

Table 1: Baseline assessment details for variables analyzed in the current study.

Variable	Assessment details
<i>Touch-screen self-administered questionnaire</i>	
Ethnicity	Response options included: White (English/Irish or other white background), Asian or British Asian (Indian/Pakistani/Bangladeshi or other Asian background), Black or Black British (Caribbean, African, or other black background), Chinese, mixed (White and Black Caribbean or African, White and Asian, or other mixed background), or other ethnic group (not defined).
Smoking status	Determined by response to “Do you smoke tobacco now?” and “In the past, how often have you smoked tobacco?”.
Alcohol intake	Determined by response to “About how often do you drink alcohol?” (options: Daily or almost daily; Three or four times a week; Once or twice a week; One to three times a month; Special occasions only; Never).
Townsend deprivation index	Determined according to participant postcode at recruitment and the corresponding output area from the preceding national census. The index was calculated based on the output area’s employment status, home and car ownership, and household condition; the higher and more positive the index, the more deprived an area.
Education level	Determined by response to “Which of the following qualifications do you have? (You can select more than one)” (options: College or University degree; A levels/AS levels or equivalent; O levels/GCSEs or equivalent; CSEs or equivalent; NVQ or HND or HNC or equivalent; Other professional qualifications e.g. nursing, teaching; None of the above). For analyses, qualifications lower than “O level/GCSEs or equivalent” were considered together as “Less than O level”.
Diabetes status	Determined as those who answered yes to “Has a doctor ever told you that you have diabetes?”.
<i>Physical measures</i>	
Weight	BV-418 MA body composition analyzer (Tanita, Arlington Heights, IL)
Height	Seca 202 height measure (Seca, Birmingham, UK)

Table 2: Demographic, systemic and ocular characteristics for included participants (N=42,044). Mean (SD) is presented for continuous variables and count (%) is presented for categorical variables.

	Mean (SD) or count (%)
Age	56.4 (8.1)
Sex	
Women	22,332 (53%)
Men	19,712 (47%)
Ethnicity	
White	38509 (92%)
Asian	1163 (3%)
Black	1234 (3%)
Other/mixed	1138 (3%)
Weight (Kg)	78.1 (15.3)
Height (cm)	169.0 (9.2)
Body mass index (Kg/m²)	27.3 (4.4)
Smoking status	
Never	23052 (55%)
Previous	14869 (35%)
Current	4123 (10%)
Alcohol intake	
Never or special occasion only	8237 (20%)
One to three times a month	4771 (11%)
Once or twice a week	10557 (25%)
Three or four times a week	9610 (23%)
Daily or almost daily	8869 (21%)
Townsend deprivation index	
Least deprived quartile	10721 (25%)
2 nd quartile	10748 (26%)
3 rd quartile	10487 (25%)
Most deprived quartile	10088 (24%)
Education level	
Less than O level	13215 (31%)
O level	8919 (21%)
A Level	5007 (12%)
Degree	14903 (35%)
Diabetes (self-report)	
No	39955 (95%)
Yes	2089 (5%)
Spherical equivalent (dioptries)	0.001 (1.9)
IOPg (mmHg)	15.66 (3.59)
IOPcc (mmHg)	15.83 (3.60)
mRNFL (µm)	28.91 (3.83)
GCC (µm)	104.15 (7.56)
GCIPL (µm)	75.24 (5.19)

GCC – ganglion cell complex; GCIPL – ganglion cell inner plexiform layer; IOPcc – corneal-compensated intraocular pressure; IOPg – Goldmann-correlated intraocular pressure; mRNFL – macular retinal nerve fiber layer

Table 3: Univariable associations with average macular retinal nerve fiber layer (mRNFL), ganglion cell complex (GCC) and ganglion cell inner plexiform layer (GCIPL) thicknesses. Results are from linear regression models ($N=42,044$). P -values <0.0020 are in bold, representing significance at a Bonferroni-corrected threshold for 25 statistical tests.

