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Home Self-tonometry Trials Compared with Clinic Tonometry in Patients with Glaucoma

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Purpose: This study examined characteristics of intraocular pressure (IOP) as measured during home tonometry in comparison with in-clinic tonometry in patients with glaucoma.

Design: Retrospective cross-sectional study of glaucoma patients who completed 1 week of self-tonometry at a single academic center.

Participants: Patients with glaucoma who completed home tonometry trials with the iCare HOME tonometer (iCare USA) for any reason.

Methods: Home IOP measurements were compared with in-clinic tonometry performed during the 5 visits preceding home tonometry. Maximum daily IOP was correlated to time of day. Generalized estimating equations were used to evaluate patient characteristics and clinic-derived variables that predicted differences between home and clinic IOP.

Main Outcome Measures: IOP mean, maximum, minimum, range, standard deviation and coefficient of variation were compared between clinic and home tonometry. IOP mean daily maximum (MDM) and mean daily range were calculated to describe recurrent IOP spiking.

Results: A total of 107 eyes from 61 patients were analyzed. Mean age was 63.2 years (standard deviation [SD], 14.0 years) and 59.0% were women. Mean clinic and home IOPs were 14.5 mmHg (SD, 4.7 mmHg) and 13.6 mmHg (SD, 5.1 mmHg). Home tonometry identified significantly higher maximum IOP, lower minimum IOP, and greater IOP range than clinic tonometry ($P < 0.001$). Maximum daily IOP occurred outside of clinic hours (8 AM–5 PM) on 50% of days assessed and occurred between 4:30 AM and 8 AM on 24% of days. Mean daily maximum IOP exceeded maximum clinic IOP in 44% of patients and exceeded target IOP by 3 mmHg, 5 mmHg, or 10 mmHg in 31%, 15%, and 6% of patients, respectively. Patient characteristics that predicted significant deviations between MDM and mean clinic IOP or target IOP in multivariate models included younger age, male gender, and absence of prior filtering surgery.

Conclusions: Self-tonometry provides IOP data that supplements in-clinic tonometry and would not be detectable over daytime in-clinic diurnal curves. A subset of patients in whom home tonometry was ordered by their glaucoma clinician because of suspicion of occult IOP elevation demonstrated reproducible IOP elevation outside of the clinic setting. Such patients tended to be younger and male and not to have undergone previous filtering surgery. *Ophthalmology Glaucoma 2021;4:569-580 © 2021 by the American Academy of Ophthalmology*

Intraocular pressure (IOP) reduction is the only treatment proven to ameliorate glaucoma worsening,[1–4] with treatment decisions typically based on periodic IOP measurement obtained during clinic visits. However, IOP varies from day to day and throughout the day,[5–7] making in-office tonometry an incomplete representation of overall IOP-mediated glaucoma risk.[8,9] Studies of 24-hour IOP monitoring using a variety of methods have demonstrated that most patients manifest greater mean, peak, and range of IOP outside of office hours and that knowledge of out-of-office IOP behavior warrants glaucoma management change for a subset of patients.[10,11] Out-of-office IOP measurements have been advocated for patients progressing despite low in-office IOP.[12] Nonetheless, 24-hour IOP monitoring by clinical staff is prohibitively resource intensive for routine practice, and clinical diurnal curves obtained during working hours often are used as a surrogate. The advent of new devices to permit routine home self-tonometry may fill an important need in glaucoma clinical care, but empiric data that can guide best practices for who should undergo home self-tonometry and to establish expected out-of-office IOP benchmarks are lacking.

Home self-tonometry presents an opportunity to capture 24-hour IOP data noninvasively in a natural setting that is more convenient to patients than clinic-based diurnal curves or 24-hour tonometry. However, it requires a tonometry device that patients can self-administer. In 1973, Jensen and Maumenee[13] published the first trial of home tonometry using the Schiotz tonometer; despite some limitations of the device, they believed that this was a potentially useful source of information in guiding glaucoma treatment. In 1983, Zeimer et al[14] reported the self-use of an automated applanation tonometer by patients with glaucoma, and a subsequent version of the instrument produced data

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suggesting that large out-of-office IOP variability is an independent risk factor for glaucomatous visual field progression. Although this device was commercialized, it was not adopted for widespread clinical use.[15]

The iCare HOME (iCare USA) is a rebound tonometer approved by the Food and Drug Administration for home self-use by patients. With training, more than 75% of patients can obtain IOP measurements[16] that are accurate in comparison with Goldmann applanation tonometry (GAT).[16–18] The iCare HOME is compact, rapid, acceptable to most patients, and requires no anesthesia.[19–21]

It is now well established that home self-tonometry with the iCare HOME tonometer is feasible and accurate.[22,23] However, data to guide physicians in how best to integrate home self-measured IOP into clinical practice for evaluation or monitoring of glaucoma patients are lacking, except for specific indications, such as assessing luminal opening of ligated tube shunts,[24] responses to laser trabeculoplasty,[25] or IOP lowering after initiation of topical therapy.[23,26] Prospective studies using the iCare HOME highlighted the ability of self-tonometry to capture more IOP data than is feasible in the clinic and identified higher IOP peak and fluctuation at home than in the clinic.[20,22,27] However, important unanswered questions remain including: (1) Which home tonometry metrics are most useful for reliably identifying clinically relevant IOP fluctuations? (2) Does rebound self-tonometry provide information that is independent of data ascertainable in the clinic? (3) What proportion of glaucoma patients receiving care are likely to manifest clinically meaningful differences in IOP inside versus outside of clinic hours? and (4) Can discrepancies between clinic and home tonometry be predicted by patient or ocular characteristics?

