

# Comparison of Rates of Fast and Catastrophic Visual Field Loss in Three Glaucoma Subtypes

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**PURPOSE.** To compare the distribution of visual field progression rates in three subgroups of glaucoma, being primary angle-closure glaucoma (PACG), POAG, and juvenile open-angle glaucoma (JOAG).

**METHODS.** We assessed glaucoma patients treated in an Indian tertiary care setting with at least four visual field assessments. We determined rates from a single eye of each of 525 patients using linear regression of the summary index mean deviation (MD) over time. The main outcome measures were the proportions of fast ( $<-1.0$  to  $-2.0$  dB/y) and catastrophic ( $<-2$  dB/y) visual field progression. Bootstrapped 95% CIs allowed comparison with published data from a large clinical cohort in Canada.

**RESULTS.** The combined proportion of fast and catastrophic progressors in our cohort was less than half that in the Canada dataset (2.3% vs. 5.8%), despite median progression rates differing by only 0.03 dB/y. PACG, POAG, and JOAG represented 45%, 32%, and 12% of our cohort, respectively. Baseline MD values were similarly distributed between these subtypes. All subtypes showed a similar shaped distribution for progression rates, with median progression rates of  $-0.03$ ,  $-0.05$ , and  $0.02$  dB/y for PACG, POAG, and JOAG, respectively. Combined proportions of fast and catastrophic progression rates did not significantly differ between subtypes.

**CONCLUSIONS.** Differences in fast and catastrophic visual field progression can exist despite only small changes in median progression rates, highlighting the importance of considering the full shape of the progression rate distribution when comparing the risk of devastating visual field loss.

Keywords: glaucoma, progression rate, visual field, juvenile open angle glaucoma, angle-closure glaucoma

Most patients with treated glaucoma show rates of visual field progression substantially slower than  $-1.0$  dB/y, although a small percentage will show more rapid rates.<sup>1-3</sup> A formal analysis of the distribution of progression rates may be useful for several reasons. Firstly, knowing the likelihood of particular progression rates in the population can be used to constrain rate estimates in individuals, thereby potentially improving their reliability.<sup>4</sup> Distributions of rates can also be used to calculate the proportion of patients likely to develop visual impairment in their lifetime.<sup>5</sup> An analysis of distributions can also highlight differences in visual outcomes for glaucoma patients in different geographic locations.<sup>6</sup> Distributional differences between populations likely reflect, at least in part, that the proportions of glaucoma subtypes and the presence of risk factors for rapid progression differ between populations. For example, rapid visual field progression was more common in a Swedish hospital-based cohort<sup>1</sup> than for similar cohorts from North America.<sup>2,3</sup> This may be due to the large proportion (38%) of the Swedish cohort that had pseudoexfoliation glaucoma, which is associated with increased progression rates.<sup>7</sup>

Although the distribution of visual field progression rates for several large datasets from North America and Europe have

been compared recently,<sup>6</sup> a greater proportion of glaucoma in Asia consists of angle-closure glaucoma.<sup>8</sup> A recent analysis found that average visual field progression rates in glaucoma subtypes, including angle-closure glaucoma, did not significantly differ after adjustment for other covariates (e.g., age, IOP, and central corneal thickness).<sup>9</sup> Such an analysis of average rates does not address potential differences in progression rate distributions between subtypes. Distributional differences may be important, particularly if they occur predominantly in the distributions' tails where rapid progressors lie. For example, an extended tail of fast progressors is seen in pseudoexfoliation glaucoma.<sup>7</sup> Furthermore, even if glaucoma subtype is not an independent risk factor, differences in progression rates between subtypes will likely still occur in a clinical setting due to differences in other risk factors that covary with glaucoma subtype. For example, pseudoexfoliative glaucoma was not found to be an independent risk factor for progression (i.e., when covariates were controlled for in a statistical study), but patients with pseudoexfoliation progressed more often than other subtypes (i.e., in a univariate analysis) in part because pseudoexfoliation is associated with significantly increased mean, peak, and IOP fluctuations relative to these other subtypes.<sup>9</sup>



The distribution of progression rates for one glaucoma subtype in India has recently been published. Gupta et al.<sup>10</sup> analyzed the distribution of visual field progression rates in a group of juvenile open-angle glaucoma (JOAG) patients from India, and predicted the likely incidence of perimetric blindness as such patients aged. These incidences were either higher or lower than estimates based on a comparison with published rates for POAG patients from other countries, highlighting the challenge of comparing rates between glaucoma subtypes when the subtypes are investigated in differently constructed studies (e.g., different inclusion and exclusion criteria, or different regression analysis methods) performed on geographically differing populations. Such challenges would be avoided through a comparison of visual field progression distributions for common glaucoma subtypes, taken from a single clinical database of patients from a similar geographic region and subject to a common standard of care.