	mRNFL thickness (μm)		GCC thickness (μm)		GCIPL thickness (μm)	
	β (95% CI)	P -value	β (95% CI)	P -value	β (95% CI)	P -value
Age (per decade)	-0.57 (-0.61, -0.52)	<0.001	-1.73 (-1.82, -1.64)	<0.001	-1.17 (-1.22, -1.10)	<0.001
Sex						
Women	Ref		Ref		Ref	
Men	-0.70 (-0.77, -0.63)	<0.001	-1.00 (-1.14, -0.85)	<0.001	-0.30 (-0.39, -0.19)	<0.001
Ethnicity						
White	Ref		Ref		Ref	
Asian	-0.75 (-0.97, -0.53)	<0.001	-1.28 (-1.72, -0.84)	<0.001	-0.53 (-0.83, -0.22)	0.001
Black	-1.46 (-1.68, -1.24)	<0.001	-1.20 (-1.62, -0.77)	<0.001	0.27 (-0.03, 0.55)	0.08
Other/mixed	-0.21 (-0.43, 0.01)	0.07	0.64 (0.19, 1.08)	0.005	0.84 (0.53, 1.14)	<0.001
Weight (per 10 Kg)	-0.12 (-0.14, -0.09)	<0.001	-0.21 (-0.25, -0.15)	<0.001	-0.08 (-0.11, -0.05)	<0.001
Height (per 10 cm)	0.02 (-0.02, 0.05)	0.37	0.04 (-0.03, 0.11)	0.30	0.02 (-0.03, 0.07)	0.40
Body mass index (per 5 Kg/m ²)	-0.26 (-0.30, -0.22)	<0.001	-0.46 (-0.53, -0.37)	<0.001	-0.19 (-0.25, -0.13)	<0.001
Smoking status						
Never	Ref		Ref		Ref	
Previous	-0.22 (-0.29, -0.13)	<0.001	-0.45 (-0.60, -0.29)	<0.001	-0.24 (-0.34, -0.13)	<0.001
Current	-0.28 (-0.40, -0.15)	<0.001	0.04 (-0.21, 0.29)	0.75	0.32 (0.14, 0.49)	<0.001
Alcohol intake						
Never or special occasion only	Ref		Ref		Ref	
One to three times a month	0.26 (0.12, 0.39)	<0.001	0.42 (0.15, 0.69)	0.002	0.16 (-0.02, 0.34)	0.09
Once or twice a week	0.24 (0.12, 0.34)	<0.001	0.40 (0.18, 0.61)	<0.001	0.16 (0.01, 0.31)	0.032
Three or four times a week	0.16 (0.04, 0.27)	0.005	0.07 (-0.15, 0.29)	0.54	-0.09 (-0.24, 0.06)	0.25
Daily or almost daily	-0.02 (-0.13, 0.09)	0.68	-0.62 (-0.84, -0.39)	<0.001	-0.60 (-0.75, -0.44)	<0.001
Townsend deprivation index						
Least deprived quartile	Ref		Ref		Ref	
2 nd quartile	-0.06 (-0.16, 0.04)	0.27	-0.03 (-0.23, 0.17)	0.76	0.03 (-0.11, 0.16)	0.71
3 rd quartile	-0.08 (-0.18, 0.02)	0.12	-0.10 (-0.30, 0.10)	0.32	-0.02 (-0.16, 0.11)	0.76
Most deprived quartile	-0.20 (-0.30, -0.09)	<0.001	-0.19 (-0.39, 0.01)	0.07	0.02 (-0.12, 0.15)	0.83
<i>Test of trend</i>	-0.06 (-0.09, -0.03)	<0.001	-0.06 (-0.12, 0.00)	0.06	0.00 (-0.04, 0.04)	0.99
Education level						
Less than O level	Ref		Ref		Ref	
O level	0.47 (0.37, 0.57)	<0.001	0.69 (0.48, 0.89)	<0.001	0.22 (0.08, 0.35)	0.002
A Level	0.85 (0.72, 0.96)	<0.001	1.11 (0.86, 1.35)	<0.001	0.26 (0.09, 0.42)	0.003
Degree	0.83 (0.74, 0.92)	<0.001	0.99 (0.81, 1.16)	<0.001	0.16 (0.03, 0.28)	0.010
Diabetes status						
No	Ref		Ref		Ref	
Yes	-0.95 (-1.12, -0.78)	<0.001	-1.92 (-2.25, -1.59)	<0.001	-0.97 (-1.19, -0.74)	<0.001
Spherical equivalent (diopters)	-0.40 (-0.41, -0.38)	<0.001	0.20 (0.16, 0.23)	<0.001	0.60 (0.57, 0.62)	<0.001
IOPg (mmHg)	-0.01 (-0.01, 0.00)	0.15	-0.11 (-0.12, -0.08)	<0.001	-0.10 (-0.11, -0.08)	<0.001
IOPcc (mmHg)	-0.01 (-0.01, 0.00)	0.12	-0.11 (-0.13, -0.09)	<0.001	-0.10 (-0.11, -0.09)	<0.001