We hypothesized that among a group of glaucoma patients whose glaucoma physicians ordered a home tonometry trial, a substantial proportion would exhibit self-measured IOP outside of the clinic setting that differed in important ways from in-clinic IOP. We predicted that relevant measurements may include IOP repeatedly and significantly above the average in-clinic IOP or the target IOP, or particularly large IOP fluctuations. Herein, we performed a retrospective analysis as a foundation for future prospective studies by reviewing the data from a large group of patients for whom home tonometry was ordered by a glaucoma physician (including E.J.M., P.Y.R., and T.V.J.). We calculated relevant metrics that are representative of clinically meaningful IOP excursions outside of office hours. These included 2 novel metrics we developed for the interpretation of home tonometry data: mean daily maximum (MDM) IOP and mean daily range (MDR) of IOP. We described the 24-hour distributions of IOP variability in these self-tonometry trials and compared them with in-clinic IOP within individual eyes.

Methods

We retrospectively reviewed the clinical records of all 61 patients who underwent home self-tonometry using the iCare HOME rebound tonometer while receiving care at the Johns Hopkins Wilmer Eye Institute between October 2018 and October 2020. The Johns Hopkins Institutional Review Board approved this study, which adhered to the tenets of the Declaration of Helsinki. Informed consent was not required for this retrospective study because all data were de-identified.

Table 1. Characteristics of Study Participants

Characteristic	Data
Age (yrs), mean (SD)	63.2 (14.0)
Gender, no. (%)	
Female	36 (59.0)
Male	25 (41.0)
Race/ethnicity, no. (%)	
White	44 (72.1)
Black	6 (9.8)
Latino	1 (1.6)
Asian	8 (13.1)
Other	2 (3.3)
Type of glaucoma, no. (%)	
Primary open-angle glaucoma	69 (64.5)
Primary open-angle glaucoma suspect	9 (8.4)
PAC or PAC glaucoma	4 (3.7)
Pseudoexfoliative glaucoma	1 (0.9)
Pigmentary glaucoma	4 (3.7)
Uveitic glaucoma	6 (5.6)
Other secondary glaucoma	14 (13.1)
Previous trabeculectomy, no. (%)	13 (12.5)
Previous tube shunt, no. (%)	8 (7.5)
Pseudophakic, no. (%)	54 (50.5)
No. of glaucoma medications, mean (SD)	2.4 (1.5)
Target IOP (mmHg; n = 74 eyes), mean (SD)	15.0 (4.1)
Central corneal thickness (μm), mean (SD)	537.3 (46.3)
Visual acuity (logMAR), mean (SD)	0.18 (0.35)
Visual field mean deviation (dB), mean (SD)	−8.9 (8.7)

IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; PAC = primary angle closure; SD = standard deviation.
Data are representative of 107 eyes of 61 patients unless otherwise stated.

Patients with manifest or suspected primary or secondary glaucoma were selected for home tonometry by their ophthalmologist. Patients performed self-tonometry using an iCare HOME tonometer after (1) in-office teaching with an ophthalmic technician certified for iCare HOME training and (2) successful demonstration of accurate self-measurement as described previously.[16] Notably, to be certified for participation, patients obtained 3 sequential IOP self-measurements that were within 5 mmHg of a concomitant GAT measurement, and the range of the 3 IOP self-measurements was < 7 mmHg. Patients then were instructed to obtain at least 4 daytime measurements daily for the following week. Nighttime measurements were optional but encouraged. Tonometry data were downloaded from each device and only measurements that were rated as excellent, good, or satisfactory were included. Home IOP measurements obtained 30 minutes or more apart were analyzed as distinct data points. Multiple measurements obtained in a period of 30 minutes or less were averaged.

Chart review was performed to ascertain age, gender, past medical history, prior ophthalmic surgeries, and ophthalmic and systemic medications. Clinical data were obtained from the 5 clinic visits preceding home tonometry, or if fewer than 5 visits preceded home tonometry, then all preceding clinic visits. Clinic tonometry typically was performed by a certified ophthalmic technician using GAT, and only rarely by iCare tonometry. Clinic notes were reviewed to identify explicit statements describing reasons for ordering self-tonometry and how the self-tonometry results

Table 2. Comparisons between Home Tonometry and Clinic Tonometry

Metric	Home Tonometry	Clinic Tonometry*	P Value†
Mean of IOP measurements	13.6 (5.1)	14.5 (4.7)	**0.02**
Maximum of IOP measurements	20.8 (9.0)	17.6 (7.6)	**< 0.001**
Minimum of IOP measurements	8.0 (3.6)	12.1 (3.7)	**< 0.001**
Range of IOP measurements	12.9 (7.6)	6.1 (5.9)	**< 0.001**
Standard deviation of IOP measurements	3.3 (2.0)	2.6 (2.4)	**0.02**
Coefficient of variation‡ of IOP measurements	0.24 (0.10)	0.17 (0.10)	**< 0.001**

IOP = intraocular pressure.
Data are presented as mean (standard deviation) among all eyes (n = 107).
Boldface indicates $P < 0.05$.
*Intraocular pressure recorded in the medical record during the 5 clinic visits preceding the home tonometry trial.
†Related samples Wilcoxon signed-rank test.
‡Standard deviation divided by the mean.

interpreted by the ophthalmologist (including E.J.M., P.H.R., and T.V.J.) at the subsequent clinic visit influenced treatment recommendations.