Here, we analyzed the distribution of visual field progression rates in a cohort of glaucoma patients from a single tertiary care setting in India. We also compared progression rates for common glaucoma subtypes within the cohort, allowing us to test the hypothesis that predicted visual impairment in the common subgroup JOAG is greater than for those with POAG when compared within a similar geographic and clinical care setting, due to an anticipated increased residual life expectancy in the former. We also compared key distributions from our cohort with recently published data from a tertiary care clinical setting in Canada.<sup>3</sup>

## METHODS

Approval for this retrospective study was provided by the Ethics Committee of the All India Institute of Medical Sciences, Delhi. Glaucoma patients treated at Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS (a tertiary referral center) between December 2003 to December 2016 were identified. Although many thousands of glaucoma patients are seen for a consultation, the center only provides follow-up care for a small minority of patients. Approximately 600 glaucoma patients undergo a perimetric examination at the center each year, being 5% of the approximately 12,000 glaucoma patients seen annually. Patients with ocular co-morbidities, except for mild lenticular sclerosis, were excluded. We initially retrieved visual field series (Humphrey Field Analyser II 30-2 SITA Standard; Carl Zeiss Meditec, Dublin, CA, USA) for 1017 eyes for those patients, after excluding those patients with ocular co-morbidities other than mild lenticular sclerosis. Unreliable visual fields (i.e., those with fixation losses >20%, false-positive rates >15%, and false-negative rates >33%) were excluded from each series. We then excluded those who had no diagnostic category (62 eyes), and then those with three or fewer fields in the series (23 eyes). We then selected a single eye from each patient (at random, if records from both eyes were available [407 patients], based on a random number generation in Excel; Microsoft, Redmond, WA, USA) to form our cohort of 525 eyes. Glaucoma diagnosis was based on the diagnostic code given for the selected eye. We then performed an ordinary least squares regression on the summary index mean deviation (MD) over time for each patient in order to determine the rate of visual field progression in decibels per year. We applied previously described limits of “fast” (<-1.0 to -2.0 dB/y) and “catastrophic” (<-2.0 dB/y) visual field progression.<sup>3</sup> In addition to the progression rates, the following data were extracted from the visual field reports: age at first visual field test, sex, and baseline MD. Where available, pretreatment IOP was also extracted from patients' records.

## Glaucoma Subtypes

As we wished to analyze glaucoma as classified in a clinical setting, we identified glaucoma subtypes in our cohort based on the diagnostic codes entered on the visual field records rather than by applying a fixed set of inclusion or exclusion criterion. These codes were assigned by the glaucoma specialist treating the patient, and then entered by the perimetrist. Our approach also facilitated comparisons with recent distributional data from Canada, which similarly used a clinical classification to select glaucoma patients and glaucoma suspects.<sup>3</sup> We assumed glaucoma was primary if a secondary cause was not given (e.g., a diagnosis of “open-angle glaucoma” was assumed to be POAG). We grouped patients into POAG (persons coded as chronic open-angle glaucoma [ $n = 1$ ], open-angle glaucoma [4], open-angle glaucoma suspect [2], POAG [134], or POAG suspect [29]), primary angle-closure glaucoma (PACG: persons coded as angle-closure glaucoma [3], angle-closure suspect [1], chronic angle-closure glaucoma [23], chronic PACG [62], PACG [110], subacute PACG [28], and subacute angle-closure glaucoma [7]), and JOAG (persons coded as JOAG [61], and JOAG suspect [4]). These three classifications made up 89% of our cohort. We did not analyze other glaucoma subtypes in the remaining 11% due to insufficient numbers of patients to satisfactorily quantify distributions.

## Statistical Analyses

We performed a nonparametric bootstrap ( $n = 50,000$ ) to determine 95% confidence limits around proportions and median values, using custom software written in Matlab (R2015a for Macintosh; Mathworks, Natick, MA, USA). When comparing our cohort data with that of Canada, a proportion or median was judged to be different when it fell outside the 95% confidence limit of our cohort's proportion or median. As our cohort had a sample size less than the Canadian (525 vs. 2324) and so would be expected to have wider confidence limits, this approach should limit Type I errors.