IOPcc – corneal-compensated intraocular pressure; IOPg – Goldmann-correlated intraocular pressure

Table 4: Multivariable associations with average macular retinal nerve fiber layer (mRNFL), ganglion cell complex (GCC) and ganglion cell inner plexiform layer (GCIPL) thicknesses. Results are presented for 3 multivariable models with all explanatory variables presented together in the same model ($N=42,044$ for each model). P -values <0.0024 are in bold, representing significance at a Bonferroni-corrected threshold for 21 statistical tests.

	mRNFL thickness (μm)		GCC thickness (μm)		GCIPL thickness (μm)	
	β (95% CI)	P -value	β (95% CI)	P -value	β (95% CI)	P -value
Age (per decade)	-0.43 (-0.47, -0.38)	5.5×10^{-70}	-1.90 (-1.99, -1.80)	$< 1 \times 10^{-300}$	-1.51 (-1.58, -1.45)	$< 1 \times 10^{-300}$
Sex						
Women	Ref		Ref		Ref	
Men	-0.66 (-0.73, -0.58)	1.8×10^{-68}	-0.73 (-0.88, -0.59)	7.1×10^{-23}	-0.10 (-0.20, 0.00)	0.042
Ethnicity						
White	Ref		Ref		Ref	
Asian	-0.97 (-1.19, -0.75)	9.9×10^{-18}	-1.98 (-2.42, -1.54)	1.2×10^{-18}	-1.09 (-1.38, -0.79)	3.9×10^{-13}
Black	-1.65 (-1.86, -1.43)	2.4×10^{-50}	-1.95 (-2.38, -1.52)	5.7×10^{-19}	-0.38 (-0.67, -0.10)	0.009
Other/mixed	-0.48 (-0.70, -0.26)	2.1×10^{-5}	-0.12 (-0.56, 0.32)	0.58	0.39 (0.10, 0.68)	0.009
Body mass index (per 5 Kg/m^2)	-0.12 (-0.16, -0.08)	1.5×10^{-8}	-0.29 (-0.37, -0.21)	5.9×10^{-12}	-0.18 (-0.24, -0.13)	1.1×10^{-10}
Smoking status						
Never	Ref		Ref		Ref	
Previous	0.02 (-0.06, 0.10)	0.65	0.02 (-0.14, 0.18)	0.80	0.00 (-0.10, 0.10)	0.99
Current	-0.06 (-0.18, 0.07)	0.37	-0.07 (-0.32, 0.18)	0.57	-0.01 (-0.18, 0.15)	0.89
Alcohol intake						
Never or special occasion only	Ref		Ref		Ref	
One to three times a month	0.02 (-0.11, 0.16)	0.72	0.08 (-0.19, 0.34)	0.57	0.07 (-0.11, 0.24)	0.45
Once or twice a week	0.04 (-0.07, 0.15)	0.43	0.07 (-0.15, 0.29)	0.53	0.04 (-0.11, 0.18)	0.60
Three or four times a week	-0.09 (-0.21, 0.02)	0.11	-0.24 (-0.47, -0.02)	0.036	-0.14 (-0.29, 0.02)	0.08
Daily or almost daily	-0.19 (-0.31, -0.07)	0.002	-0.63 (-0.87, -0.40)	1.4×10^{-7}	-0.46 (-0.61, -0.30)	1.1×10^{-8}
Townsend deprivation index						
Least deprived quartile	Ref		Ref		Ref	
2 nd quartile	-0.02 (-0.12, 0.08)	0.69	-0.02 (-0.22, 0.18)	0.84	0.00 (-0.14, 0.13)	0.95
3 rd quartile	-0.12 (-0.22, -0.02)	0.019	-0.25 (-0.44, -0.05)	0.016	-0.13 (-0.26, 0.00)	0.06
Most deprived quartile	-0.13 (-0.24, -0.03)	0.012	-0.41 (-0.61, -0.20)	1.2×10^{-4}	-0.28 (-0.42, -0.14)	6.6×10^{-5}
Education level						
Less than O level	Ref		Ref		Ref	
O level	0.15 (0.05, 0.25)	0.004	0.30 (0.10, 0.50)	0.003	0.16 (0.02, 0.29)	0.022
A Level	0.35 (0.22, 0.47)	3.3×10^{-8}	0.61 (0.37, 0.86)	8.4×10^{-7}	0.26 (0.09, 0.42)	0.002
Degree	0.36 (0.26, 0.45)	2.3×10^{-14}	0.65 (0.47, 0.83)	1.7×10^{-12}	0.30 (0.18, 0.42)	8.4×10^{-7}
Diabetes status						
No	Ref		Ref		Ref	
Yes	-0.54 (-0.71, -0.38)	1.5×10^{-10}	-0.83 (-1.16, -0.50)	8.5×10^{-7}	-0.34 (-0.56, -0.12)	0.003
Spherical equivalent (diopters)	-0.33 (-0.35, -0.31)	1.1×10^{-251}	0.40 (0.36, 0.43)	1.2×10^{-93}	0.73 (0.71, 0.76)	$< 1 \times 10^{-300}$
IOPcc (mmHg)	0.00 (-0.01, 0.01)	0.77	-0.03 (-0.05, -0.01)	5.8×10^{-5}	-0.04 (-0.05, -0.03)	4.0×10^{-10}
Model R-squared	6.7%		5.6%		11.2%	