Continuous variables are expressed as means with standard deviations (SDs) unless stated otherwise. Paired Wilcoxon rank-sum tests were used to compare clinic and home IOP metrics within individual patients. Chi-square tests compared the percent of patients meeting various criteria during clinic tonometry versus home tonometry. Bland-Altman plots were used to compare the difference in mean IOP as measured in clinic versus at home as a function of mean IOP. One way analyses of variance were used to assess the effect of time of day on IOP, binned into 4 time periods including office hours (8 AM–5 PM), overnight (10:30 PM–4:30 AM), and the periods in between: early morning (4:30 AM–8 AM) and evening (5 PM–10:30 PM). Generalized estimating equations were used to identify variables that predicted large deviations between home IOP and clinic IOP, or the advancement of therapy after home tonometry, while accounting for intereye correlations within individuals and controlling for potential confounders. Multivariate models predicting discrepancy between MDM and mean clinic IOP or target IOP included: demographic variables (age, gender, ethnicity), prior glaucoma filtering surgery, prior cataract surgery, number of glaucoma drops, and any other variables with an association reaching significance of $P = 0.1$ in a univariate model. In all final models, statistical significance was defined as $P < 0.05$.

Results

A total of 107 eyes of 61 patients cared for by 8 ophthalmologists (including E.J.M., P.H.R., and T.V.J.) were analyzed (Table 1). The charted reasons for ordering home tonometry included: to elucidate current IOP range or concern for occult IOP elevation in 49 eyes (45.8%), worsening visual field defect despite clinic IOP near target in 44 eyes (41.1%), progression of retinal nerve fiber layer thinning on OCT despite clinic IOP near target in 2 eyes (1.9%), patient symptoms suggestive of IOP elevation in 2 eyes (1.9%), and presence of disc hemorrhage with clinic IOP near target in 2 eyes (1.9%); no reason was stated for 8 eyes (7.5%). All patients were certified for home tonometry by demonstrating in-clinic self IOP measurements less than 5 mmHg different than a concomitant GAT measurement. If IOP self-measurements were outside this range, patients did not perform a home tonometry trial. To explore further the possible differences in tonometry methods within the study population, we reviewed charts for patients who had documented GAT and iCare rebound tonometry performed in clinic within a 5-minute span. On average, among the 12 identified study patients with dual IOP measurements, the iCare rebound tonometer measured −0.33 mmHg and +0.08 mmHg different than GAT for right and left eyes, respectively.

Home tonometry trials lasted 7.2 days (SD, 1.7 days) and included 3.8 measurements per day (SD, 1.6 measurements per day), or 30.4 measurements total per eye (SD, 15.0 measurements total per eye). In an analysis of all data from 1 randomly selected eye from each individual, we found that 15% of measurements were deemed satisfactory, 21% were good, and 64% of measurements were of excellent quality. For comparison with home tonometry, we analyzed the clinic IOP measurements from the preceding 5 visits at maximum and included 4.2 visits (SD, 1.5 visits) per patient. Mean IOP obtained in clinic was slightly higher than mean IOP obtained at home (intraeye pairwise IOP difference, 0.8 mmHg [SD, 4.1 mmHg]; $P = 0.02$; Table 2), and the 2 measures were correlated positively ($R^2 = 0.41$; $P < 0.001$; Fig 1A). Bland-Altman analyses demonstrated no systematic bias for one form of IOP to be more than the other as a function of overall IOP (Fig 1B), although the agreement between home and clinic tonometry tended to be lower when mean IOP was more than 12 mmHg (Fig 1C). Measures of IOP variability, including the SD of IOP measurements and the coefficient of variation of IOP measurements, were higher for home than clinic tonometry (Table 2). In addition, home tonometry revealed a significantly greater maximum IOP, a lesser minimum IOP, and a greater IOP range than clinic tonometry (Table 2).

Because the severity of glaucoma and target IOP of the patients in this cohort were variable, we were interested in the relationship between home IOP measurements and target IOP. Among the 74 eyes with documented target IOPs, 45 eyes (61%) showed at least 1 in-clinic IOP measurement exceeding target. In comparison, 55 eyes (74%) showed at least 1 home IOP measurement exceeding the target during self-tonometry ($P < 0.001$). Of those 55 eyes, 21 (38%) did not show any clinic IOP measured above target. Intraocular pressure was more than the target during an average of 32.5%

