Associations with Intraocular Pressure in a Large Cohort Results from the UK Biobank

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Purpose: To describe the associations of physical and demographic factors with Goldmann-correlated intraocular pressure (IOPg) and corneal-compensated intraocular pressure (IOPcc) in a British cohort.

Design: Cross-sectional study within the UK Biobank, a large-scale multisite cohort study in the United Kingdom.

Participants: We included 110,573 participants from the UK Biobank with intraocular pressure (IOP) measurements available. Their mean age was 57 years (range, 40–69 years); 54% were women, and 90% were white.

Methods: Participants had 1 IOP measurement made on each eye using the Ocular Response Analyzer noncontact tonometer. Linear regression models were used to assess the associations of IOP with physical and demographic factors.

Main Outcome Measures: The IOPg and IOPcc.

Results: The mean IOPg was 15.72 mmHg (95% confidence interval [CI], 15.70–15.74 mmHg), and the mean IOPcc was 15.95 mmHg (95% CI, 15.92–15.97 mmHg). After adjusting for covariates, IOPg and IOPcc were both significantly associated with older age, male sex, higher systolic blood pressure (SBP), faster heart rate, greater myopia, self-reported glaucoma, and colder season (all \( P < 0.001 \)). The strongest determinants of both IOPg and IOPcc were SBP (partial \( R^2 \): IOPg 2.30%, IOPcc 2.26%), followed by refractive error (IOPg 0.60%, IOPcc 1.04%). The following variables had different directions of association with IOPg and IOPcc: height (−0.77 mmHg/m IOPg; 1.03 mmHg/m IOPcc), smoking (0.19 mmHg IOPg, −0.35 mmHg IOPcc), self-reported diabetes (0.41 mmHg IOPg, −0.05 mmHg IOPcc), and black ethnicity (−0.80 mmHg IOPg, 0.77 mmHg IOPcc). This suggests that height, smoking, diabetes, and ethnicity are related to corneal biomechanical properties. The increase in both IOPg and IOPcc with age was greatest among those of mixed ethnicities, followed by blacks and whites. The same set of covariates explained 7.4% of the variability of IOPcc but only 5.3% of the variability of IOPg.

Conclusions: This analysis of associations with IOP in a large cohort demonstrated that some variables clearly have different associations with IOPg and IOPcc, and that these 2 measurements may reflect different biological characteristics.

Elevated intraocular pressure (IOP) is one of the most significant risk factors for the development and progression of open-angle glaucoma. Intraocular pressure is a multifactorial trait with a heritability of 29% to 62%. Many epidemiologic studies have examined the association of IOP with physical and sociodemographic factors across different populations, and these factors have been shown to account for approximately 10% of IOP variability. Although some associations with IOP have been demonstrated consistently, such as systolic blood pressure (SBP), other factors such as age and sex have a less consistent effect. There is also growing evidence that corneal biomechanics influence IOP measurements. The UK Biobank is one of the largest prospective cohort studies with ocular data globally and will lend statistical power to detecting weaker associations of IOP. In this study, we explore the associations of both Goldmann-correlated IOP (IOPg) and corneal-compensated IOP (IOPcc) measured by the Ocular Response Analyzer noncontact tonometer (ORA).

Methods

The UK Biobank is a large-scale multisite cohort study established by the Wellcome Trust medical charity, Medical Research Council, Department of Health, Scottish Government, and Northwest Regional Development Agency. The overall study...
power and refractive error (spherical equivalent) was calculated as sphere stretchable sprung tape measure. Autorefraction was performed level of the umbilicus was measured using a Wessex non-

United Kingdom, including Croydon and Hounslow in Greater London, Liverpool and Sheffield in Northern England, Birmingham in the Midlands, and Swansea in Wales. Participants completed a touch-screen self-administered questionnaire on their general health and socioeconomic status. The Townsend deprivation index was determined according to the participants’ postcodes at recruitment and the corresponding output areas from the pre-

ceding national census. The index was calculated on the basis of 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. The choices for ethnicity include 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 was determined by the participant’s answer to “Do you smoke tobacco now?,” from the selection of yes, on most or all days/only occasionally/no/prefer not to answer. Diabetes status was determined as those who answered yes to “Has a doctor ever told you that you have diabetes?” Glaucoma and macular degeneration statuses were determined as those who selected “glaucoma” or “macular degeneration” from a list of eye disorders to the question, “Has a doctor told you that you have any of the following problems with your eyes?”

Measurements

Blood pressure and heart rate were measured using the HEM-70151T digital blood pressure monitor (Omron, Hoofddorp, The Netherlands). Two measurements of each were taken, and the mean was used in subsequent analysis. Weight was measured with the BV-418 MA body composition analyzer (Tanita, Arlington Heights, IL). Height was measured using a Seca 202 height measure (Seca, Birmingham, UK). Body mass index (BMI) was calculated as weight (kg)/height (m)². Waist circumference at the level of the umbilicus was measured using a Measuring tape. Body mass index was examined between 20 and 40 kg/m² (95% of the study population), because BMI outside this range showed a nonlinear relationship with IOP. Smoking status was dichotomized to regular (smokes on most or all days) and current nonsmokers (ex-smokers and never smokers) to maximize the potential to detect an effect. Season of IOP measurement was categorized into spring (March to May), summer (June to August), autumn (September to November), and winter (December to February).

The variables to be examined for associations with IOP were decided a priori on the basis of previous published studies. The possibility of clustering of IOP within each center of assessment was explored, but the intraclass correlation coefficients were very low (0.004 for IOPg; 0.0005 for IOPc), which indicated that clustering accounted for a very small proportion of the variance in IOP. Therefore, we elected to proceed with multiple regression analysis using the center of assessment as a covariable to account for the potential underlying small differences in associations with IOP. Variations in characteristics between the centers were explored using multiple 1-way analysis of variance with Bonferroni correction for continuous variables and chi-square test for categoric variables.

