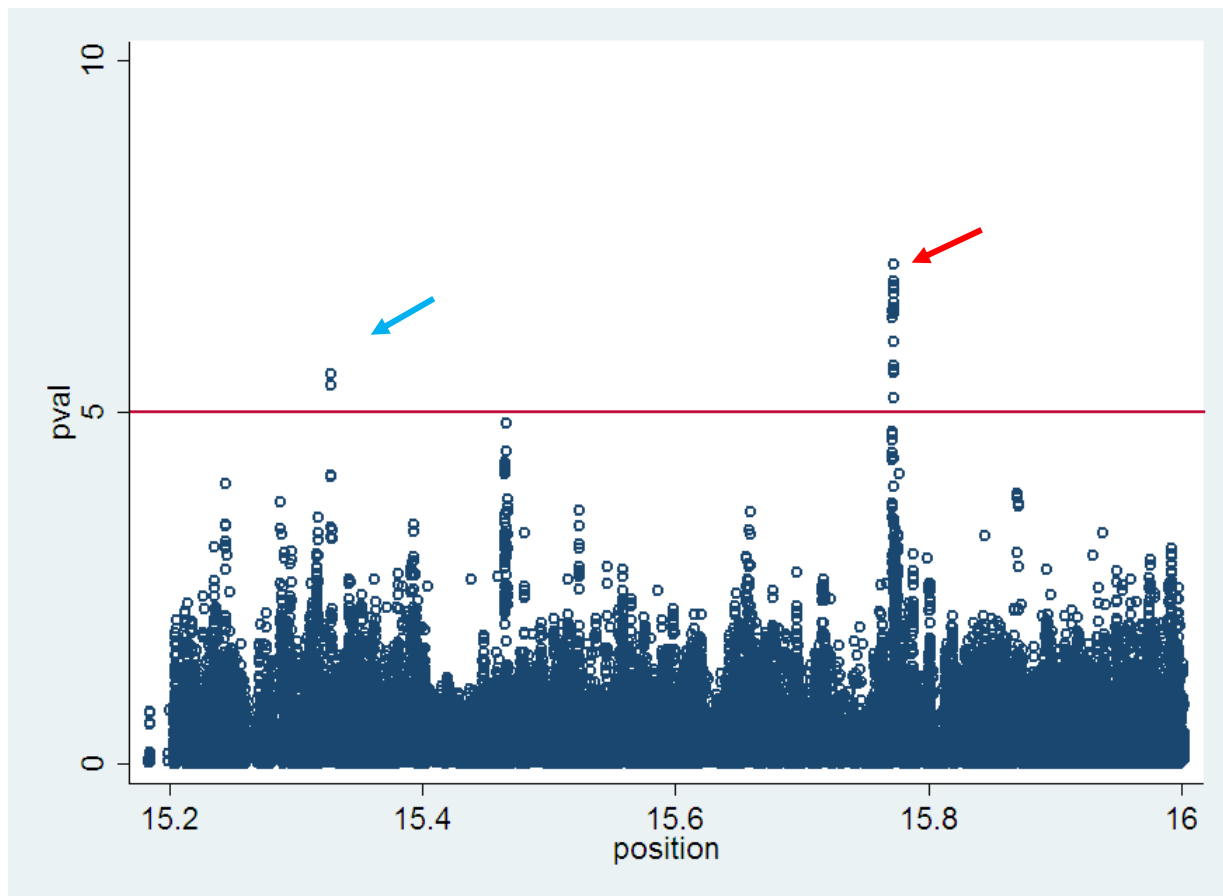
(a)

(b)