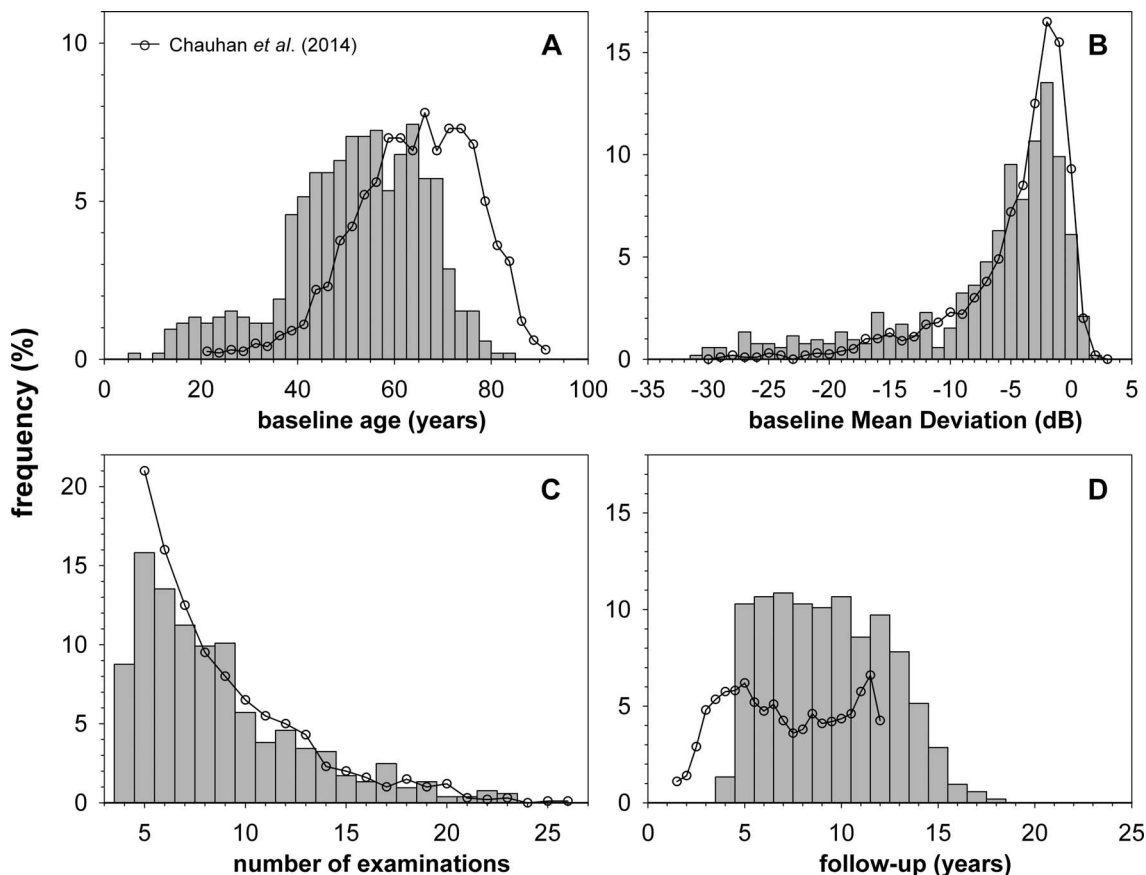
We also performed a Fisher's exact test to compare the combined proportion of fast and catastrophic progressors in each subgroup. Fast and catastrophic groups were combined given the low sample numbers, particularly in the catastrophic progression category. Previous work found a combined proportion of fast and catastrophic observers of approximately 6% in a Canadian population,<sup>3</sup> and 30% in a Swedish population.<sup>1</sup> This 5-fold difference is likely to reflect, at least in part, the presence of a large subpopulation of pseudoexfoliation glaucoma in the Swedish group, as noted earlier. Assuming a smaller 3-fold difference in combined fast and catastrophic rates between subtypes in our cohort, we estimated sample sizes of 125 per subgroup in order to find this difference ( $P < 0.05$ ) with a power of 0.80.<sup>11</sup> As we analyzed all available data meeting our inclusion criteria, our sample sizes were necessarily fixed. Both our POAG and PACG subgroups substantially exceeded the sample sizes estimated from our power analysis.