Associations between IOP and continuous variables were first explored graphically. The relationship with sex, age, Townsend deprivation index, center of assessment, weight, height, waist circumference, SBP and diastolic blood pressure (DBP), BMI, refractive error, smoking status, diabetes, glaucoma, macular degeneration, and season of IOP measurement were explored with univariable linear regression. All examined variables were included in a multivariable regression model. All statistical analyses were performed using STATA (Stata/IC 12.0; StataCorp LP, College Station, TX). A more robust statistical significance threshold of \( P < 0.001 \) was used to avoid false-positives due to the large number of tests carried out. Further details of the derivation of the variables and missing data can be found on the UK Biobank online data showcase (http://biobank.ctsu.ox.ac.uk/crystal/label.cgi).

Results

Of the 502 656 participants in the whole UK Biobank cohort, 112 690 underwent IOP measurements, and 112 285 had valid measurements. Table 1 summarizes their mean IOP stratified by age, sex, and laterality. Mean IOP was slightly higher in the right eye than the left eye for both IOPg and IOPcc (mean difference, 0.14 mmHg IOPg; 95% confidence interval [CI], 0.12–0.16 mmHg, paired \( t \) test \( P < 0.001; \) 0.07 mmHg IOPcc; 95% CI, 0.05–0.09 mmHg; \( P < 0.001 \)). Therefore, left eye values were used in all subsequent analyses because they were measured after the right eye and were possibly less prone to artifacts with the participant more familiar with the test. The mean left IOPg was 15.72 mmHg (95% CI, 15.70–15.74 mmHg), and the mean left IOPcc was 15.95 mmHg (95% CI, 15.92–15.97 mmHg). The IOPg and IOPcc increased linearly with age, SBP, DBP, pulse rate, and BMI (Fig 1A–D) and decreased linearly with refractive error (Fig 1E).
Table 1. Intracocular Pressure Stratified By Age, Sex, and Eye

| IOPg, mmHg (SD, 95% CI) | IOPcc, mmHg (SD, 95% CI) |
|-------------------------|--------------------------|
| **Right** (n=111 434)   | **Left** (n=111 049)     |
| **Men**                 |                          |
| 40–49 yrs               | 15.4 (3.7, 15.4–15.5)    | 15.6 (3.6, 15.5–15.6)    |
| 50–59 yrs               | 15.9 (4.0, 15.8–16.0)    | 16.1 (3.9, 16.1–16.2)    |
| 60–69 yrs               | 16.3 (4.0, 16.2–16.3)    | 16.8 (4.0, 16.7–16.8)    |
| **Women**               |                          |
| 40–49 yrs               | 15.3 (3.6, 15.2–15.3)    | 15.0 (3.5, 15.0–15.1)    |
| 50–59 yrs               | 15.6 (3.7, 15.6–15.7)    | 15.6 (3.6, 15.5–15.6)    |
| 60–69 yrs               | 16.2 (3.8, 16.1–16.2)    | 16.3 (3.8, 16.3–16.4)    |
| **Total**               | 15.3 (3.7, 15.3–15.4)    | 15.2 (3.7, 15.1–15.2)    |
| 40–49 yrs               | 15.8 (3.9, 15.7–15.8)    | 15.8 (3.8, 15.5–15.6)    |
| 50–59 yrs               | 15.6 (3.8, 15.7–15.8)    | 16.5 (3.9, 16.5–16.6)    |
| 60–69 yrs               | 16.2 (3.9, 16.2–16.2)    | 16.0 (3.9, 16.2–16.4)    |
| All                     | 15.86 (3.8, 15.84–15.88) | 15.72 (3.9, 15.70–15.74) |
| **Difference (right-left)** | 0.14 (0.12–0.16), P < 0.001 | 0.07 (0.05–0.09), P < 0.001 |

CI = confidence interval; IOPcc = corneal-compensated intraocular pressure; IOPg = Goldmann-correlated intraocular pressure; SD = standard deviation.

Table 2 summarizes the characteristics of the 110 573 study participants, which excluded those whose left eye has had laser refractive surgery or corneal graft surgery. The completeness of each variable is included in Table 2, which is generally high (98.6%–100% complete). Their mean age was 57.3 years (range, 40–70 years), 54.1% were women, and the majority were white (89.6%). Significant differences between men and women were found for age, distribution of participants among the centers of assessment, ethnicity, deprivation index, height, weight, BMI, waist circumference, SBP, DBP, pulse rate, smoking status, and the percentage with self-reported glaucoma and diabetes.

Among the 6 centers of assessment, mean IOPcc was significantly different (P < 0.001, analysis of variance) but not mean IOPg (P = 0.046). Specifically, IOPcc was significantly lower in Birmingham than every center except Swansea by 0.05 to 0.41 mmHg (P < 0.001). The centers were also different in ethnicity, deprivation index, height, weight, BMI, waist circumference, SBP, DBP, pulse rate, smoking status, and the percentage with self-reported glaucoma and diabetes.

The associations of IOP with physio-demographic factors were tested using univariable linear regression stratified by Table 3 and 4) and multivariable regression (Table 5). All covariates in the univariable model were included in the multiple regression model to allow direct comparisons between IOPg and IOPcc. The DBP and waist circumference were excluded because of collinearity between DBP and SBP, and waist circumference with BMI. After adjusting for covariates, the following were significantly associated with both IOPg and IOPcc: older age (0.18 mmHg IOPg/decade, P < 0.001; 0.49 mmHg IOPg/decade, P < 0.001), male sex (0.18 mmHg IOPg, P < 0.001; 0.35 mmHg IOPcc P < 0.001), SBP (0.035 mmHg IOPg, P < 0.001; 0.033 mmHg IOPcc, P < 0.001), pulse rate (0.023 mmHg IOPg, P < 0.001; 0.018 mmHg IOPcc, P < 0.001), myopic refractive error (−0.11 mmHg IOPg/diopter, P < 0.001; −0.14 mmHg IOPcc/diopter, P < 0.001), self-reported glaucoma (1.97 mmHg IOPg, P < 0.001; 2.30 mmHg IOPcc, P < 0.001), and colder season (baseline winter; IOPg −0.14 mmHg spring, −0.27 mmHg summer; IOPcc −0.29 mmHg spring, −0.37 mmHg summer, P < 0.001). Systolic blood pressure was the most important determinant of both IOPg and IOPcc, accounting for 2.3% and 2.26% (partial R²) of their variations, respectively, followed by refractive error (IOPg 0.60%, IOPcc 1.04%) (Table 5).