Figure 5a. Distribution of age at the moment of visit in the UK Twin Cohort. Each bar represents a category of 5 years; numbers of individual are shown by a label on top of each bar.
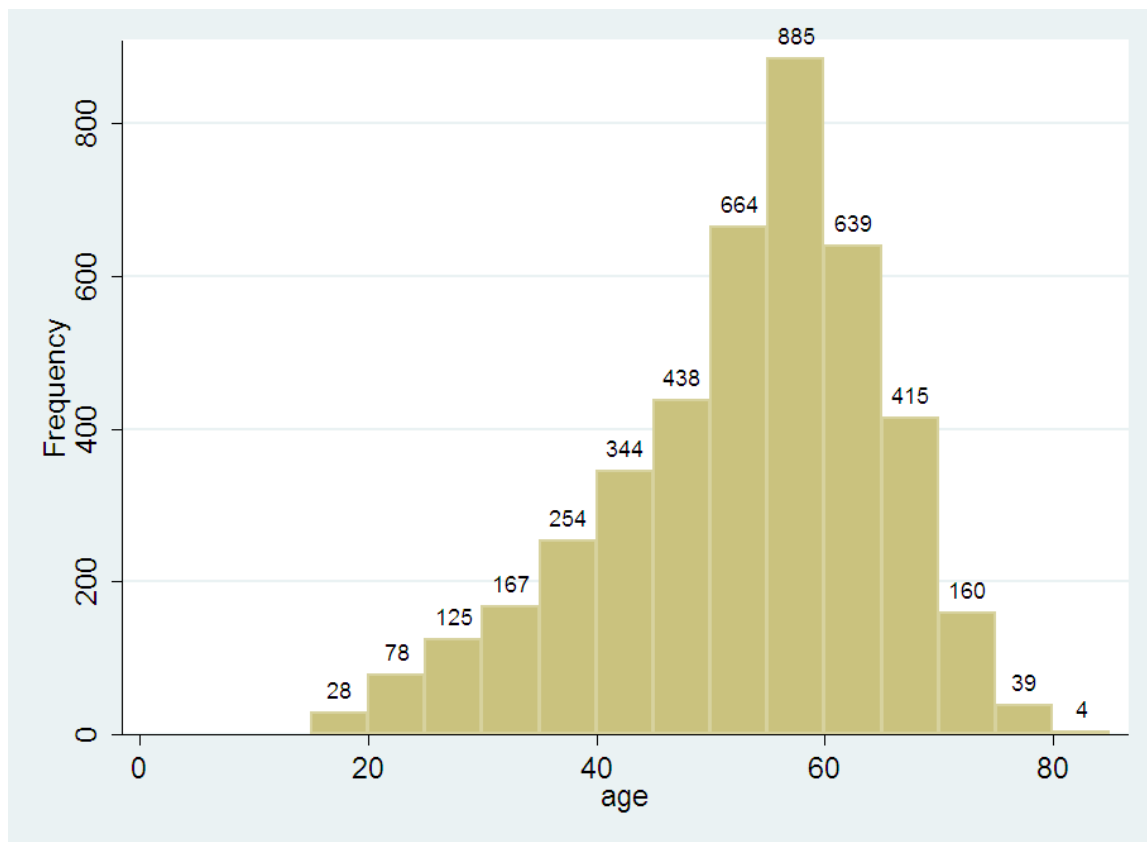
Figure 5b Each bar represents a range within 1 Diopter and the number of individuals within that interval is shown on top of the respective bar.
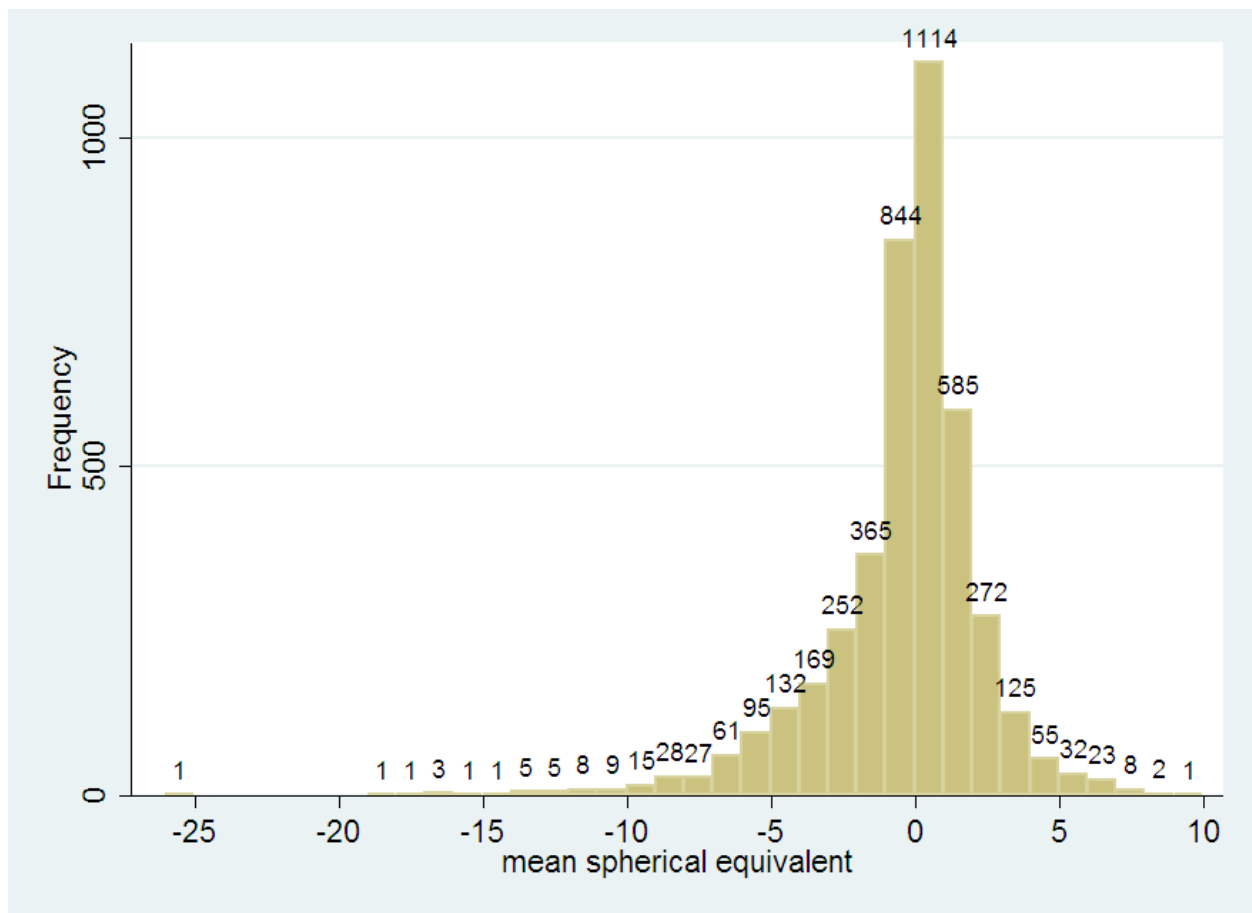
Table 1. Detailed results of association of SNPs in the associated region regressing over observed phenotypes in the TwinsUK cohort