## Predicted MD at Life Expectancy

Life expectancy in India is approximately 68 years.<sup>12</sup> We estimated the MD value at this age ( $MD_{68}$ ) for our cohort using a linear model:

$$MD_{68} = MD_{baseline} + (68 - baseline\ age) \times rate \quad (1)$$

where  $MD_{baseline}$  was the patient's initial MD value, baseline age was the age when visual field testing was commenced, and rate was the rate of MD progression in dB/y. Simulation work



**FIGURE 1.** Distributions of baseline age (A), baseline MD (B), number of visual field examinations (C), and follow-up duration (D) for a cohort of 525 patients from India. Lower limits of the histogram bins are applied inclusively. Unfilled circles and lines show data from a large clinical population in Canada, as visually estimated from figures presented in Chauhan et al.,<sup>3</sup> where the symbol gives the height of each bin's midpoint. Of note is follow-up frequencies for the Canadian dataset are in half-yearly, rather than yearly, bins, and so would be expected to be half as high.

has demonstrated that progression rate estimates above +1.0 dB/y can occur when visual field results are noisy and/or visual field series are short, despite a patient's true, underlying progression rate being below +1.0 dB/y.<sup>13</sup> Such positive progression rates estimates could potentially produce large, and unrealistic, improvement in visual fields when extrapolated over an extended time. Therefore, we capped the maximum improvement at 2 dB above baseline; this was done for reasons of physiological plausibility, but does not actually influence our reported frequencies of visual impairment, which are driven solely by negative progression rates. One hundred eighteen eyes (22%) from our cohort had improvements greater than 2 dB that were then capped at 2 dB, consistent with the high proportion of people with positive progression rates in our data (see Results). We also capped the minimum MD allowable to -30 dB, and set the  $MD_{68}$  for any patients already 68 years or older to their baseline MD. We defined visual impairments as an MD less than -20 dB, being a level previously used to define visual impairment<sup>14</sup> and close to the level used to mark statutory blindness by Saunders et al.<sup>5</sup>

**RESULTS**

Figure 1 shows the distribution of baseline age, MD, number of visual field examinations, and follow-up duration for the cohort (histogram bars) along with comparison data from a cohort of clinical patients from a tertiary care setting in Canada.<sup>3</sup> Of note was the upper half of the baseline age distribution was shifted

left by approximately a decade, consistent with the age expectancy in India being approximately 14 years less than in Canada.<sup>12</sup> In addition, our cohort contained a more substantial lower tail of patients older than 40 years. The median baseline MD was lower for the Canadian dataset, and lay outside the 95% confidence limit for our cohort data (Table). The number of examinations was broadly similar, although the frequency distribution of follow-up years was shifted to the left for the Canadian dataset, consistent with visual fields being performed more frequently for that group.

The distribution of progression rates is shown in Figure 2. A linear regression showed a significant relationship between age and progression rate for our cohort, with a regression slope of -0.047 dB/decade ( $P < 0.001$ ). A similar linear regression found no significant relationship between baseline MD and rate of progression (slope 0.003,  $P = 0.21$ ). The median rate, and proportion of fast and catastrophic progressors, for the Canadian dataset fell outside the 95% confidence limits for our cohort, with the Canadian group showing faster median progression, and a larger proportion of fast and catastrophic progressors (Table). Given the median age for the Canadian group was 12 years greater than for our cohort (Table), along with the significant relationship between age and progression rate we found, we modelled what might be the proportion of fast and catastrophic progressors if our cohort were 12 years older (i.e., if progression rates were all adjusted by -0.056 dB/y [= 1.2 decades × -0.047 dB/decade]). The proportion of fast and catastrophic progressors in this adjusted data was 3.24

TABLE. Proportions and Median Parameters for the Entire Cohort as Well as Subgroups Classified as POAG, PACG, or JOAG