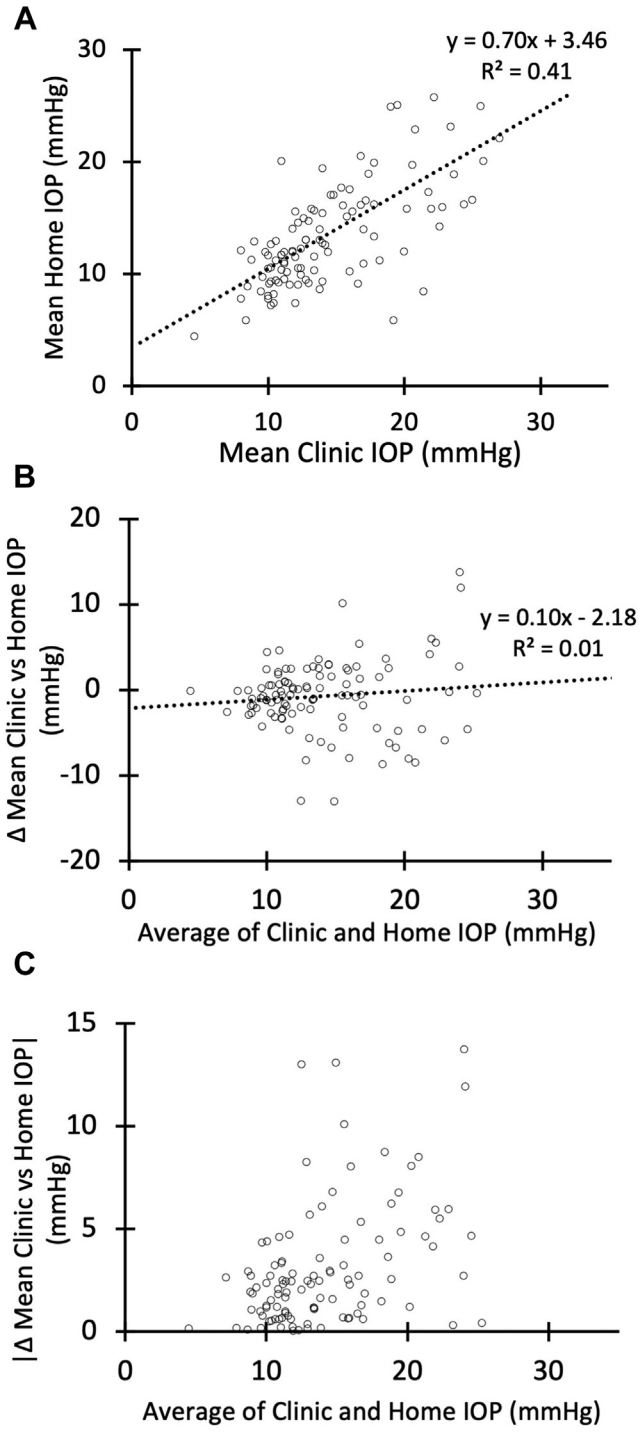

Figure 1. Comparison of mean clinic versus home intraocular pressure (IOP) measurements among individual patients. **A**, Linear regression analysis showing the positive correlation between mean home IOP and mean clinic IOP ($P < 0.001$). **B**, Bland-Altman plot showing the difference between mean home IOP and mean clinic IOP as a function of the average IOP. **C**, Bland-Altman plot showing the absolute value of the difference between mean home IOP and mean clinic IOP as a function of the average IOP.

(29.6%) of patients' home tonometry measurements. The maximum home IOP exceeded any recorded historic maximum clinic IOP, thereby setting a new maximum IOP, in 32 eyes (29.9%).

Intraocular Pressure Monitoring over 24 Hours

Home tonometry provides an opportunity to capture IOP at times of day that are outside of typical ophthalmology clinic hours (assumed here to be 8:00 AM–5:00 PM), which could explain discrepancies between clinic and home IOP data. We examined the 24-hour IOP profiles of patients who underwent home tonometry by dividing the day into 4 blocks of time: early morning (4:30 AM–8:00 AM), clinic hours (8:00 AM–5:00pm), evening (5:00 PM–10:30 PM), and overnight (10:30 PM–4:30 AM; Fig 2A). On average, patients obtained 13.5% of their home IOP measurements in the early morning, 42.5% during clinic hours, 31.8% in the evening, and 12.3% overnight. We detected a statistically significant variation in IOP over these 4 time points, with the highest mean IOP occurring in the morning ($P = 0.02$; Fig 2A).

We next examined the timing of maximum daily IOP among the cohort. For patients who performed home tonometry on both eyes, peak IOP occurred in 1 eye within 2 hours of the fellow eye on 68% of days assessed, suggesting moderate correlation between eyes of individual patients. We considered eyes to have consistent maximum IOP timing if the daily peak IOP occurred within a single 2-hour window on at least 70% of days assessed. Sixty-three percent of eyes met this definition, suggesting a moderate degree of internal consistency in the timing of peak IOP within individual patients. The timing of peak IOP over the 24-hour period fell outside of the 8:00 AM to 5:00 PM clinic hours window on 50% of days assessed. It occurred between 4:30 AM and 8:00 AM (early morning) 24% of the time, between 5 PM and 10:30 PM (evening) 21% of the time, and between 10:30 PM and 4:30 AM (overnight) 5% of the time (Fig 2B). Detection of early morning IOP spiking at this frequency is out of proportion to the 13.5% of measurements obtained during this period, suggesting that this was not simply a sampling artifact.

Mean Daily Maximum Intraocular Pressure

In clinical practice, an often-cited use for home tonometry is to detect out-of-office IOP spikes. Therefore, we sought to identify metrics that would capture this phenomenon and would determine the proportion of patients in this cohort who exhibit IOP spikes. Although IOP measurements are given individual quality scores by the iCare HOME device and only quality scores of satisfactory or better were included in our analysis, we were concerned that single spurious home tonometry readings could increase the home IOP absolute maximum and IOP range artifactually. Moreover, absolute maximal IOP discards a considerable amount of useful data obtained over multiple days. Therefore, we calculated the MDM IOP of home tonometry measurements, in which the maximal IOP value obtained over each 24-hour period (12:01 AM–11:59 PM) was averaged for the course of the multiday trial. By taking the mean over multiple days, this metric is protected from artifactual inflation by individual spurious readings. Indeed, the MDM IOP was 16.6 mmHg (SD, 7.0 mmHg), significantly lower than the absolute home IOP maximum of 20.8 mmHg (SD, 9.0 mmHg; $P < 0.001$). Similarly, we calculated the MDR IOP, which was 6.5 mmHg (SD, 4.7 mmHg), significantly lower than the absolute home IOP range of 12.9 mmHg (SD, 7.6 mmHg; $P < 0.001$).