IOPcc – corneal-compensated intraocular pressure

Table 5: Associations of intraocular pressure (IOP) with average macular retinal nerve fiber layer (mRNFL), ganglion cell complex (GCC) and ganglion cell inner plexiform layer (GCIPL) thicknesses. Results are from linear regression models adjusted for age, sex and spherical equivalent. Six different associations with IOP are presented: either Goldmann-correlated (IOPg) or corneal compensated (IOPcc) IOP, and three methods for handling IOP values for patients on IOP-lowering treatment (1. including participants on IOP-lowering medication and imputing pre-treatment IOP; 2. including participants on IOP-lowering medication and using current IOP rather than imputing; 3. excluding participants using IOP-lowering medications [see Methods]).

	mRNFL thickness (μm)			GCC thickness (μm)			GCIPL thickness (μm)		
	β (95% CI)	<i>P</i> -value	<i>R</i> ²	β (95% CI)	<i>P</i> -value	<i>R</i> ²	β (95% CI)	<i>P</i> -value	<i>R</i> ²
1. IOP imputed if using IOP-lowering medication (<i>n</i> = 42,044)									
IOPg (mmHg)	-0.01 (-0.02, 0.00)	0.042	5.6%	-0.07 (-0.09, -0.05)	7.8×10^{-13}	4.8%	-0.06 (-0.08, -0.05)	2.7×10^{-20}	10.8%
IOPcc (mmHg)	0.00 (-0.01, 0.01)	0.55	5.6%	-0.05 (-0.07, -0.03)	1.4×10^{-6}	4.8%	-0.05 (-0.06, -0.03)	1.1×10^{-11}	10.8%
2. Current IOP analyzed regardless of IOP-lowering medication (<i>n</i> = 42,044)									
IOPg (mmHg)	0.00 (-0.01, 0.01)	0.56	5.6%	-0.06 (-0.08, -0.04)	3.5×10^{-8}	4.8%	-0.05 (-0.07, -0.04)	4.4×10^{-15}	10.8%
IOPcc (mmHg)	0.01 (-0.01, 0.02)	0.31	5.6%	-0.03 (-0.05, -0.01)	0.003	4.7%	-0.04 (-0.05, -0.02)	1.4×10^{-7}	10.8%
3. Excluded if using IOP-lowering medication (<i>n</i> = 41,770)									
IOPg (mmHg)	0.00 (-0.01, 0.01)	0.72	5.6%	-0.05 (-0.07, -0.03)	1.6×10^{-7}	4.7%	-0.05 (-0.07, -0.04)	2.8×10^{-14}	10.7%
IOPcc (mmHg)	0.01 (0.00, 0.02)	0.15	5.6%	-0.03 (-0.05, -0.01)	0.012	4.6%	-0.03 (-0.05, -0.02)	1.2×10^{-6}	10.6%