SNP	Reference Allele	Second Allele	Freq. for Ref. Allele	Regression Coefficient	Standard Error	p-value	Genotyped or Imputed
rs8027411	T	G	0.52	-0.351	0.065	7.91E-08	Partly Imputed
rs11072826	A	G	0.52	-0.344	0.065	1.38E-07	Fully Imputed
rs17175798	C	T	0.52	-0.344	0.065	1.38E-07	Fully Imputed
rs8033963	T	C	0.519	-0.342	0.065	1.59E-07	Partly Imputed
rs12439908	C	T	0.519	-0.342	0.065	1.69E-07	Fully Imputed
rs11629665	A	G	0.519	-0.342	0.065	1.69E-07	Fully Imputed
rs8031019	G	A	0.519	-0.342	0.065	1.69E-07	Fully Imputed
rs8031504	T	G	0.519	-0.342	0.065	1.69E-07	Fully Imputed
rs939658	G	A	0.52	-0.34	0.065	2.09E-07	Fully Imputed
rs939661	A	G	0.525	-0.332	0.065	2.73E-07	Genotyped
rs4778924	T	C	0.524	-0.329	0.064	3.34E-07	Fully Imputed
rs11631411	C	T	0.524	-0.329	0.064	3.34E-07	Fully Imputed
rs1915726	C	G	0.525	-0.329	0.065	3.69E-07	Fully Imputed
rs12902831	G	A	0.525	-0.328	0.065	3.82E-07	Fully Imputed
rs11630571	C	A	0.525	-0.328	0.065	3.82E-07	Fully Imputed
rs11635757	T	C	0.525	-0.328	0.065	3.83E-07	Fully Imputed
rs11634679	T	C	0.525	-0.328	0.065	3.83E-07	Fully Imputed
rs8024813	A	G	0.525	-0.327	0.065	3.93E-07	Fully Imputed
rs11634903	A	G	0.524	-0.327	0.065	3.94E-07	Fully Imputed
rs11638625	T	G	0.524	-0.327	0.065	3.96E-07	Fully Imputed
rs8031638	C	T	0.578	-0.331	0.066	4.48E-07	Partly Imputed
rs4778651	G	A	0.523	-0.318	0.065	9.81E-07	Genotyped
rs2204069	G	A	0.523	-0.318	0.065	1.00E-06	Fully Imputed
rs12903747	C	A	0.523	-0.318	0.065	1.01E-06	Fully Imputed
rs11634726	G	A	0.574	0.312	0.066	2.21E-06	Partly Imputed
rs11072829	G	A	0.575	0.311	0.066	2.49E-06	Fully Imputed
rs1434459	C	T	0.575	0.311	0.066	2.49E-06	Fully Imputed
rs8024572	A	G	0.575	0.309	0.066	2.67E-06	Genotyped
rs1474256	C	T	0.575	0.311	0.066	2.77E-06	Fully Imputed
rs8038464	T	A	0.586	0.305	0.068	6.35E-06	Fully Imputed
rs12595749	A	G	0.569	0.293	0.065	6.39E-06	Partly Imputed
rs2102999	T	C	0.512	0.276	0.065	1.95E-05	Genotyped
rs8035606	C	T	0.518	-0.355	0.083	2.06E-05	Partly Imputed
rs2049176	A	C	0.586	0.278	0.066	2.54E-05	Fully Imputed
rs6495367	G	A	0.583	0.27	0.066	3.86E-05	Genotyped
rs13380104	C	T	0.584	0.275	0.067	4.42E-05	Fully Imputed
rs1560895	C	T	0.585	0.346	0.085	4.52E-05	Partly Imputed
rs1007365	T	G	0.584	0.274	0.067	4.77E-05	Fully Imputed

Table 2. Transcription Factor Binding sites that are altered by the SNPs in the RASGRF1 promoter associated region .

