The Accuracy and Clinical Application of Predictive Models for Primary Open-Angle Glaucoma in Ocular Hypertensive Individuals

The Ocular Hypertension Treatment Study Group and the European Glaucoma Prevention Study Group

Objective: This report compares the accuracy of 3 prediction models for the development of primary open-angle glaucoma (POAG). The models differ primarily in their handling of these eye-specific variables: intraocular pressure (IOP), central corneal thickness (CCT), vertical cup-to-disc ratio (VCD), and visual field pattern standard deviation (PSD). The "means" model includes age and the means of right and left eyes; the "means plus asymmetry" model includes age, the means of right and left eyes as well as the absolute difference between eyes for eye-specific variables; and the "worse" eye model includes age and values from the eye at higher risk for developing POAG.

Design: This report uses data from the observation group of the Ocular Hypertension Treatment Study (OHTS) and the placebo group of the European Glaucoma Prevention Study (EGPS) who have complete data on both eyes at baseline. Performance of the prediction models is assessed using the c-statistic, calibration chi-square, and Pearson correlation coefficient.

Participants: The OHTS observation group (n = 717; 6.7 years median follow-up) and the EGPS placebo group (n = 324; 4.9 years median follow-up).

Testing: Baseline data included demographic characteristics, medical history, ocular examination, visual fields, and optic disc photographs.

Main Outcome Measures: Development of reproducible visual field abnormality or optic disc deterioration as determined by masked readers and attributed to POAG by a masked end point committee.

Results: Baseline factors that were statistically significant in all predictive models were age, IOP, CCT, VCD, and PSD. Also, statistically significant were baseline asymmetry in IOP and asymmetry in VCD. The c-statistics for the "means" model, "means plus asymmetry" model, and "worse" eye model were 0.74, 0.77, and 0.75, respectively. The calibration chi-square values were 7.32, 11.19, and 1.81, respectively. Correlation coefficients between risk estimates calculated by different models ranged from 0.94 to 0.98.

Conclusions: The high agreement between the risk estimates from 3 different predictive models for the development of POAG suggests little difference in their statistical or clinical performance. The predictive model that uses the means of both eyes for eye-specific variables is the simplest to use and the most robust to measurement variability and error.

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The Ocular Hypertension Treatment Study (OHTS) published a multivariate prediction model to calculate the 5-year risk for developing primary open-angle glaucoma (POAG) in ocular hypertensive individuals. Factors used to calculate risk in this prediction model included older age and several baseline eye-specific measures including vertical cup-to-disc ratio (VCD), intraocular pressure (IOP), pattern standard deviation (PSD), and central corneal thickness (CCT).[1] This prediction model has been replicated in an independent US study[2] as well as in the European Glaucoma Prevention Study (EGPS)[3] and further refined using the pooled OHTS and EGPS samples.[4] The OHTS/EGPS prediction model has demonstrated good predictive accuracy across the range of risk among participants in these studies.[4]

The OHTS/EGPS prediction model uses the means of the right and left eyes of each participant to calculate eye-specific predictive factors. Advantages of using the means of right and left eyes include the use of all relevant data from both eyes of each participant and the reduction of measurement variability. The disadvantages of using the means of both eyes include the loss of predictive accuracy from information unique to each eye and from the differences between the eyes. This report assesses whether the accuracy and clinical application of the OHTS/EGPS predictive model based on the means of right and left eyes, "means model," as described, is equal, superior, or inferior to predictive models that includes eye-specific information: (1) a "means plus asymmetry" model, which includes the

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means of both eyes as well as the absolute differences between right and left eyes for eye-specific variables; and (2) a "worse" eye model which includes baseline information only from the eye at higher risk of developing POAG.[4]

Methods

The OHTS[5] and the EGPS[6] are both randomized clinical trials that tested the safety and efficacy of topical ocular hypotensive medication in delaying or preventing the development of POAG in individuals with ocular hypertension. The OHTS and the EGPS protocols are described in their respective baseline design papers.[7,8] The OHTS protocol is also available online at https://vrcc.wustl.edu (accessed August 1, 2006). The protocol is compliant with the Health Insurance Portability and Accountability Act of 1996 and was approved by the institutional review boards of all participating clinics and resource centers. The OHTS registration number is NCT00000125 and can be found at www.clinicaltrials.gov (accessed March 18, 2008).

In the OHTS and the EGPS, participants were randomized in equal proportions to a control or medication group. In the OHTS, the control group was an observation group that received no ocular hypotensive medication or placebo. In the EGPS, the control group was a placebo group, which received the diluent for the medication. This report uses data from participants in the OHTS and the EGPS who were randomized to the control group and did not receive active ocular hypotensive treatment. Data from these control groups provide information on the relationship of baseline factors to the true, natural (untreated) history of the risk of developing POAG.

The analysis dataset for this report includes baseline and POAG outcomes data for OHTS observation participants from the start of randomization in February 1994 to June 2002 (median follow-up of 6.7 years), and EGPS placebo group participants from the start of randomization in January 1997 to May 2004 (median follow-up of 4.9 years). Only participants with complete baseline data for both eyes were included in this report so that the same sample of participants would be used to compare the performance of the different predictive models (OHTS, n = 717; EGPS, n = 324). In the section that follows, we briefly describe the protocol for the measurement of eye-specific factors and POAG end points for OHTS and EGPS. Procedures for the resolution of differences between the OHTS and EGPS protocols are described in detail in a previous publication.[4]

1. Intraocular pressure measurements by Goldman tonometry. In the OHTS, the mean IOP for each eye was calculated using 2–3 IOP measurements from each of the 2 qualifying visits and the randomization visit. Thus, the mean pressure for each eye was calculated from 6–9 IOP measurements and the 2 means were averaged to create a new baseline IOP. In the EGPS, the mean IOP for each eye was calculated using 2–3 measurements per eye at the eligibility visit and 1 measurement per eye at the 6-month follow-up visit. Thus, the pressure for each eye was calculated from 3–4 IOP measurements and the means for the 2 eyes were averaged.
2. The CCT measurements were made using the same protocol and same model pachymeter (DGH Pachette Model 500). The CCT for each eye was the mean of 5 measurements taken of each eye completed on a single visit and the means for the 2 eyes were averaged.
3. For the optic disc, the VCD was estimated by masked readers from stereoscopic slides taken by certified study photographers.
4. In the OHTS, all visual fields were assessed using full-threshold white on white Humphrey standard program 30-2. In the EGPS, visual fields were assessed using Humphrey 30-2 visual fields for 80% of the participants and Octopus 32 visual fields for 20% of the participants. We converted the baseline Octopus mean defect to Humphrey mean deviation by changing the sign and the loss variance to PSD by taking the square root of the loss variance.[9] The baseline visual field score for each eye is the mean of 2–3 visual fields completed at 2–3 visits and the means for the 2 eyes were averaged.

In both the OHTS and the EGPS, the date of onset for POAG is the date of the first of 3 consecutive abnormal visual fields or the first optic disc photograph that masked readers classified as meeting the definition for change and that was subsequently attributed to POAG by a masked end point committee. In OHTS, a technically acceptable visual field was considered abnormal if $P<5\%$ for the corrected PSD or if the glaucoma hemifield test was outside normal limits by STATPAC 2.[7] In EGPS, a visual field was considered abnormal if $\geq$3 adjacent points were reduced by $\geq$5 dB from baseline, or were reduced by $\geq$2 adjacent points differ $\geq$10 dB from baseline.[8]

Baseline demographic and clinical information in both the OHTS and EGPS was collected on each participant before randomization, except for CCT measurements, which were performed 1–3 years after randomization.

Statistical Analysis

The prediction models for the development of POAG differ in their handling of eye-specific measures (IOP, CCT, VCD, and PSD). Eye-specific variables in the "means" model were the means of right and the left eyes of each participant. Eye-specific variables in the "means plus asymmetry" model were the means of right and left eyes and their absolute differences for each participant.