Group	Age, y	n	Progression Rate, dB/y	Any, %	Fast, %	Catastrophic, %	Exams	Follow-up, y	IOP, mm Hg	Baseline MD, dB
Cohort	53.0 [51.5–54.5]	525	-0.02 [-0.04 to -0.01]	55.2 [51.0–59.4]	1.7 [0.8–2.9]	0.6 [0.0–1.3]	8 [7–8]	9 [9–10]	25.0 [24.0–26.0]	-4.42 [-4.90 to -4.04]
POAG	53.5 [52.0–55.3]	170	-0.05 [-0.09 to -0.01]	60.0 [52.4–67.1]	1.2 [0.0–2.9]	1.2 [0.0–2.9]	7 [7–9]	10 [9–10]	26.0 [24.0–26.0]	-4.47 [-5.16 to -3.30]
PACG	56.5 [55.0–58.8]	234	-0.03 [-0.08 to -0.01]	56.8 [50.4–63.2]	1.7 [0.4–3.4]	0.0 [0.0–0.0]	7 [7–8]	9 [8–9]	24.0 [22.0–24.4]	-4.23 [-4.84 to -3.37]
JOAG	32.5 [28.5–37.0]	65	0.02 [-0.08 to 0.08]	43.1 [30.8–55.4]	3.1 [0.0–7.7]	1.5 [0.0–4.6]	9 [7–10]	9 [8–12]	28.0 [26.0–32.0]	-4.25 [-7.44 to -3.11]
Chauhan et al. <sup>3</sup>	65	2324	-0.05	57.8	4.3	1.5	8	7.1	17.1	-2.44
De Moraes et al. <sup>2</sup>	64.9 (mean)	587	-0.45	78.5	12.6	3.1	11.1 (mean)	6.4 (mean)	15.2 (mean follow-up)	-7.1
Heijl et al. <sup>1</sup>	71.4 (mean)	583	-0.62	89.4	4.2	8.6	8.9 (mean)	7.8 (mean)	20.2 (mean)	-10.0

“Age” is the age at the first visual field, and the “Any,” “Fast,” and “Catastrophic” columns give the percentage of visual fields showing progression rates <0.0, <-1.0 to -2.0, and <-2.0 dB/y, respectively. Values in square brackets give 95% confidence limits derived from a nonparametric bootstrap procedure of 50,000 resamples with replacement. Pretreatment IOP were not available in 56, 21, 23, and 6 people in the cohort, POAG, PACG, JOAG, respectively. Values from the clinical cohorts of Chauhan et al.,<sup>3</sup> De Moraes et al.,<sup>2</sup> and Heijl et al.<sup>1</sup> are given for comparison with our cohort data. For the data of Chauhan et al.,<sup>3</sup> the percentage for “Any” progression taken as the sum of histogram bin frequencies ≤ -0.1 dB/y, plus half of the bin centered on 0 dB/y.

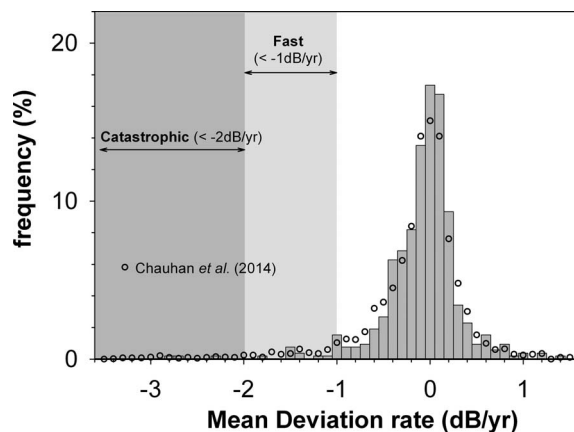


FIGURE 2. Distribution of rates of visual field progression. Data estimated from Chauhan et al.,<sup>3</sup> is given in comparison (unfilled circles).

(95% CI: 1.90–4.76) and 0.57 (0.00–1.33), respectively, which are similar to those in the Canadian group.

The most common glaucoma subtype in our cohort was PACG (45%), followed by POAG (32%) and JOAG (12%). Although we did not extract data for our particular cohort, we estimate that 18% of POAG patients, 32% of PACG patients, and no JOAG patients, are pseudophakic at baseline in our hospital. The distribution of baseline age, MD, number of visual field examinations, and follow-up duration for these subgroups can be seen in Figure 3. Overall, there was little difference between subgroups, except for the marked shift in the age distribution seen in JOAG. Compared with PACG, neither POAG ( $P = 0.73$ ) nor JOAG ( $P = 0.18$ ) had a significantly increased combined proportion of fast and catastrophic progressors (Fisher's exact test; Fig. 4), and this combined proportion was not associated with the length of the visual field series (Supplementary Table S1).

As JOAG patients were significantly younger (Table), yet had similar rates of visual field progression to other glaucoma subtypes (Fig. 4) and similar baseline MD values (Fig. 3), it would be anticipated that a greater proportion of these patients would have an MD less than -20 dB at 68 years (i.e., have visual impairment). The proportion of glaucoma subtypes with a MD<sub>68</sub> less than -20 dB was 10% (18/170), 6% (13/234), and 27% (17/64) for POAG, PACG, and JOAG, respectively. The proportions were significantly different ( $\chi^2 [23.53, 2], P < 0.0001$ ). Subsequent paired Fisher tests found the proportion for JOAG was significantly higher compared with both POAG ( $P = 0.004$ ) and PACG ( $P < 0.0001$ ), but that POAG and PACG did not significantly differ ( $P = 0.09$ ).