To determine the extent of out-of-office IOP spikes, we calculated the difference between the MDM and the mean clinic IOP (Fig 3A), the maximum clinic IOP, and the target IOP

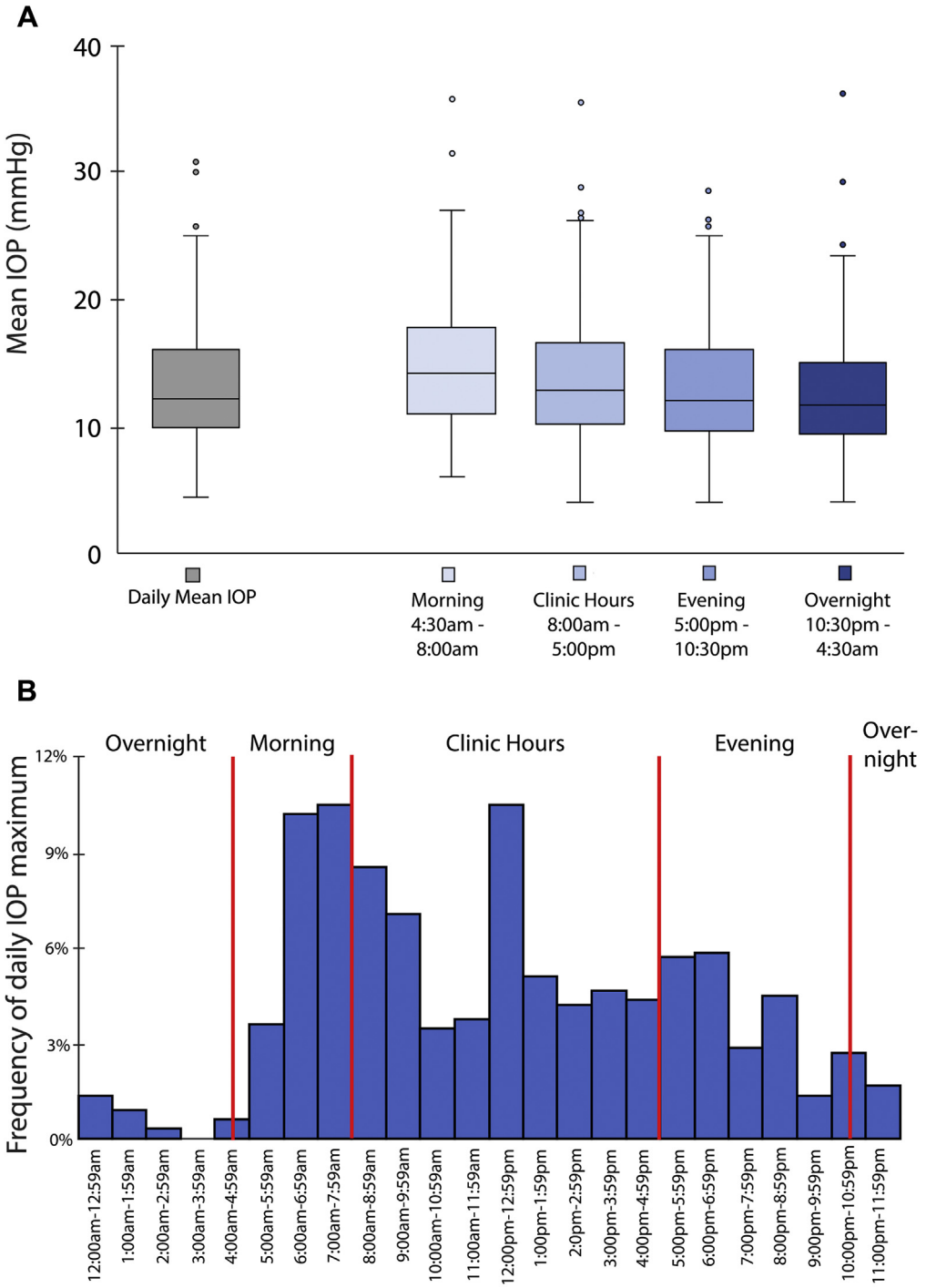

Figure 2. Home intraocular pressure (IOP) measurements and time of day. **A**, Boxplot showing IOP for each patient according to time of day as indicated. Boxes are centered on the mean and bounded by the twenty-fifth and seventy-fifth percentiles, with the median indicated by the central line and outliers indicated by circles. One-way analysis of variance demonstrated a statistically significant ($P = 0.02$) association between home IOP and time of day. **B**, Histogram showing the timing of the maximum home IOP measurement for each person by day recorded (n = 691 days).

(Fig 3B). Moreover, we calculated the proportion of patients that manifested MDM IOPs of varying degrees over clinic mean, clinic maximum, and target IOP (Table 3). Most eyes showed an MDM IOP of more than the mean clinic IOP, and almost one third of eyes showed an MDM IOP that was more than 30% greater than mean clinic IOP (Fig 3; Table 3). In addition, almost two thirds of eyes showed an MDM IOP that was greater than the target IOP, and nearly one quarter showed an MDM IOP that exceeded the target IOP by more than 30% (Fig 3; Table 3). Critically, among the eyes in which MDM IOP exceeded the target IOP, 18 eyes (24.3%) had not registered a previous clinic IOP over target. Therefore, in a substantial