Eye-specific variables in the "worse" eye model first required that we identify which eye is "worse" based on 4 eye-specific factors: IOP, CCT, VCD, and PSD. No one factor captured the risk status of an eye. The risk of each eye was calculated using the OHTS/EGPS multivariate prediction model and the eye with the higher risk was selected as the "worse" eye. The 5-year risk of developing POAG of each eye could range from 0.00 to 1.00 or 0% to 100%. If both eyes had equal (2 decimal places) risk of developing POAG, 1 eye was selected randomly. Because the OHTS/EGPS multivariate model, which was used to calculate the risk for the worse eye, was developed from this same sample of participants, statistical circularity is introduced. This statistical circularity could increase the apparent accuracy of the "worse" eye model.

Multivariate Cox proportional hazards models were used to calculate hazard ratios for baseline factors predictive for the development of POAG for each of the different models, the "means" model, the "means plus asymmetry" model, and the "worse eye" model. The accuracy of each prediction model in discriminating between participants who did or did not develop POAG was assessed using the c-statistic.[10] The c-statistic ranges from 0.50 (chance) to 1.00 (perfect agreement). The rate of over- or underestimation of the actual number of POAG events compared with the observed number of POAG events was calculated for each prediction model using the calibration chi-square.[11] The calibration chi-square divides the sample into 10 levels of risk; for each decile, the predicted risk of developing POAG is compared with the observed proportion of participants developing POAG. A calibration chi-square of $\leq$20.00 indicates good agreement between the predicted and the observed event rate.[11]

The agreement between the risk estimates calculated for each participant by the 3 predictive models was assessed using Pearson correlation coefficients and Spearman rank-order correlation coefficients.

The clinical application of each model was assessed by examining the stability of the risk estimates. In both OHTS and EGPS, an emphasis was placed on measurement reliability. For instance, 2 to 9 measurements of IOP were performed per eye to get a stable estimate of baseline IOP. However, 1 IOP measurement per eye is typically performed in clinical practice. Thus, to investigate the stability of the "means plus asymmetry" model in a clinical setting, we calculated baseline IOP and asymmetry of IOP using only the first of 2–9 IOP measurements per eye. We compared the results of the "means plus asymmetry" model based on 2–9 IOP measurements per eye with the same model based on 1 IOP measurement per eye. A similar analysis with VCD could not be conducted because only 1 grading of VCD is available at baseline in OHTS and in EGPS.

The clinical application of the "worse" eye model was assessed by examining whether the same eye was selected the "worse" eye at baseline and at 12 months. We calculated the risk estimate for right and left eyes using data at baseline and recalculated the risk estimate again using data at 12 months. We determined whether the same eye was designated the "worse" eye at both the baseline and at the 12-month follow-up visit. This analysis was conducted using data from the OHTS observation group because all data on predictive factors were available for both eyes of all participants at both baseline and 12 months.

Results

Baseline demographic and clinical features of participants who did or did not develop POAG in the OHTS observation group and the EGPS placebo group are reported in Table 1.

"Means" Prediction Model

In the "means" prediction model, which used the means of right and left eyes for eye-specific variables, statistically significant baseline predictors for the development of POAG in the multivariate Cox proportional hazards model included baseline age, mean IOP, mean CCT, mean VCD, and mean PSD.

"Means Plus Asymmetry" Prediction Model

The range and magnitude of asymmetry between eyes in IOP, CCT, VCD and PSD were modest (Tables 1 and 2). Twelve percent (121 of 1041) of the participants had an IOP difference between eyes at baseline of >3 mmHg (Table 2). Six percent (64 of 1041) of the participants had a difference between eyes at baseline of >0.2 in VCD.

In the "means plus asymmetry" prediction model, statistically significant baseline predictors for the development of POAG in the multivariate Cox proportional hazards model included baseline age, mean IOP, mean CCT, mean VCD, mean PSD, the absolute difference between eyes in IOP, and the absolute difference between eyes in VCD (Table 3) . The absolute differences between eyes in CCT and PSD were not statistically significant in the prediction model.

When the "means plus asymmetry" model was recalculated using only the first of 2–9 IOP measurements per eye to mimic clinical practice, baseline IOP remained statistically significant in univariate and multivariate Cox proportional hazards models. However, the absolute difference in IOP between eyes was no longer statistically significant (hazard ratio of 0.99; 95% confidence limits, 0.90–1.10; $P = 0.94$) and was not selected for inclusion in the multivariate model (Table 3). A parallel analysis on VCD could not be performed because only 1 assessment of VCD was available at baseline.

"Worse Eye" Prediction Model

The selection of the "worse" eye proved difficult because the eyes of many participants had nearly identical risk estimates at baseline. Nineteen percent (194 of 1041) of the participants had the same risk score in both eyes to 2 decimal places. Of the 847 participants with an eye that could be defined as "worse," 90% (763 of 847) had a difference in risk between eyes of <0.10, that is, a 5-year risk of developing POAG of 5% in 1 eye versus 15% in the fellow eye. Only 2% (17 of 847) of the participants had a difference in risk between eyes of ≥0.20.

Primary open-angle glaucoma developed in 11.0% (94 eyes of 847 participants) of the "worse" eyes at baseline, in 6.0% (51 eyes of 847 participants) of the "better" eyes and in 8.2% (16 eyes of 194 participants) of the eyes that had the same risk estimate.

In the "worse eye" prediction model, statistically significant baseline predictors for the development of POAG in the multivariate Cox

Table 1. Comparison of Baseline Risk Factors for Participants Who Did and Did Not Develop Primary Open-Angle Glaucoma

	Develop POAG						All		
	No			*Yes*					
	n	*Mean*	*SD*	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*
Age	898	55.8	9.7	143	59.18	9.2	1041	56.22	9.7
Mean OU IOP	898	24.2	2.3	143	25.14	2.7	1041	24.33	2.4
Mean OU CCT	898	577.6	36.3	143	552.1	35.8	1041	574.1	37.3
Mean OU VCD	898	0.4	0.2	143	0.45	0.2	1041	0.37	0.2
Mean OU PSD	898	1.93	0.4	143	2.02	0.3	1041	1.94	0.4
Absolute difference between eyes, IOP	898	1.33	1.3	143	1.93	1.7	1041	1.41	1.4
Absolute difference between eyes, CCT	897	8.69	7.6	142	8.57	7.9	1039	8.67	7.7
Absolute difference between eyes, VCD	898	0.07	0.1	143	0.11	0.1	1041	0.08	0.1
Absolute difference between eyes, PSD	897	0.25	0.3	141	0.28	0.2	1038	0.25	0.3
Worse eye IOP	898	24.6	2.5	143	25.71	3.0	1041	24.71	2.6
Worse eye CCT	898	575.4	36.8	143	550.2	36.8	1041	572.0	37.8
Worse eye VCD	898	0.38	0.2	143	0.49	0.2	1041	0.39	0.2
Worse eye PSD	898	2.00	0.5	143	2.10	0.4	1041	2.02	0.5

CCT = central corneal thickness; IOP = intraocular pressure; OU = both eyes; POAG = primary open-angle glaucoma; PSD = pattern standard deviation; SD = standard deviation; VCD = vertical cup-to-disc ratio.

Table 2. Distribution of Absolute Differences between Right and Left Eyes for Intraocular Pressure, Central Corneal Thickness, Vertical Cup-to-Disc Ratio, Pattern Standard Deviation, and the Development of Primary Open-Angle Glaucoma in 1 or Both Eyes

			At POAG End Point in 1 or Both Eyes?			
			No		*Yes*	
	N	**%**	*n*	*%*	*n*	*%*
Absolute difference in IOP						
≤2	793	76.2	701	88.4	92	11.6
>2–3	127	12.2	109	85.8	18	14.2
>3–4	69	6.6	53	76.8	16	23.2
>4	52	5.0	35	67.3	17	32.7
Absolute difference in CCT						
≤10	699	67.3	607	86.8	92	13.2
>10–15	172	16.6	146	84.9	26	15.1
>15–20	80	7.7	66	82.5	14	17.5
>20	88	8.5	78	88.6	10	11.4
Absolute difference in VCD						
≤0.1	732	70.3	652	89.1	80	10.9
>0.1–0.2	245	23.5	197	80.4	48	19.6
>0.2–0.3	42	4.0	35	83.3	7	16.7
>0.3	22	2.1	14	63.6	8	36.4
Absolute difference in PSD						
≤2	1034	99.6	893	86.3	141	13.6
>2–3	2	0.2	2	100.0	.	.
>4	2	0.2	2	100.0	.	.

CCT = central corneal thickness; IOP = intraocular pressure; POAG = primary open-angle glaucoma; PSD = pattern standard deviation; VCD = vertical cup-to-disc ratio.

proportional hazards model included baseline age, IOP, CCT, VCD, and PSD for the worse eye as defined by the risk model (Table 3).

The stability of the "worse" eye model was assessed in the OHTS observation group by determining whether the same eye defined as "worse" at baseline continued to be the "worse" eye at 12 months. Of the 649 OHTS observation participants, 81% (524 of 649) had an eye that could be designated the "worse" eye. In these 524 eyes that were defined as the "worse" eye at baseline, 22% (116 of 524) were defined as the "better" eye at 12 months and 10% (55 of 524) were identical in risk (to 2 decimal places) as the fellow eye at 12 months.

Comparison of Prediction Models for Primary Open-Angle Glaucoma

The c-statistics for concordance between observed and predicted development of POAG for the "means" model, the "means plus asymmetry" model, and "worse eye" model were 0.74, 0.77, and

Table 3. Hazard Ratios and 95% Confidence Intervals for Baseline Predictors for the Development of Primary Open-Angle Glaucoma in the "Means" Model, the "Means Plus Asymmetry" Model, and the "Worse Eye" Model

Hazard Ratio and 95% CI	**5-Variable Model (n = 1041)**	**5-Variable Model + Asymmetry in IOP and VCD (n = 1041)**	**"Worse" Eye Model**
Age decade	1.27 (1.07–1.51)	1.27 (1.06–1.52)	1.29 (1.09–1.54)
IOP*	1.11 (1.04–1.19)	1.10 (1.03–1.18)	1.12 (1.05–1.19)
Mean CCT per 40-micron decrease	1.98 (1.64–2.40)	1.91 (1.58–2.31)	1.92 (1.59–2.31)
VCD per 0.1	1.22 (1.11–1.34)	1.24 (1.12–1.37)	1.27 (1.16–1.39)
PSD per 0.2	1.17 (1.06–1.29)	1.18 (1.07–1.31)	1.13 (1.07–1.20)
Absolute difference IOP		1.13 (1.03–1.24)	N/A
Absolute difference CCT per 40 micron decrease		N/A	N/A
Absolute difference VCD per 0.1		1.48 (1.25–1.76)	N/A
Absolute difference PSD per 0.2		N/A	N/A
C-statistic with 95% CI	0.74 (0.70–0.79)	0.77 (0.72–0.81)	0.75 (0.71–0.80)
Calibration chi-square	7.32	11.19	1.81

CI = confidence intervals; CCT = central corneal thickness; IOP = intraocular pressure; POAG = primary open-angle glaucoma; PSD = pattern standard deviation; VCD = vertical cup-to-disc ratio.
*The IOP is the mean of the initial IOP per eye for the participant at the baseline visit.

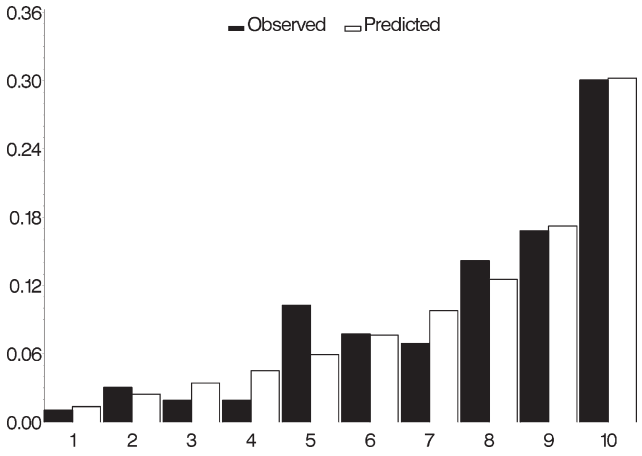

Figure 1. Comparison of observed and predicted 5-year incidence of POAG for the OHTS-EGPS pooled "mean" model. The *x*-axis refers to the predicted probability of risk divided into 10 groups of approximately 90 participants each. EGPS = European Glaucoma Prevention Study; OHTS = Ocular Hypertension Treatment Study; POAG = primary open-angle glaucoma.