Some examined factors had different relationships with IOPg and IOPcc in the multivariable model. Self-reported diabetes was significantly associated with IOPg (0.41 mmHg, P < 0.001) but not with IOPcc (−0.05 mmHg, P = 0.38). The following covariates had different directions of association with IOPg and IOPcc: height (−0.77 mmHg/m IOPg, P < 0.001; 1.03 mmHg/m IOPcc, P < 0.001), smoking (0.19 mmHg IOPg, P < 0.001; −0.35 mmHg IOPcc, P < 0.001), and ethnicity, where IOPg was highest among whites (baseline) and lowest among blacks (−0.80 mmHg, P < 0.001), but IOPcc was highest among blacks (0.77 mmHg, P < 0.001) and lowest among the Chinese (−0.74 mmHg, P < 0.001) (Fig 2). This suggests that height, smoking, and ethnicity are strongly related to corneal biomechanical properties. The same set of covariates explained 7.4% of the variability of IOPcc, but only 5.3% of the variability of IOPg.

The association of IOP and age was examined for each ethnic group. Figure 3 demonstrates how changes in mean IOP with age varies across the ethnic groups, showing a linear increase among whites, Asians, blacks, and those of mixed ethnicities, and the trends are similar between IOPg and IOPcc. The increase was greatest among those of mixed ethnicities after adjusting for covariates (mixed 0.55 mmHg IOPg/decade, 0.64 mmHg IOPcc/ decade), followed by black participants (0.42 mmHg IOPg/ decade, 0.54 mmHg IOPcc/decade) (Table 6). There was no statistically significant trend among Chinese and “other” ethnicities for IOP and age.

Sensitivity analysis using right eye IOP values and right eye-specific variables (e.g., refraction) was performed for the regression analysis. The only different results were for sex, which was no longer significantly associated with IOPg (0.09 mmHg; 95% CI, 0.03–0.16 mmHg; P = 0.007), and with BMI, which
Figure 1. Graphs showing that Goldmann-correlated intraocular pressure (IOPg) and corneal-compensated intraocular pressure (IOPcc) increase linearly with (A) age, (B) systolic blood pressure, (C) pulse rate, (D) body mass index (BMI). (E) The IOPg and IOPcc show an inverse relationship with refractive error. (F) Height has an insignificant relationship with IOPg and IOPcc in univariable regression, but a differential relationship with IOPg and IOPcc in multivariable regression. The error bars represent the 95% confidence intervals (CIs).
was no longer significant with IOPcc (−0.005 mmHg, 95% CI, −0.011 to 0.001 mmHg; \( P = 0.11 \)).

**Discussion**

We examined the physical and demographic associations with IOP in one of the largest cohort studies in recent years. This is also one of the few studies that examined and contrasted the associations of IOPg and IOPcc together in a large cohort.

**Goldmann-Correlated Intraocular Pressure versus Corneal-Compensated Intraocular Pressure**

In this study, the associations of most variables with IOPg and IOPcc were similar. However, after adjusting for confounders, there were clear differences in the association of IOPg and IOPcc with self-reported diabetes (positively and significantly associated with IOPg but not with IOPcc), height (positively associated with IOPcc, negatively associated with IOPg), smoking (positively associated with...
### Table 3. Univariable Linear Regression with Goldmann-Correlated Intraocular Pressure (Left Eye) as the Dependent Variable

|                        | All (β [95% CI]) | P     | Women (β [95% CI]) | P     | Men (β [95% CI]) | P     |
|------------------------|------------------|-------|-------------------|-------|------------------|-------|
| **Age, decade**        | 0.45 (0.43–0.48) | <.0001| 0.50 (0.46–0.53)  | <.0001| 0.4 (0.36–0.44)  | <.0001|
| **Sex (baseline = female)** | 0.25 (0.20–0.30) | <.0001| –                  | –     | –                | –     |
| **Ethnicity (baseline = white)** | –              | –     | –                 | –     | –                | –     |
| **Asian**              | –0.52 (–0.64 to –0.40) | <.0001| –0.65 (–0.82 to –0.48) | <.0001| –0.44 (–0.61 to –0.27) | <.0001|
| **Black**              | –0.71 (–0.83 to –0.58) | <.0001| –0.83 (–0.99 to –0.67) | <.0001| –0.50 (–0.70 to –0.30) | <.0001|
| **Chinese**            | –0.55 (–0.90 to –0.21) | 0.001| –0.72 (–1.14 to –0.31) | 0.001| –0.19 (–0.78 to 0.40) | 0.53  |
| **Mixed**              | –0.58 (–0.82 to –0.34) | <.0001| –0.58 (–0.88 to –0.28) | <.0001| –0.52 (–0.93 to –0.11) | 0.012 |
| **Others**             | –0.58 (–0.77 to –0.39) | <.0001| –0.69 (–0.93 to –0.46) | <.0001| –0.37 (–0.68 to 0.068) | 0.017 |

### Assessment center (baseline = Croydon)

|                        |                |       |
|------------------------|----------------|-------|
| Sheffield              | 0.088 (0.20–0.16) | 0.012|
| Birmingham             | 0.011 (–0.06 to 0.08) | 0.76  |
| Hounslow               | 0.044 (–0.028 to 0.12) | 0.23  |
| Liverpool              | 0.14 (0.057–0.21) | 0.001|
| Swansea                | 0.19 (–0.18 to 0.57) | 0.31  |
| Deprivation index      | –0.010 (–0.018 to –0.002) | 0.011|
| Weight, kg             | 0.08 (0.062–0.091) | <.0001|
| Height, m              | 0.09 (–0.16 to 0.34) | 0.47  |
| BMI, kg/m²             | 0.033 (0.027–0.038) | <.0001|
| Waist, cm              | 0.014 (0.013–0.016) | <.0001|
| SBP, mmHg              | 0.039 (0.038–0.040) | <.0001|
| DBP, mmHg              | 0.054 (0.052–0.056) | <.0001|
| Pulse, min⁻¹           | 0.030 (0.028–0.032) | <.0001|
| Refractive error, D    | –0.085 (–0.093 to –0.077) | <.0001|
| Smoking                |                |       |
| Nonsmoker = 0          | –              | –     |
| Regular smoker = 1     | 0.12 (0.026–0.20) | 0.011|
| Diabetes               | 0.69 (0.60–0.79) | <.0001|
| Glaucoma               | 2.34 (2.15–2.53) | <.0001|
| Macular degeneration   | 0.51 (0.26–0.80) | <.0001|
| Seasons (baseline = winter) |                |       |
| Spring                 | –0.20 (–0.26 to –0.14) | <.0001|
| Summer                 | –0.43 (–0.50 to –0.36) | <.0001|
| Autumn                 | –0.13 (–0.19 to –0.57) | <.0001|

BMI = body mass index; CI = confidence interval; D = diop ters; DBP = diastolic blood pressure; IOPg = Goldmann-correlated intraocular pressure; SBP = systolic blood pressure.

P < 0.001 shown in bold. BMI between 20 and 40 kg/m² was analyzed.

### OIPg but negatively associated with IOPECc, and black ethnicity (negatively associated with IOPg, positively associated with IOPECc). Previous studies using Goldmann applanation tonometry found higher IOP to be associated with self-reported diabetes, whereas no association had been found with height, including 1 study that used IOPg. A recent study comparing ORA data among 2 groups of diabetic patients (HbA1c <7% and HbA1c ≥7%) and healthy controls did demonstrate similar differential associations and found that IOPECc was not significantly different among the 3 groups, whereas IOPg was significantly higher in the diabetic patients than in the controls. For smoking, findings have been variable, with some studies reporting no association and other studies reporting higher IOP in smokers. Among women, IOPg in this study was not significantly associated with smoking in univariable (P = 0.004) or multiple regression (P = 0.41, not shown in tables), a finding also seen in the Gutenberg Health Study using noncontact tonometry. The differential systemic associations of IOPg and IOPECc demonstrated probably mean these 2 IOP measures reflect different biological features. The IOPg is calibrated against the Goldmann applanation tonometer, whereas IOPECc is derived by modeling IOP of patients who underwent laser-assisted in situ keratomileusis to minimize the difference in measured pressure before and after surgery, therefore reflecting an IOP measure with minimal influence from corneal biomechanics. In particular, central corneal thickness (CCT) is correlated with IOPg but not IOPECc, and IOPECc is not correlated with corneal resistance factor. However, it is not clear exactly which parameters of corneal biomechanics best describe the difference between IOPg and IOPECc.

Height is related to a longer axial length, deeper anterior chamber, and flatter cornea. Therefore, height is plausibly related to determinants of collagen-related processes, which may explain the different associations with IOPg and IOPECc. There is a clear trend for men being taller than women in our study, and that resulted in paradoxical results in the univariable analysis when the sexes were separated. This was resolved when sex was adjusted for in the model. Chronic high serum glucose in diabetes and the
Table 4. Univariable Linear Regression with Corneal-Compensated Intraocular Pressure (Left Eye) as the Dependent Variable

|                      | All       | Women    | Men       |
|----------------------|-----------|----------|-----------|
| **β (95% CI)**       | **P**     | **β (95% CI)** | **P**     | **β (95% CI)** | **P**  |
| Age, decade          | 0.67 (0.64–0.70) | <0.001 | 0.70 (0.67–0.73) | <0.001 | 0.61 (0.57–0.65) | <0.001 |
| Sex (female = 0, male = 1) | 0.61 (0.56–0.66) | <0.001 | — | — | — | — |
| Ethnicity (baseline = white) | — | — | — | — | — | — |
| Asian                | −0.16 (−0.28 to −0.04) | 0.009 | −0.25 (−0.42 to −0.08) | 0.004 | −0.15 (−0.32 to 0.02) | 0.08 |
| Black                | 0.56 (0.44–0.69) | <0.001 | 0.49 (0.33–0.65) | <0.001 | 0.74 (0.54–0.94) | <0.001 |
| Chinese              | −0.77 (−1.11 to −0.44) | <0.001 | −0.80 (−1.21 to −0.39) | <0.001 | −0.55 (−1.13 to 0.03) | 0.06 |
| Mixed                | −0.31 (−0.55 to −0.07) | 0.013 | −0.18 (−0.48 to 0.12) | 0.23 | −0.38 (−0.79 to 0.02) | 0.06 |
| Others               | −0.22 (−0.41 to −0.035) | 0.020 | −0.13 (−0.36 to 1.02) | 0.27 | −0.26 (−0.57 to 0.04) | 0.09 |
| Center of assessment (baseline = Croydon) | — | — | — | — | — | — |
| Sheffield            | 0.053 (−0.015 to 0.12) | 0.13 | 0.028 (−0.06 to 0.12) | 0.53 | 0.042 (−0.061 to 0.15) | 0.42 |
| Birmingham           | −0.37 (−0.44 to −0.30) | <0.001 | −0.39 (−0.48 to −0.30) | <0.001 | −0.40 (−0.51 to −0.30) | <0.001 |
| Hounslow             | −0.014 (−0.086 to 0.057) | 0.69 | −0.042 (−0.13 to 0.051) | 0.38 | 0.002 (−0.11 to 0.11) | 0.98 |
| Liverpool            | 0.042 (−0.036 to 0.12) | 0.29 | −0.041 (−0.14 to 0.061) | 0.43 | 0.098 (−0.02 to 0.22) | 0.10 |
| Swansea              | 0.065 (0.30 to 0.43) | 0.73 | 0.19 (−0.32 to 0.70) | 0.46 | −0.13 (−0.67 to 0.40) | 0.63 |
| Deprivation index    | −0.02 (−0.03 to −0.01) | <0.001 | −0.02 (−0.03 to −0.01) | <0.001 | −0.02 (−0.04 to −0.01) | <0.001 |
| Weight, 10 kg        | 0.12 (0.10–0.13) | <0.001 | 0.08 (0.06–0.10) | <0.001 | −0.0004 (−0.02 to 0.02) | 0.10 |
| Height, m            | 2.02 (1.77–2.23) | <0.001 | −0.91 (−1.38 to −0.43) | <0.001 | −0.18 (−0.69 to 0.33) | 0.48 |
| BMI, kg/m²           | 0.025 (0.019–0.030) | <0.001 | 0.030 (0.023–0.037) | <0.0008 | −0.0013 (0.01 to 0.009) | 0.87 |
| Waist, cm            | 0.018 (0.017–0.20) | <0.001 | 0.015 (0.013–0.017) | <0.001 | 0.004 (0.001–0.007) | 0.007 |
| SBP, mmHg            | 0.042 (0.040–0.045) | <0.001 | 0.040 (0.039–0.042) | <0.001 | 0.040 (0.038–0.042) | <0.001 |
| DBP, mmHg            | 0.058 (0.056–0.061) | <0.001 | 0.057 (0.054–0.060) | <0.001 | 0.053 (0.049–0.056) | <0.001 |
| Pulse, min⁻¹         | 0.021 (0.019–0.023) | <0.001 | 0.031 (0.028–0.033) | <0.001 | 0.016 (0.013–0.019) | <0.001 |
| Refractive error, D  | −0.11 (−0.12 to −0.11) | <0.001 | −0.63 (−0.75 to −0.50) | <0.001 | −0.14 (−0.15 to −0.13) | <0.001 |

- **Nonsmoker = 0**
- **Regular smoker = 1**
- **Diabetes**
- **Glaucoma**
- **Macular degeneration**
- **Seasons (baseline = winter)**
- **Spring**
- **Summer**
- **Autumn**

BMI = body mass index; CI = confidence interval; D = dipters; DBP = diastolic blood pressure; SBP = systolic blood pressure.

P < 0.001 shown in bold. BMI between 20 and 40 kg/m² was analyzed.

Toxicity from smoking could directly influence the cornea to cause the differential associations with IOPg and IOPcc. Diabetes is known to cause corneal epithelial and endothelial dysfunction and thickening of the basement membrane, postulated to occur from advanced glycation end products and changes in the polyol pathway. Although the damage of cigarette smoke on the cornea is rarely examined, smoking induces oxidative stress on lens protein and the retina, thought to be related to cataract formation and increased risk of age-related macular degeneration. These tissue effects could be replicated in the cornea.

Overall, the list of systemic and ocular factors examined explained only a small proportion of IOPg and IOPcc variation (adjusted $R^2$: 5.3% IOPg, 7.4% IOPcc). Other published studies reported similarly low explanatory power in their models ($R^2$ of 10.19%–11.0% using Goldmann IOP), although the list of explanatory variables varies greatly among studies, and therefore the $R^2$ values cannot be directly compared. Nevertheless, the power of large population studies is to allow small effects to be detected, and these small effects could be biologically important. By focusing on the magnitudes of association, self-reported glaucoma has the greatest effect on IOP ($β$=1.97 mmHg IOPg, 2.30 mmHg IOPcc), which is equivalent to a 5- to 10-fold effect on IOP compared with a decade increase in age ($β$=0.18 mmHg IOPg, 0.49 mmHg IOPcc). It is also notable that the effect of seasonal change in IOP between winter and summer ($β$=−0.27 mmHg IOPg, −0.37 mmHg IOPcc) is comparable to the difference in IOP between women and men ($β$=0.18 mmHg IOPg, 0.35 IOPcc), as well as the difference between smokers and nonsmokers ($β$=0.19 mmHg IOPg, −0.35 mmHg IOPcc).

**Ethnicity**

For ethnicity, the differential associations with IOPg and IOPcc could be related to ethnic differences in corneal hysteresis or CCT. Thick or thin CCT is known to cause overestimation or underestimation, respectively, of the true IOP by Goldmann applanation tonometers and corneal curvature. Studies have consistently found CCT to be thinner in Africans than in white subjects.
## Table 5. Multivariable Linear Regression with Goldmann-Correlated Intraocular Pressure and Corneal-Compensated Intraocular Pressure (Left Eye) as the Dependent Variables

|                        | IOPg   |                      | IOPcc  |                      |
|------------------------|--------|----------------------|--------|----------------------|
|                        | \( \beta \) (95% CI) | \( P \) | Standard Coefficient* | \( \beta \) (95% CI) | \( P \) | Standard Coefficient* |
| Age, decade            | \( 0.18 \) (0.15-0.21) | \( <0.001 \) | 0.15 | 0.12 | \( 0.49 \) (0.46-0.52) | \( <0.001 \) | 0.39 | 0.9 |
| Sex (baseline = female)| \( 0.18 \) (0.11-0.25) | \( <0.001 \) | n/a  | 0.03 | \( 0.35 \) (0.28-0.42) | \( <0.001 \) | n/a  | 0.1 |
| Ethnicity (baseline = white) |          |                      |        |        |                        |        |        |        |
| Asian                  | \( -0.61 \) (-0.74 to -0.48) | \( <0.001 \) | 0.09 | 0.13 | \( 0.042 \) (-0.09 to 0.17) | 0.52 | 0 |
| Black                  | \( -0.80 \) (-0.94 to -0.66) | \( <0.001 \) | 0.13 | 0.77 | \( 0.63-0.90) \) | \( <0.001 \) | 0.13 |
| Chinese                | \( -0.72 \) (-1.08 to -0.36) | \( <0.001 \) | 0.02 | 0.74 | \( -1.10 \) to \( -0.38) \) | \( <0.001 \) | 0.02 |
| Mixed                  | \( -0.55 \) (-0.80 to -0.29) | \( <0.001 \) | 0.02 | 0.39 | \( -0.50 \) (0.39 to 0.70) | \( <0.001 \) | 0.28 |
| Others                 | \( -0.50 \) (-0.70 to -0.30) | \( <0.001 \) | 0.02 | 0.11 | \( -0.088 \) to \( -0.30) \) | 0 | 0 |
| Center of assessment   | (baseline = Cryoodon) |          |        |        |                        |        |        |        |
| Sheffield              | \( -0.07 \) (-0.14 to 0.002) | 0.058 | 0 | 0.012 | \( -0.06 \) to \( 0.83) \) | 0.74 | 0 |
| Birmingham             | \( -0.056 \) (-0.13 to 0.017) | 0.13 | n/a  | 0 | \( -0.32 \) (-0.39 to -0.25) | \( <0.001 \) | n/a  | 0.08 |
| Hounslow               | \( -0.05 \) (-0.07 to 0.08) | 0.89 | 0 | \( -0.04 \) (-0.11 to 0.04) | 0.32 | 0 |
| Liverpool              | \( -0.12 \) (-0.21 to -0.04) | 0.005 | 0.01 | \( -0.15 \) (-0.23 to -0.06) | 0.001 | 0.01 |
| Swansea                | \( -0.24 \) (-0.63 to 0.15) | 0.23 | 0 | \( -0.014 \) (-0.39 0.37) | 0.94 | 0 |
| Deprivation index      | \( 0.007 \) (-0.001 to 0.016) | 0.10 | 0.02 | 0 | \( -0.004 \) (-0.013 to 0.004) | 0.32 | \( <0.001 \) |
| Height, m              | \( -0.77 \) (-1.14 to -0.39) | \( <0.001 \) | \( -0.07 \) | 0.02 | 1.03 | \( 0.65 \) to \( 1.40) \) | \( <0.001 \) | 0.095 | 0.03 |
| BMI, kg/m²              | \( -0.028 \) (-0.014 to -0.002) | 0.029 | \( -0.03 \) | 0.01 | \( -0.016 \) (-0.022 to -0.011) | \( <0.001 \) | -0.067 | 0.03 |
| SBP, mmHg              | \( 0.35 \) (0.033-0.036) | \( <0.001 \) | 0.63 | 2.29 | \( 0.033 \) (0.032-0.034) | \( <0.001 \) | 0.60 | 2.16 |
| Pulse, min⁻¹            | \( 0.023 \) (0.021-0.025) | \( <0.001 \) | 0.26 | 0.43 | \( 0.018 \) (0.016-0.02) | \( <0.001 \) | 0.20 | 0.28 |
| Refractive error, D     | \( -0.11 \) (-0.12 to -0.10) | \( <0.001 \) | -0.30 | 0.58 | \( -0.14 \) (-0.15 to -0.13) | \( <0.001 \) | -0.39 | 1.04 |
| Smoking (baseline = nonsmoker) |          |                      |        |        |                        |        |        |        |
| Regular smoker         | \( 0.19 \) (0.097-0.28) | \( <0.001 \) | n/a  | 0.02 | \( -0.35 \) (-0.44 to -0.26) | \( <0.001 \) | n/a  | 0.06 |
| Self-reported diabetes  | \( 0.41 \) (0.3-0.52) | \( <0.001 \) | n/a  | 0.06 | \( -0.05 \) (-0.15 to 0.06) | 0.38 | n/a  | 0 |
| Self-reported glaucoma  | \( 1.97 \) (1.77-2.17) | \( <0.001 \) | n/a  | 0.38 | 2.30 | \( 2.11 \) to \( 2.50) \) | \( <0.001 \) | 0.54 |
| Self-reported macular degeneration | \( 0.21 \) (-0.053 to 0.47) | 0.12 | n/a  | 0 | \( 0.34 \) (0.087-0.60) | 0.009 | n/a  | 0.01 |
| Seasons (baseline = winter) |          |                      |        |        |                        |        |        |        |
| Spring                 | \( -0.14 \) (-0.21 to -0.075) | \( <0.001 \) | 0.02 | -0.29 | \( -0.35 \) to \( -0.22) \) | \( <0.001 \) | 0.08 |
| Summer                 | \( -0.27 \) (-0.35 to -0.20) | \( <0.001 \) | n/a  | 0.05 | \( -0.37 \) (-0.44 to -0.30) | \( <0.001 \) | n/a  | 0.1 |
| Autumn                 | \( -0.04 \) (-0.11 to 0.03) | 0.30 | 0 | \( 0.056 \) (-0.003 to 0.14) | 0.06 | 0 |

BMI = body mass index; CI = confidence interval; D = diopters; DBP = diastolic blood pressure; IOPcc = corneal-compensated intraocular pressure; IOPg = Goldmann-correlated intraocular pressure; n/a = not available; SBP = systolic blood pressure.

*For continuous covariates, standardized coefficient represents change in IOP (mmHg) per standard deviation of the covariate. \( P < 0.001 \) shown in bold. BMI between 20 and 40 kg/m² was analyzed.

The effects of smoking and ethnicity were consistent with other studies. Smoking is a well-documented risk factor for open-angle glaucoma, and ethnicity is associated with the prevalence of glaucoma. The results of this study support the possibility that the effect of smoking and ethnicity on IOP is mediated by corneal biomechanics.

### Age

Studies in the past have found inconsistent relationships of IOP with age in regression analyses, ranging from a positive association,7–10,18,28 an inverse relationship,11,12 and no association.6,13,29 For subjects aged 40 to 69 years, this study found a positive relationship with IOP, which persisted after adjusting for confounders. The Beijing Eye study found IOP increasing up to age 60 to 64 years and decreasing thereafter to age 75 years.30 The EPIC-Norfolk Eye Study also found the same trend among women,18 and there is a hint of the same “inverted U” trend in our data as IOPg reaches a plateau at age 65 (Fig 1A), although there were no data beyond age 69 years. Corneal-compensated IOP continues to increase at age 65 years or more, and this trend mirrors the increasing prevalence of glaucoma with age. Age is one of the most important risk factors for open-angle glaucoma (OAG), and the results of this study support the possibility that the effect
could be mediated partly by higher IOP in older people. In sensitivity analysis using right eye IOP values, the association with age was less significant with IOPg ($P = 0.007$), although the direction of association remains. It was the introduction of SBP into the model that attenuated the effect of age on right eye IOPg.