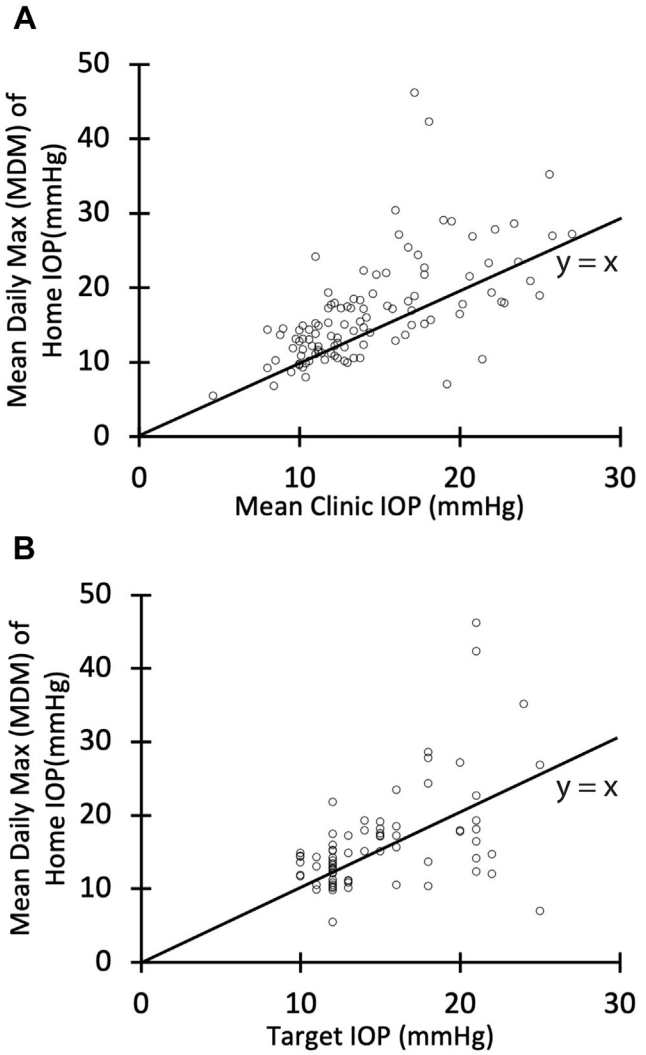

Figure 3. Scatterplots comparing mean daily maximum (MDM) intraocular pressure (IOP) with home tonometry versus mean clinic IOP and target IOP among individual patients. Solid lines represent unity (y = x), where MDM equals (**A**) mean clinic IOP or (**B**) target IOP. Points above the solid line represent patients in whom MDM IOP exceeded mean clinic IOP or target IOP.

minority of patients who underwent home tonometry, clinically significant IOP elevation was detected only by home tonometry and not by clinic tonometry.

Predictors of Discrepancy between Home and Clinic Tonometry

Whereas agreement between clinic and home tonometry generally was good, it is clear that an important subset of patients demonstrated significant discrepancy between these 2 tonometric approaches, which manifests as occult IOP elevation (i.e., IOP elevated above desirable levels not identified by clinic tonometry). We were interested in determining whether any patient or ocular characteristics might have predicted discrepancies between clinic and home IOP, and therefore used generalized estimating equations with the difference between MDM and either mean clinic IOP or target IOP as a continuous dependent variable, while accounting for correlation between eyes of single patients (Table 4). Univariate models suggested that younger age, male gender, phakic lens status, and absence of previous glaucoma filtering surgery predicted a greater discrepancy between MDM and mean clinic IOP, although only age and male gender remained significant in the multivariate model (Table 4). In contrast, history of previous glaucoma filtering surgery was the only significant predictor of MDM IOP being closer to target IOP in both univariate and multivariate models (Table 4).

Table 3. Quantification of Patients Whose Mean Daily Maximum Intraocular Pressure during Home Tonometry Exceeded Mean Clinic Intraocular Pressure* and Target Intraocular Pressure

Mean Daily Maximum Intraocular Pressure	No. (%)
MDM > mean clinic IOP (n = 107 eyes)	70 (65.4)
MDM > mean clinic IOP + 3 mmHg	39 (36.4)
MDM > mean clinic IOP + 5 mmHg	23 (21.5)
MDM > mean clinic IOP + 10 mmHg	6 (5.6)
MDM > mean clinic IOP × 120%	45 (42.1)
MDM > mean clinic IOP × 130%	32 (29.9)
MDM > maximum clinic IOP (n = 107 eyes)	47 (43.9)
MDM > maximum clinic IOP + 3 mmHg	22 (20.6)
MDM > maximum clinic IOP + 5 mmHg	11 (10.3)
MDM > maximum clinic IOP + 10 mmHg	4 (3.4)
MDM > maximum clinic IOP × 120%	23 (21.5)
MDM > maximum clinic IOP × 130%	15 (14.0)
MDM > target IOP (n = 74 eyes)	47 (63.5)
MDM > target IOP + 3 mmHg	23 (31.5)
MDM > target IOP + 5 mmHg	11 (15.1)
MDM > target IOP + 10 mmHg	4 (5.5)
MDM > target IOP × 120%	23 (31.1)
MDM > target IOP × 130%	18 (24.3)

IOP = intraocular pressure; MDM = mean daily maximum intraocular pressure during home tonometry trial.
Data are presented as number of eyes (percent) meeting the indicated criterion.
*Intraocular pressure recorded in the medical record during the 5 clinic visits preceding the home tonometry trial.

Glaucoma Management after Home Tonometry

Given that most home tonometry trials were ordered out of concern for disease progression or occult IOP elevation, we were interested in whether clinical management was changed for patients after their home tonometry trials and how that correlated with home tonometry metrics. Home tonometry trials were followed by advancement of glaucoma therapy for 55 of 95 eyes (58%). Therapy included surgery in 23 of 55 eyes (42%), addition of medication in 21 of 55 (38%), and laser trabeculoplasty in 11 of 55 eyes (20%). In 40 eyes, the ongoing treatment plan remained unchanged after home tonometry, and in 12 eyes, the results of self-tonometry were not specifically acknowledged as playing role in clinical decision making in the subsequent clinic note.

We next constructed generalized estimating equations that assessed the predictive values of various IOP metrics on the likelihood that glaucoma therapy was advanced, while accounting for intereye correlations of individual patients and controlling for potential confounding factors including age, gender, ethnicity, glaucoma type, specific ophthalmologist ordering the self-tonometry trial, history of glaucoma filtering surgery, pseudophakia, number

Table 4. Associations between Mean Daily Maximum Intraocular Pressure during Home Tonometry and Mean Clinic Intraocular Pressure or Target Intraocular Pressure*

	Univariable Analysis		Multivariable Analysis†	
	Coefficient	*P Value*	*Coefficient*	*P Value*
Dependent variable: difference between MDM and mean clinic IOP				
Age (yrs)	−0.11	**0.02**	−0.11	**0.02**
Female gender	−2.80	**0.03**	−2.88	**0.02**
White ethnicity	−2.18	0.14	−0.53	0.7
Glaucoma physician	0.36	0.3	—	—
Glaucoma type	0.03	0.9	—	—
Prior glaucoma filtering surgery	−2.53	**0.04**	−2.27	0.07
Pseudophakia	−2.69	**0.01**	−1.95	0.09
No. of glaucoma drops	0.20	0.5	0.38	0.2
Central corneal thickness (μm)	0.01	0.3	—	—
Visual field mean deviation	0.08	0.14	—	—
Dependent variable: difference between MDM and target IOP				
Age (yrs)	−0.09	0.2	−0.13	0.06
Female gender	−1.27	0.5	−2.29	0.2
White ethnicity	−2.03	0.3	0.59	0.8
Glaucoma physician	0.48	0.3	—	—
Glaucoma type	0.02	0.9	—	—
Prior glaucoma filtering surgery	−3.39	**0.02**	−3.97	**0.01**
Pseudophakia	−1.53	0.3	−0.51	0.7
No. of glaucoma drops	0.22	0.6	0.04	0.9
Central corneal thickness (μm)	0.02	0.13	—	—
Visual field mean deviation	0.10	0.2	—	—

IOP = intraocular pressure; MDM = mean daily maximum; — = not included in the multivariable model.
Boldface indicates $P < 0.05$.
*Results of generalized estimating equations, accounting for intereye correlations of individual patients.
†Multivariate analysis includes age, gender, ethnicity, prior glaucoma filtering surgery, pseudophakia, and number of glaucoma drops.

of glaucoma medications prescribed, central corneal thickness, and visual field mean deviation. As predicted, because clinicians ordered home tonometry trials to help guide clinical decision making, multiple home IOP metrics including mean daily IOP, home MDM IOP, home MDR IOP, and percentage of home IOP measurements more than the clinic average and clinical target IOP each were associated strongly with the ophthalmologist's recommendation to advance management, with odds ratios that ranged from 1.18 to 1.5 (Table 5). More importantly, however, our analyses demonstrated that no clinic-based IOP metrics predicted therapy advancement, suggesting that the home tonometry data provided information to the clinicians that was not captured in the clinic. Because of a high degree of colinearity between the variables, we were unable to assess all the IOP metrics in a multivariate model to

Table 5. Associations between Therapy Advancement and Various IOP Metrics Evaluated Using Adjusted* Generalized Estimating Equations, Accounting for Intereye Correlations of Individuals Using Advancement of Therapy after Home Tonometry Trial as the Dependent Variable

	No.	Odds Ratio	95% CI	*P* Value
Clinic IOP (mmHg)				
Mean	91	0.98	0.87–1.10	0.7
Range	82	0.96	0.86–1.06	0.4
Maximum	91	0.96	0.89–1.04	0.4
Home IOP (mmHg)				
Mean	91	1.25	1.08–1.44	**0.002**
Daily range	91	1.18	1.07–1.31	**0.001**
MDR	91	1.31	1.09–1.58	**0.004**
Daily MDM	91	1.22	1.08–1.37	**0.001**
Home MDM IOP minus clinic mean IOP	91	1.51	1.21–1.87	**< 0.001**
Home MDM IOP minus target IOP	67	1.34	1.10–1.64	**0.004**

CI = confidence interval; IOP = intraocular pressure; MDM = mean daily maximum; MDR = mean daily range.
Boldface indicates $P < 0.05$.
Association of each IOP measure with the outcome is derived from a separate multivariate model.
*Adjusted for age, gender, ethnicity, glaucoma type, specific physician making management decisions, prior glaucoma filtering surgery, pseudophakia, number of glaucoma medications, central corneal thickness, and visual field mean deviation.