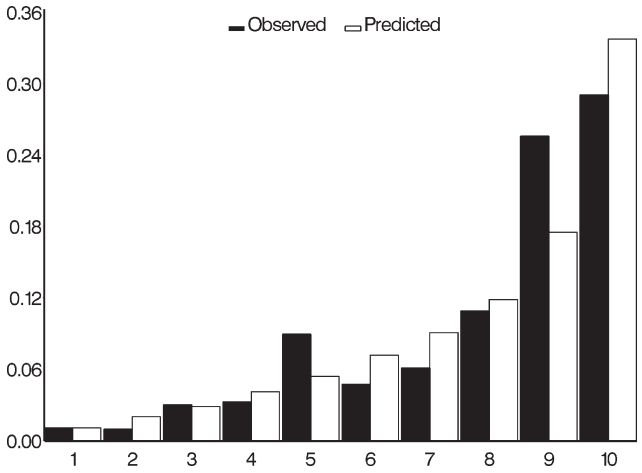

Figure 2. Comparison of observed and predicted 5-year incidence of POAG for the OHTS-EGPS pooled "asymmetry" model. The *x*-axis refers to the predicted probability of risk divided into 10 groups of approximately 90 participants each. EGPS = European Glaucoma Prevention Study; OHTS = Ocular Hypertension Treatment Study; POAG = primary open-angle glaucoma.

0.75 respectively (higher values indicate better concordance). The calibration chi-squares for "means" model, the "means plus asymmetry" model and "worse eye" model were 7.32, 11.19, and 1.81, respectively, where lower values indicate less over- or underestimation (Figs 1, 2, and 3).

The Pearson correlation coefficient for the risk of developing POAG calculated by each model for each participant were high, ranging from 0.94 to 0.98 and the Spearman rank order correlation coefficient had the identical range.

Discussion

The OHTS/EGPS collaborative prediction model uses 5 baseline factors—age, IOP, CCT, VCD, and PSD—to predict the 5-year risk of developing POAG. All eye-specific factors in this model were calculated as the means of right and left eyes; thus, information about differences between eyes was not used.[4] We undertook this reanalysis to determine if the predictive accuracy of the OHTS/EGPS prediction model could be improved by incorporating eye-specific information. The prognostic value of asymmetry between right and left eyes for the development of POAG in ocular hypertension has been reported for IOP,[12] cup-to disc ratio,[3,13] and visual field threshold.[12] In addition, greater asymmetry between eyes of established glaucoma patients compared with controls has been reported for many ocular measures including disc parameters,[14–18] IOP,[19] contrast sensitivity,[20] visual evoked response,[21] and blood velocity.[22] These studies suggest that asymmetry between eyes may be a sentinel for incipient glaucoma and/or a marker for established glaucoma.

We found that the performance of the OHTS/EGPS prediction model based on the means of right and left eyes for eye-specific variables was remarkably comparable with prediction models that included additional information on baseline differences between eyes. The correlation coefficients for risk scores of each participant calculated from the "means," "means plus asymmetry," and "worse" eye models ranged between 0.94 and 0.98 and were statistically equivalent. The 3 predictive models for the development of POAG identified the same 5 baseline risk factors: age, IOP, CCT, VCD, and PSD. In addition, the "means plus asymmetry" model identified larger baseline asymmetry in IOP and larger asymmetry in VCD as statistically significant predictors for the development of POAG. In a given participant, the risk of developing POAG increased 13% for every 1 mmHg an eye was higher than the fellow eye. The risk of developing POAG also increased almost 50% for every 0.1 difference between eyes in cup-to-disc ratio. Baseline asym-