	Ancestral Allele	Derived Allele
	TF	TF
rs6495366|C/T		V$CREL.01
		V$IK2.01
		V$CEBP.02
rs13380104|C/T	V$ZFX.01	V$TCF11MAFG.01
	V$AIRE.01	V$ESRRB.01
	V$NFY.02	V$MEIS1A_HOXA9.01
		V$AIRE.01
		V$PBX1_MEIS1.02
rs2049176|A/C	V$CMYB.01	V$HOXC8.01
rs2102999|T/C	V$HOX_PBX.01	V$VMYB.05
	V$HBP1.01	
	V$NANOG.01	
	V$HNF6.01	
rs8031638|C/T	V$REV-ERBA.03	
rs8024813|A/G	V$GATA1.06	
	V$EVI1.05	
	V$SL1.01	
rs939661|A/G	V$DELTAEF1.01	V$NBRE.01
	V$DEC1.01	V$PTF1.01
	V$MIT.01	
	V$SREBP.03	
	V$TR2.01	
	V$RORA.01	
	V$NBRE.01	
	V$ESRRB.01	
	V$PPAR_RXR.01	
	V$RAR_RXR.01	
rs4778651|A/G		V$DMRT1.01
		V$SIX4.01
rs8033963|C/T	V$SRF.01	O$VTATA.01
	V$OCT1.01	V$BRN5.02
	V$DBP.01	V$BRN2.01
	V$OCT3_4.02	
	V$FHXB.01	
	V$GSH1.01	V$XFD2.01
	V$BRN3.03	
		O$PTATA.01
		V$GSH1.01

Table 3. Comparison in eye growth parameters between Wild Type and RASGRF1 Knock-Out mice

Observation Number	Sex	Body Weight (g)	Average Eye Weight (g)	Cross Dimension (mm)	Longitudinal Dimension (mm)	Average Crystalline Weight (mg)	Wild Type or Knockout
1	F	22.2	20	1.54	1.55	8.45	WT
2	F	23.08	20	1.58	1.61	7.45	WT
3	F	22.51	21	1.62	1.61	8.1	WT
4	M	27.55	20	1.64	1.62	7.25	WT
5	M	28.32	20.5	1.61	1.57	7.7	WT
6	M	29.46	20.5	1.52	1.61	7	WT
7	M	28.93	21	1.64	1.66	6.9	WT
8	F	20.98	20	1.63	1.6	8.35	KO
9	F	24.06	21.5	1.59	1.63	8.2	KO
10	F	20.73	19.5	1.6	1.57	8.45	KO
11	F	23.53	21	1.6	1.6	7.95	KO
12	F	23.37	21	1.67	1.61	7.75	KO
13	M	13.97	20	1.57	1.55	8.45	KO
14	M	29.04	19	1.55	1.59	7.85	KO
15	F	21.47	20	1.62	1.6	7	WT
16	F	21.74	20	1.6	1.61	6.95	WT
17	M	28.2	21	1.63	1.63	6.8	WT
18	M	30.45	20.5	1.62	1.64	7.25	WT
19	M	28.19	21	1.67	1.67	7.1	WT
20	M	25.98	21	---	---	6.8	WT
21	F	22.39	20	1.6	1.6	6.6	WT
22	M	26.04	20.5	1.6	1.61	7.05	WT
23	M	25.72	20	1.64	1.6	6.3	WT
24	M	26.14	21	1.64	1.66	6.65	WT
25	M	28.86	22	1.62	1.64	6.9	WT
26	M	28.99	21	1.62	1.63	6.65	WT
27	F	21.6	21	1.6	1.61	7.65	KO
28	F	21.69	21	1.62	1.65	7.4	KO
29	M	33.42	21.5	1.63	1.65	7.3	KO
30	M	23.76	20.5	1.59	1.62	7.35	KO
31	M	30.16	19.5	1.52	1.55	7.6	KO
32	F	26.2	19.5	1.55	1.6	7.55	KO
33	M	30.54	21	1.63	1.6	6.8	KO
34	M	33.11	21.5	1.62	1.65	7.2	KO
35	M	33.1	19.5	1.58	1.58	7.55	KO

Supplementary Note

In addition to the Acknowledgements in the main manuscript: