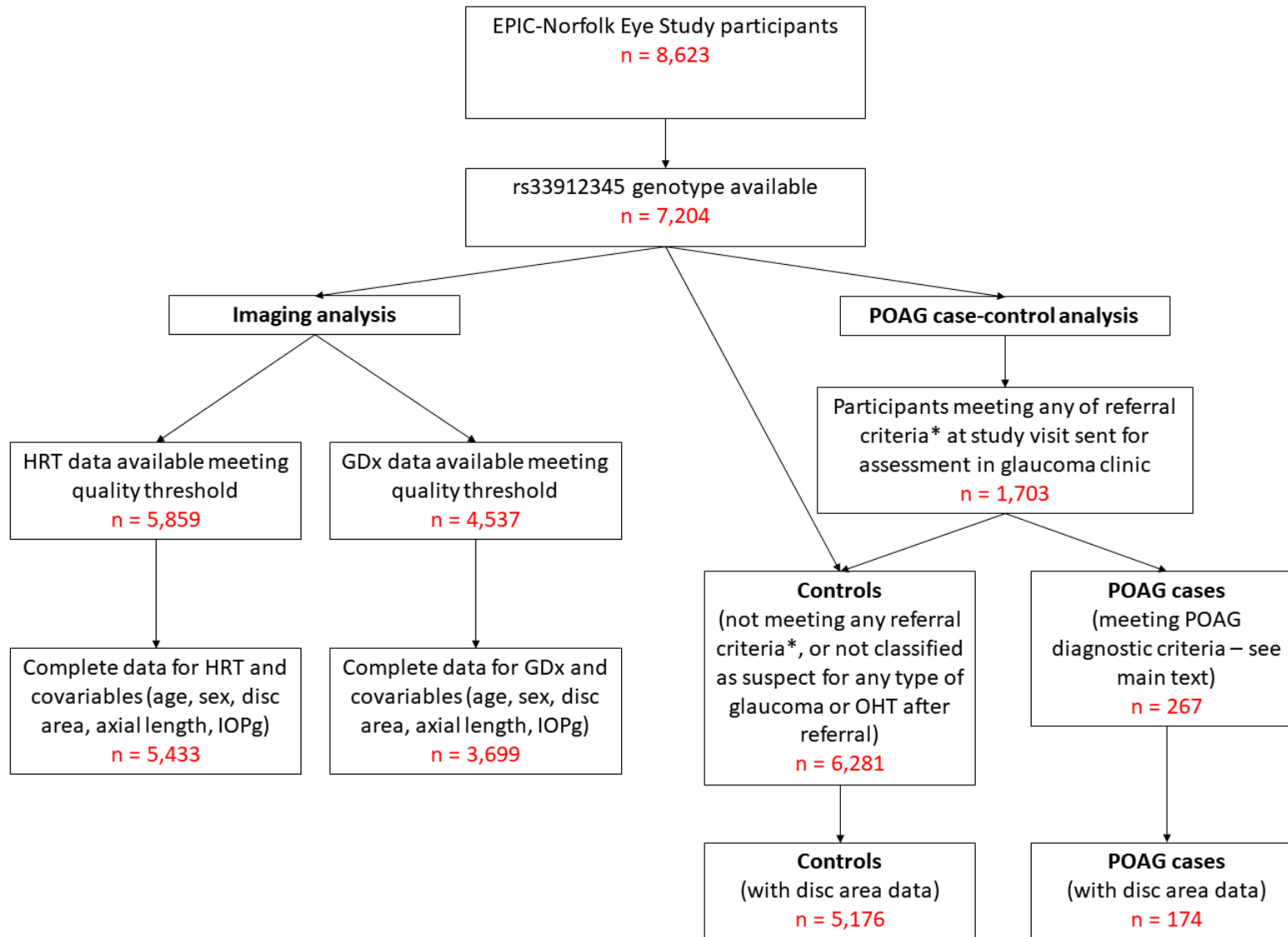


Supplementary Figure A: Flow chart describing the derivation of participants included in the primary analyses. *referral criteria were any one of: best-corrected visual acuity >0.34 LogMAR in either eye, IOP >24mmHg in either eye, IOP >21mmHg in either eye with ≥ 3 borderline HRT II sectors on Moorfields Regression Analysis, GDx RNFL average thickness/standard deviation/superior thickness/inferior thickness measures outside normal limits in either eye (1 reading at $P < 0.5\%$ or 2 readings $P < 1\%$ or 3 readings $P < 5\%$), any HRT II sector Moorfields Regression Analysis outside normal limits, manifest abnormalities on fundus photography in either eye.