## DISCUSSION

We found that our three glaucoma subtypes, POAG, PACG and JOAG, had similar median progression rates, and comparable levels of visual field loss at baseline (Table). This finding is similar to that reported by De Moraes et al.<sup>2</sup> where there was no difference in the average rate of visual field progression between these subgroups for a US-based cohort. Although De Moraes et al.<sup>2</sup> did find that pseudoexfoliation glaucoma gave significantly higher rates of visual field progression in their univariate analysis, this association was no longer significant after adjusting for covariates. With regard to POAG and PACG cohorts drawn from India, our findings agree with those of Rao et al.<sup>15</sup> who did not find significant differences in progression rates between POAG and PACG among patients from Southern

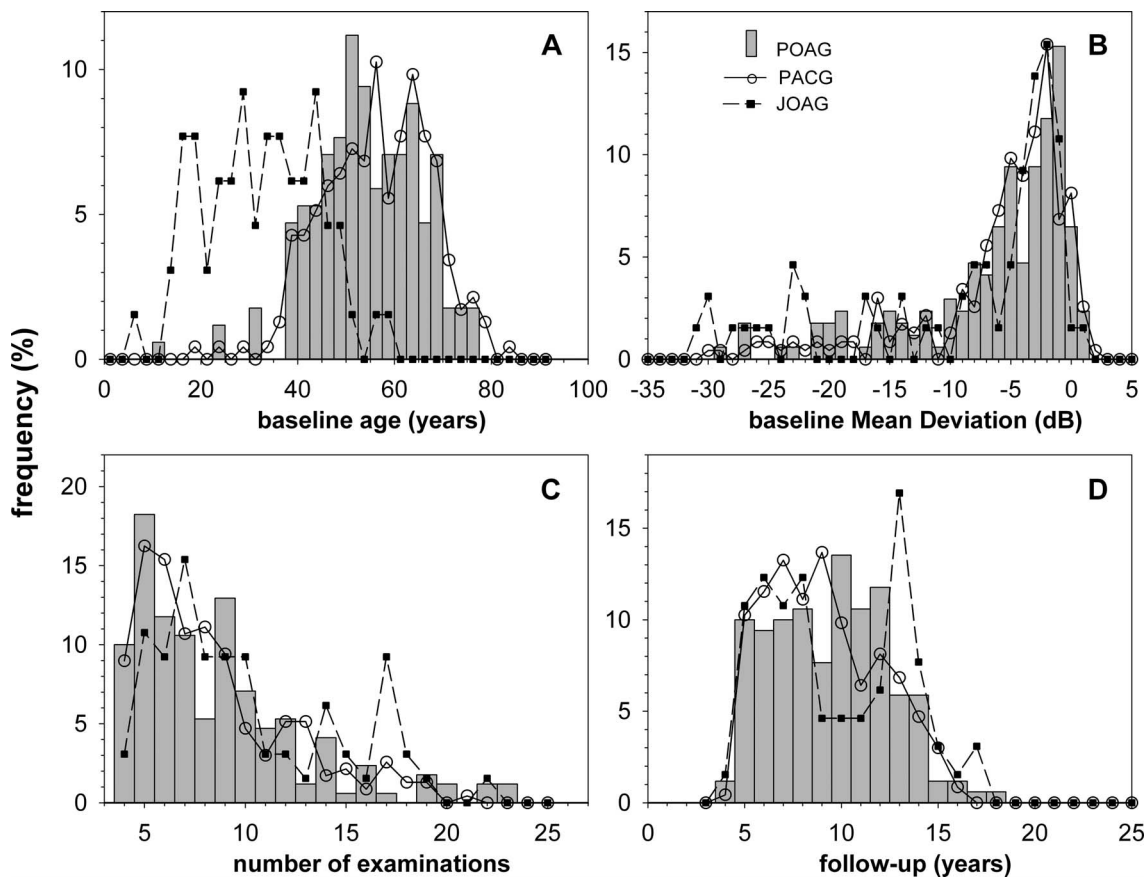


FIGURE 3. Distributions of baseline age (A), baseline MD (B), number of visual field examinations (C), and follow-up duration (D) for cohorts with POAG, PACG, and JOAG. Remaining details are as given in Figure 1.