The large size of this study allows us to further examine the relationship of age with IOP in different ethnic groups. The increase in both IOPg and IOPcc with age was greatest among those of mixed ethnicities, followed by blacks and whites. The trend among Chinese and "other" ethnicities was not clear, and this in part could be due to these 2 groups having relatively smaller numbers, and the size of the change in IOP per decade of age could inherently be small.

The trend of increase in OAG prevalence with age has been examined in 2 recently published meta-analyses, and both studies found Hispanics to have the steepest rate of increase in OAG cases with age.31,32 However, both studies also confirmed that the prevalence of OAG was actually highest among blacks, followed by Hispanics and Asians, and lowest among white subjects.

Although we cannot relate the observations of Hispanics to our study because they were not identified as a separate group, it seems that the trend in OAG prevalence found in recent studies mirrors our findings in ethnic differences in IOPcc. Elevated IOPcc could be a useful indicator of OAG risk.

**Sex**

We found IOP to be higher in men than in women after adjusting for confounders. This contrasts with several studies that found IOP to be higher in women than in men.2,8,10,19 or found no difference,5,9,13,30,40 but it is supported by 1 study that used noncontact tonometry.21 In addition, meta-analyses of the prevalence of OAG have consistently shown men to be 1.36 to 1.37 times more likely than women to have OAG after adjusting for age, race, and study design.32,33 A possible reason other studies found different associations with IOP could be their smaller sample sizes, which could be underpowered to detect the difference, although there could be true differences in the populations surveyed.

**Blood Pressure**

Systolic blood pressure was the strongest determinant of IOP in this study, which is in agreement with most other studies reporting similar analyses.3,5,10,13,18,30 Other hemodynamic factors such as DBP2,13,30 and pulse rate2,10,13 were also associated with IOP in this study and previous publications. This reflects the dynamic role they have in aqueous production, which is mediated by ciliary blood flow and ciliary oxygen delivery, as well as in regulating aqueous outflow by their effects on episcleral venous pressure and pulse-dependent motion of the trabecular meshwork.34

**Body Mass Index**

In the univariable regression model, IOPg and IOPcc had a positive relationship with BMI, but after adjusting for confounders, they were associated with lower BMI (IOPg $P = 0.009$, IOPcc $P < 0.001$). This contrasts with all previous studies that found IOP to be associated with higher BMI,2,8,10,11,21,35 even if not statistically significant.8 It was the introduction of SBP into the model that switched the direction of association, indicating that SBP was a major confounder in the relationship between IOP and BMI in this study. In the sensitivity analysis using right eye IOP values, a similar attenuation effect was found, where BMI was positively associated with both IOPg and IOPcc in the univariable model ($P < 0.0001$), but the association was no longer significant in the multivariable model (IOPg $0.005$ mmHg, 95% CI, $–0.0005$ to 0.011 mmHg, $P = 0.073$; IOPcc $–0.005$ mmHg, 95% CI, $–0.02$ to 0.001 mmHg, $P = 0.11$). Again, it was the introduction of SBP (IOPg) and SBP and pulse rate (IOPcc) into the model that negated the association with BMI.

**Refractive Error**

Refractive error was the second most important predictor of both IOPg and IOPcc. Higher IOP was associated with increasing myopic refraction, which persisted even if pseudophakic participants were excluded (results not shown). This corroborates other studies that reported refractive error2,8,13,18,30 and studies that reported IOP increases with longer axial length.2,12,18 Myopia is a well-established risk factor for glaucoma,36–38 although the exact mechanism is unknown. The current results support, at least in part, an IOP-related mechanism.

**Season**

The effect of seasonality on IOP has been shown in longitudinal studies in Sweden41 and Shanghai,44 and among ocular hypertensives in Pakistan41 and the United States, as well as cross-sectional population studies in the United States2 and Barbados.10 These studies all demonstrated higher IOP in the colder months than the warmer months. Our IOPg and IOPcc data also corroborated these findings and showed that the trend is not restricted to applanation tonometry. Temperature, hydration, and daylight hours41,42 all have been suggested as possible explanations.
The 6 centers are widely distributed geographically within the United Kingdom, covering the midlands (Birmingham), northern England (Liverpool, Sheffield), Wales (Swansea), and Greater London (Hounslow, Croydon). They each contributed different proportions of subjects to the study cohort, with Swansea accounting for only 0.4% of the study. Participants in these centers also differed in many physical characteristics. Initial analysis of variance analysis showed IOPg to be similar between the centers, but IOPcc was significantly higher in Birmingham than all centers except Swansea. The findings remain in multivariable regression, in which IOPg was similar between the baseline center of Croydon and all other centers, and IOPcc was significantly lower in Birmingham than Croydon. Sensitivity analysis was performed by excluding data from Birmingham, and the main findings of differential associations of IOPg and IOPcc with the physical characteristics remained.

Study Strengths and Limitations
The strength of this study is the large sample size of 110,573 participants, which is 19 to 55 times larger than to most

**Figure 3.** Variation of Goldmann-correlated intraocular pressure (IOPg) and corneal-compensated intraocular pressure (IOPcc) with age for each ethnic group. The error bars represent the 95% confidence intervals (CIs).
population studies that reported associations with IOP. This allows weaker associations to be shown. However, the price of achieving such a large sample size efficiently is a low study response rate (5.5%). Together with the volunteer nature and the relatively young age group of <70 years, the study participants are likely to be a healthier sample of the UK population, and therefore are unrepresentative of the general population. Nevertheless, a diverse range of exposures and characteristics are likely to have been captured in such a large study, such that the results reported can still be applicable to other populations with a different distribution of these exposures. The self-reported nature of diabetes, glaucoma, and macular degeneration could affect the observed associations because of recall and misclassification errors. However, more advanced diseases were likely to be included and to bias the outcome by increasing the likelihood of an association being found.