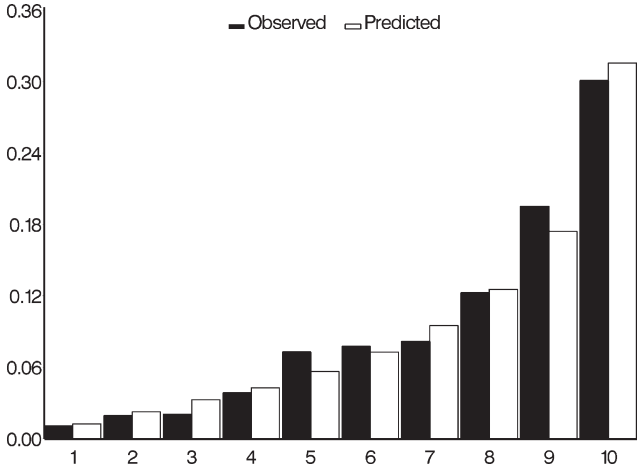

Figure 3. Comparison of observed and predicted 5-year incidence of POAG for the OHTS-EGPS pooled "worse eye" model. The *x*-axis refers to the predicted probability of risk divided into 10 groups of approximately 90 participants each. EGPS = European Glaucoma Prevention Study; OHTS = Ocular Hypertension Treatment Study; POAG = primary open-angle glaucoma.

metry in VCD was 0.1±0.1 SD among participants who developed POAG and 0.07±0.1 SD among participants who did not. It should be noted that the cup-to-disc ratio was not adjusted for optic disc area because it was not assessed in either OHTS or EGPS.

The predictive accuracy of all 3 models was good. The "worse" eye model seems to have the best predictive accuracy based on its low (good) calibration chi-square (1.81) compared with 11.19 and 7.32 for the "means plus asymmetry" model and the "means" model, respectively. However, the good predictive accuracy of the "worse" eye model may be partly due to statistical circularity. The "worse" eye was selected using the OHTS/EGPS prediction model, which was developed from the same sample. To some extent, the worse eye model becomes a self-fulfilling prophecy and may not perform equally well in an independent sample.

We examined whether the 3 predictive models would perform equally in a clinical setting. The "means" model, which has 5 factors, was the simplest to calculate and yielded the most stable estimate of risk. The "means plus asymmetry" model, which has 7 factors, requires calculation of the means of 4 eye-specific variables and the absolute differences in IOP and VCD. Reliable assessment of asymmetry in IOP and VCD is critical because measurement variability can easily obscure or conflate the true magnitude of asymmetry and result in erroneous calculations of risk. The range of IOP asymmetry was small with 76% of the participants having IOP asymmetry of ≤2 mmHg and 70% having VCD asymmetry of ≤0.1. When we reran the "means plus asymmetry" prediction model using only the first of 6–9 IOP measurements per eye to mimic the clinical setting (rather than the mean of 6–9 IOP measurements per eye as done in this study), IOP asymmetry was not statistically significant. We were unable to evaluate the impact of variability in cup-to-disc estimates because only 1 grading by trained readers using stereophotographs was performed in the OHTS and the EGPS. However, numerous studies have reported differences of ≥0.2 disc diameters among skilled graders in 13%–19% of the readings of VCD gradings from optic disc photographs.[23–26] These studies suggest that variability in the clinical evaluation of VCD could reduce the reliability of the risk estimate.

We encountered an unexpected limitation in the application of the "worse" eye model in this study. The "worse" eye model requires calculation of risk for each eye using IOP, CCT, PSD, and VCD and then the selection of the eye with the higher risk. No one variable could be used to identify the "worse" eye. Only 2% (17 of 847) of the participants in this study were found to have a difference between eyes of ≥20% in the 5-year risk of developing POAG. The application of the "worse" eye prediction model in clinical practice may be limited by the fact many ocular hypertensive individuals may not have an eye that is materially "worse" at baseline. Thus, advantages of the "worse" eye model over the "means" prediction model are not clear.

The OHTS/EGPS prediction model is among the first ophthalmic models to be developed and confirmed in a large, independent sample. As new information about risk factors emerge, the prediction model for the development of POAG will be further refined. We evaluated whether adding asymmetry between eyes at baseline or using the "worse" eye at baseline improved the OHTS/EGPS prediction model, which uses the means of right and left eyes for eye-specific variables. We conclude that the "means plus asymmetry" and "worse" eye prediction models were statistically equivalent to the "means" model, but that the "means" prediction model, which uses the mean of right and left eyes for eye-specific predictors, is the most robust to measurement variability and error.

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