India. Increased rates of visual field loss in PACG compared with POAG in a Korean cohort have been reported by Lee et al.<sup>16</sup> based on gradings of Goldmann visual fields, although of note is that their PACG patients had significantly higher number of surgeries and had significantly higher IOP throughout the study, compared with their POAG patients. In our clinical setting, PACG patients are generally treated with surgery earlier, using either a cataract extraction or filtering surgery. This higher rate of early surgical intervention may explain why we do not predict a greater level of visual impairment in PACG compared with POAG in our current

study, in contrast to the greater blindness found from PACG compared with POAG in population-based studies.<sup>17-19</sup>

### Proportion of Fast and Catastrophic Progression in Glaucoma Subtypes

Based on our results, we believe that giving the proportion of fast ( $<-1.0$  to  $-2.0$  dB/y) and catastrophic ( $<-2$  dB/y) progressors may be a more meaningful summary statistic for rate-of-change distributions than the median rate of change. Identification of rapid progressors is important for stratification of resources toward this small population of patients. Boodhna et al.<sup>20</sup> found that while overall progression rates have improved over the years due to better management of glaucoma, the prevalence of rapid progressors remained unchanged, indicating that preserving vision in such patients remains a significant clinical challenge. The proportion of catastrophic rates of progression in our cohort was slightly lower than that from Canada,<sup>3</sup> and were substantially lower than those from a hospital-based cohort in Southern Sweden<sup>1</sup> (fast  $\sim 30\%$ , catastrophic  $\sim 9\%$ ) which is likely due to the substantial proportion of fast progressing pseudoexfoliation glaucoma in this latter cohort.

The proportion of fast and catastrophic progressors in the Canada dataset was over double that for our cohort (5.8% vs. 2.3%), despite median progression rates differing by only 0.03 dB/y. This highlights how a comparison of median progression rates may not reflect behavior in the tails of progression rate distributions. It is unlikely that this difference is attributable to increased noise in the Canadian dataset artificially broadening the tails of the distribution, and so increasing the proportion of

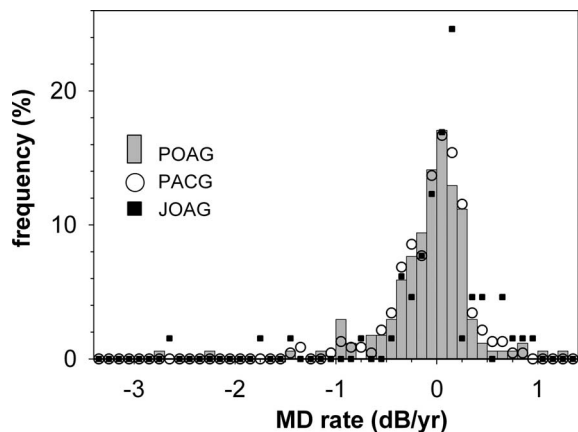


FIGURE 4. Distribution of rates of visual field progression for persons with POAG, PACG, and JOAG.

fast and catastrophic progressors. The Canadian study employed a robust regression method, in contrast to the more common ordinary least-squares method we employed, and had a larger sample size than our study. Both of these factors should reduce noise, and so should produce a narrower distribution of progression rates<sup>13</sup> rather than the broader-tailed distribution we found. When we adjusted our cohort to account for the 12-year age difference between our cohort and that from Canada, proportions of fast and catastrophic progressors become similar. Although an interesting finding, we caution against concluding that the difference in rates between our groups is therefore due to age. While the groups differ substantially in terms of absolute age, they are reasonably well matched in terms of age relative to life expectancy. Increasing age has been found by some to increase the rate of visual field loss within a given population,<sup>21-23</sup> although the validity of using this relationship to adjust for age differences between populations with different life expectancies remains necessarily speculative.

Our comparison of glaucoma subtypes revealed no significant difference in the combined rates of fast and catastrophic progressors. Importantly, these comparisons were made between subgroups drawn from within a single cohort of shared geography (Northern India) and subject to similar standards of care (a single hospital-based setting), thereby avoiding the challenges faced when trying to compare progression rate distributions in subgroups drawn from different studies.<sup>10</sup> With regard to our POAG subgroup, we did not show a significant increase in the proportion showing visual impairment (MD < -20 dB) at life expectancy compared with PACG. Such longitudinal analysis stands in contrast to the findings of Garudadri et al.,<sup>18</sup> who found a greater proportion of blindness from PACG than POAG in a cross-sectional study in India. The large majority of people in their study were previously unaware of their disease, and so the difference between our results and theirs may in part reflect differences between the natural and treated histories of PACG versus POAG.