Another limitation of this study is that only 1 IOP measurement was made for each participant, rendering the data more prone to measurement error than if multiple measurements were taken. However, it is reassuring that the standard deviation of 3.8 to 3.9 mmHg for IOP in this study is comparable to 3.7 mmHg reported in another population study using the ORA, which used an average of 3 measurements.

In conclusion, this is the largest study of associations of IOP with demographic and systemic factors to date. It has confirmed many known associations and demonstrated previously unknown differential associations with IOPg and IOPcc. The findings provide insight into the relationship between corneal biomechanics with systemic factors and their effect on IOP measurements.

References

1. de Voogd S, Ikram MK, Wolfs RC, et al. Incidence of open-angle glaucoma in a general elderly population: the Rotterdam Study. Ophthalmology 2005;112:1487–93.

2. Leske MC, Heijl A, Hyman L, et al. Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 2007;114:1965–72.

3. Carbonaro F, Andrew T, Mackey DA, et al. Heritability of intraocular pressure: a classical twin study. Br J Ophthalmol 2008;92:1125–8.

4. Chang TC, Congdon NG, Wojciechowski R, et al. Determinants and heritability of intraocular pressure and cup-to-disc ratio in a defined older population. Ophthalmology 2005;112:1186–91.

5. Weih LM, Makesh BN, McCarty CA, et al. Association of demographic, familial, medical, and ocular factors with intraocular pressure. Arch Ophthalmol 2001;119:875–80.

6. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: the Liwan eye study. Am J Ophthalmol 2011;152:454–462 e1.

7. Memarzadeh F, Ying-Lai M, Azen SP, et al. Associations with intraocular pressure in Latinos: the Los Angeles Latino Eye Study. Am J Ophthalmol 2008;146:69–76.

8. Klein BE, Klein R, Linton KL. Intraocular pressure in an American community. The Beaver Dam Eye Study. Invest Ophthalmol Vis Sci 1992;33:2224–8.

9. Foster PJ, Machin D, Wong T-Y, et al. Determinants of intraocular pressure and its association with glaucomatous optic neuropathy in Chinese Singaporeans: the Tanjong Pagar Study. Invest Ophthalmol Vis Sci 2003;44:3885–91.

10. Wu SY, Leske MC. Associations with intraocular pressure in the Barbados Eye Study. Arch Ophthalmol 1997;115:1572–6.

11. Kawase K, Tomidokoro A, Araie M, et al. Ocular and systemic factors related to intraocular pressure in Japanese adults: the Tajimi study. Br J Ophthalmol 2008;92:1175–9.

12. Tomoyose E, Higa A, Sakai H, et al. Intraocular pressure and related systemic and ocular biometric factors in a population-based study in Japan: the Kumejima study. Am J Ophthalmol 2010;150:279–86.

13. Jonas JB, Nangia V, Matin A, et al. Intraocular pressure and associated factors: the central India eye and medical study. J Glaucoma 2011;20:405–9.

14. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measurements: a review and meta-analysis approach. Surv Ophthalmol 2000;44:367–408.

15. Liu J, Roberts CJ. Influence of corneal biomechanical properties on intraocular pressure measurement: quantitative analysis. J Cataract Refract Surg 2005;31:146–55.

16. Medeiros FA, Weinreb RN. Evaluation of the influence of corneal biomechanical properties on intraocular pressure measurements using the ocular response analyzer. J Glaucoma 2006;15:364–70.

17. Luce D. Methodology for cornea compensated IOP and corneal resistance factor for the Reichert Ocular Response Analyzer. Invest Ophthalmol Vis Sci 2006;47. E-Abstract 2266.

18. Foster PJ, Broadway DC, Garway-Heath DF, et al. Intraocular pressure and corneal biomechanics in an adult British population: the EPIC-Norfolk eye study. Invest Ophthalmol Vis Sci 2011;52:8179–85.

19. Yazgan S, Celik U, Kaldırım H, et al. Evaluation of the relationship between corneal biomechanic and HbA1C levels in type 2 diabetes patients. Clin Ophthalmol 2014;8:1549–53.

20. Lee AJ, Rochtchina E, Wang JJ, et al. Does smoking affect intraocular pressure? Findings from the Blue Mountains Eye Study. J Glaucoma 2003;12:209–12.

21. Hoehn R, Mirshahi A, Hoffmann EM, et al. Distribution of intraocular pressure and its association with ocular features and cardiovascular risk factors: the Gutenberg Health Study. Ophthalmology 2013;120:961–8.

22. Nangia V, Jonas JB, Matin A, et al. Body height and ocular dimensions in the adult population in rural Central India. The
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Abbreviations and Acronyms:

- **BMI** = body mass index
- **CCT** = central corneal thickness
- **CI** = confidence interval
- **DBP** = diastolic blood pressure
- **IOP** = intraocular pressure
- **IOPcc** = corneal-compensated intraocular pressure
- **IOPg** = Goldmann-correlated intraocular pressure
- **OAG** = open-angle glaucoma
- **ORA** = Ocular Response Analyzer
- **SBP** = systolic blood pressure

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Central India Eye and Medical Study. Graefes Arch Clin Exp Ophthalmol 2010;248:1657–66.

23. Wong TY, Foster PJ, Johnson GI, et al. The relationship between ocular dimensions and refraction with adult stature: the Tanjong Pagar Survey. Invest Ophthalmol Vis Sci 2001;42:1237–42.

24. Kaji Y. Prevention of diabetic keratopathy. Br J Ophthalmol 2005;89:254–5.

25. Galor A, Lee DJ. Effects of smoking on ocular health. Curr Opin Ophthalmol 2011;22:477–82.

26. Brandt JD, Beiser JA, Kass MA, et al. Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS). Ophthalmology 2001;108:1779–88.

27. Detry-Morel M, Jamart J, Hautenuaeven F, et al. Comparison of the corneal biomechanical properties with the Ocular Response Analyzer (ORA) in African and Caucasian normal subjects and patients with glaucoma. Acta Ophthalmol 2012;90:e118–24.

28. Rochtchina E, Mitchell P, Wang JJ. Personal fees

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