Supplementary Table A: Sensitivity analyses for association between rs33912345 genotype and optic nerve head parameters. Results are from multivariable linear regression models with the optic nerve head parameter as the dependent variable and genotype dosage as an explanatory variable. The first model is for all included participants without excluding glaucoma (n = 5,433 for HRT, n = 3,699 for GDx) and adjustment for IOPcc rather than IOPg. The second model is for all participants following exclusion of participants with glaucoma or history of glaucoma medication or procedure (following exclusion: n = 5,196 for HRT, n = 3,572 for GDx). *P*-values < 0.01 are in bold.

	Sensitivity analysis 1: All participants with alternative IOP adjustment (adjusted for age, sex, disc area, axial length and IOPcc)			Sensitivity analysis 2: Glaucoma excluded (adjusted for age, sex, disc area, axial length and IOPg)		
	Difference per risk allele (C)	95% CI	<i>P</i>-value	Difference per risk allele (C)	95% CI	<i>P</i>-value
HRT rim area (mm²)	-0.030	(-0.040, -0.020)	5.66E-09	-0.025	(-0.034, -0.015)	3.35E-07
HRT VCDR	0.025	(0.017, 0.033)	3.62E-10	0.022	(0.014, 0.029)	4.81E-08
GDx RNFL thickness (μm)	-0.389	(-0.627, -0.151)	0.001	-0.319	(-0.549, -0.089)	0.007

Supplementary Table B: Association between rs33912345 genotype with sectoral optic nerve head (HRT) and RNFL thickness (GDxVCC) parameters. Results are from multivariable linear regression models with the sectoral optic nerve head parameter as the dependent variable and genotype dosage as an explanatory variable, adjusted for age, sex, disc area, axial length and IOPg. *P*-values < 0.01 are in bold.

	Difference per risk allele	95% CI	<i>P</i>-value
HRT rim area			
Superotemporal rim area (mm ²)	-0.006	(-0.007, -0.004)	<0.001
Temporal rim area (mm ²)	-0.007	(-0.011, -0.004)	<0.001
Inferotemporal rim area (mm ²)	-0.004	(-0.006, -0.002)	<0.001
Superonasal rim area (mm ²)	-0.005	(-0.006, -0.003)	<0.001
Inferonasal rim area (mm ²)	-0.004	(-0.005, -0.002)	<0.001
Nasal rim area (mm ²)	-0.005	(-0.007, -0.002)	<0.001
GDx RNFL thickness			
Superior thickness (μm)	-0.683	(-1.023, -0.344)	<0.001
Inferior thickness (μm)	-0.641	(-0.998, -0.284)	<0.001
Temporal thickness (μm)	-0.327	(-0.617, -0.038)	0.027
Nasal thickness (μm)	0.409	(0.051, 0.768)	0.025

Supplementary Table C: Association between rs33912345 genotype and optic nerve head parameters in participants with primary open-angle glaucoma (POAG). Results are shown for the associations among POAG patients with complete data available for genotype, optic nerve parameter and covariables (numbers included in each analysis are shown). We present results for two models: the first model is adjusted for age, sex and disc area; the second model is adjusted for age, sex, disc area, axial length and IOPg.

	Adjusted for age, sex and disc area				Adjusted for age, sex, disc area, axial length and IOPg			
	Number of participants	Change per risk allele (C)	95% CI	P-value	Number of participants	Change per risk allele (C)	95% CI	P-value
HRT rim area (mm ²)	174	-0.073	(-0.128, -0.018)	0.009	164	-0.067	(-0.123, -0.010)	0.020
HRT VCDR	174	0.044	(0.011, 0.077)	0.010	164	0.042	(0.008, 0.076)	0.015
GDx RNFL thickness (μm)	86	-1.608	(-3.230, 0.014)	0.052	81	-1.242	(-2.847, 0.362)	0.13