### Rate of VF Loss Overall

Our results show that the overall visual field progression rates for our cohort were similar to what has been reported from a Canadian tertiary care setting.<sup>3</sup> Our median rate of visual field loss was just outside the interquartile range (IQR) previously reported by Rao et al.<sup>24</sup> for an Indian population (-0.19 dB/y; IQR -0.41, -0.03) and so is likely within the 95% CI (unreported) for their data, despite their cohort having a substantially greater median MD at baseline (-16.9 vs. -4.42). This is consistent with the observation that baseline MD does not profoundly affect rate of visual field progression,<sup>3,24</sup> although floor effects will likely slow measured progression rates in those with advanced field loss.<sup>24</sup>

### Predicted Visual Impairment

We found that fewer than 0.5% of patients were above 80 years at diagnosis, compared with approximately 9% in Canada.<sup>5</sup> The main portion of the age distribution was shifted leftward in our cohort by an amount similar to the expected life-expectancy difference between India and Canada (68.3 vs. 82.2 years).<sup>12</sup> As such, the residual life expectancy for POAG and PACG patients after diagnosis might be expected to be similar between both countries. However, a slightly greater level of visual impairment over their residual life expectancy might be expected in our cohort as baseline MDs were approximately 2 dB worse. It should also be noted that our estimation of life expectancy is necessarily approximate, and could be improved by incorpo-

rating patient sex, as well as patient age so that changes in life expectancy rates over time are accounted for. However, the principal limitation in our method for estimating vision impairment at life expectancy is almost certainly not our estimate of life expectancy itself, but rather the rate of visual field loss visual used in our extrapolation.

Patients with JOAG would be expected to have an increased residual life expectancy; correspondingly, our calculations predicted that a significantly larger proportion would suffer substantial visual impairment in their lifetime. Previous modeling work has suggested that patients with JOAG might have a similar risk of visual impairment (defined as  $\leq 50\%$  on the visual field index) over their lifetime compared with other forms of glaucoma.<sup>10</sup> The conclusions of previous modeling were made based on comparisons to rates from other published studies. That the methodology in our current study avoids the potentially large between-study variations noted above may, in part, explain the difference between the current and previous<sup>10</sup> findings. In general, any such modeling should be treated with a certain degree of caution as it assumes that a patient's visual field damage will progress at a constant rate across their lifetime, even if therapeutic interventions are subsequently altered. In addition, estimates of the rate of progression are subject to substantial noise particularly when visual field series are short,<sup>25</sup> which can act to artefactually broaden the distribution of visual field progression rates.<sup>13</sup> Such noise might be expected to be slightly greater in the current study than in previous work as we allowed shorter visual field series (minimum 4 vs. 5) and had no minimum follow-up time (compared with a minimum 5 years in Gupta et al.<sup>10</sup>). Despite these caveats, our results do not appear out of step with empirical findings. We predicted visual impairment among PACG eyes to be 6% in our cohort over approximately 11.5 years (which is life expectancy minus median age at baseline). This is similar to that determined empirically by Quek et al.<sup>26</sup> who found 7% of eyes progressing to blindness among Chinese patients with treated PACG over 10 years (using a definition of blindness based on the presence of sensitivity  $\leq 10$  dB at or within 20° fixation, and/or visual acuity of 20/200 or worse). The level of the impairment for the patient is more difficult to estimate, and will be reduced if the visual field of their fellow eye is less severely damaged. A limitation of our study is that our extracted data did not include information on the state of the fellow eye for those participants who only had monocular visual fields available. While it is possible that some of these patients had monocular testing due to only monocular disease being manifest, it is also possible that some had severe visual impairment or blindness that precluded visual field assessment. A further limitation is that patients with severe vision loss or blindness upon presentation are unlikely to be those provided follow-up care with perimetry within our hospital, and so will necessarily not be represented in the selection of patients we analyzed. As such, our cohort represents a selected sample that isolates those patients who have been followed perimetrically. This is, however, the group for whom knowing the rate of visual field progression—and, therefore, the likelihood of significant visual impairment in their lifetimes—is probably most critical.

In summary, we show that differences in fast and catastrophic visual field progression may occur between cohorts with similar median progression rates, and that three common glaucoma subtypes within a single cohort have similar rates of fast and catastrophic progression. These results highlight the importance of considering the full shape of the distribution when assessing progression rates, as patients with rapidly deteriorating fields are among those whose management is the most challenging and urgent.

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