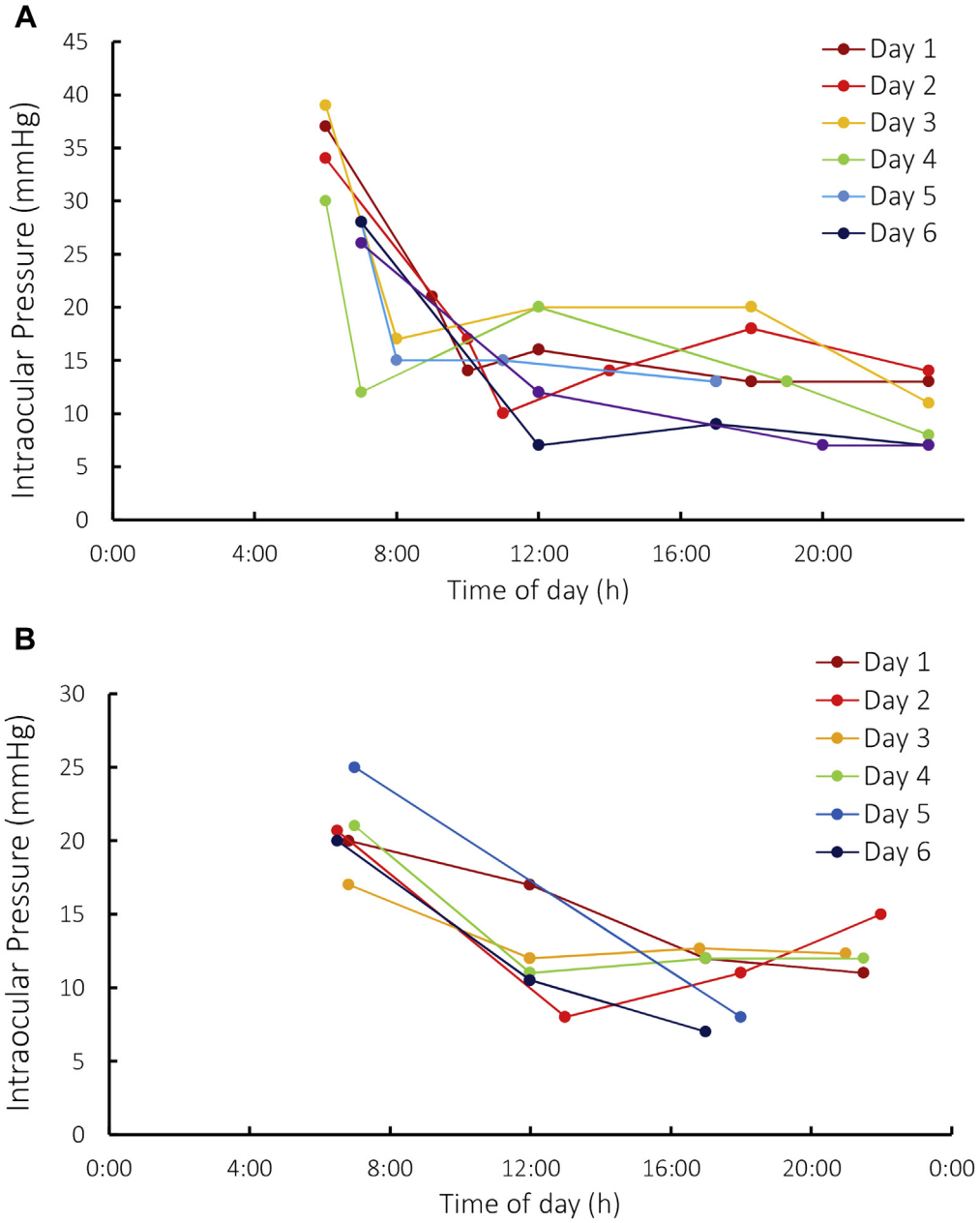

Figure 4. Line graphs showing examples of patients with reproducible out-of-office IOP spiking. **A**, This patient demonstrated reproducible elevation in intraocular pressure (IOP) to between 25 and 40 mmHg each morning at approximately 6 to 7 AM despite IOP measuring in the low teens in the clinic. **B**, This patient, with a low target pressure, demonstrated reproducible elevation in IOP to between 17 and 28 mmHg each morning at approximately 6 to 7 AM, despite IOP measurements in the low teens to single digits in the clinic. h = hours.

determine which was the most influential in the decision to change treatment.

Patient Examples

In a particularly illustrative case of a 42-year-old man with worsening glaucoma and clinic IOP in the low teens, home tonometry revealed morning home IOP consistently exceeding 25 mmHg and sometimes exceeding 35 mmHg, greatly above what was captured during clinic visits (Fig 4A). As a result of home tonometry, this patient subsequently underwent laser trabeculoplasty in both eyes. Another patient, a 69-year-old man with worsening glaucoma and clinic IOP measurements of 11 mmHg or less, exhibited a relatively sizeable spike in the morning compared with basal IOP levels throughout the day (Fig 4B). This patient subsequently underwent changes in medical management as a result of home tonometry findings. In both cases, daytime home measurements were more similar to the in-clinic IOPs recorded.

Discussion

This retrospective analysis of self-tonometry trials performed by glaucoma patients, as ordered by an ophthalmologist during the course of clinical care, provides several lines of evidence to suggest that a substantial subset of patients exhibit clinically significant IOP fluctuations that are not identified by clinic tonometry alone. First, although mean IOP actually was slightly lower during home tonometry, all measurements of IOP fluctuation and IOP spiking were significantly higher. Second, home MDM IOP exceeded the recent clinic maximum IOP in 44% of patients, and the MDM IOP was more than any historic IOP in chart data in 13% of patients. Third, MDM exceeded the target IOP in almost half of patients, and 24% of eyes manifesting MDM IOP over target showed no prior clinic IOP measured over target. Fourth, the peak home IOP occurred outside the 8:00 AM to 5:00 PM office hours window on half of the days studied. Therefore, home tonometry has potential to reveal clinically relevant IOP data not captured during clinic visits, even during clinic-based diurnal curves.

Identification of the 15% of patients whose IOP measurements routinely exceeded the IOP target by 5 mmHg and the 5.5% of patients whose IOP measurements routinely exceeded target by 10 mmHg is likely to be clinically relevant. In analyzing the current data, we aimed to develop home tonometry metrics that would be reliable (i.e., relatively resistant to artifactual inflation by spurious measurements) and clinically relevant. If further validated in prospective fashion, the MDM and MDR IOPs may meet these criteria. By averaging the daily IOP maximum or daily IOP range over several consecutive days of home tonometry, these metrics are representative of IOP exposure and fluctuation, respectively, over time. By comparing MDM IOP with the clinic IOP (Table 2), one can discern how representative a patient's clinic measured IOP is of the overall 24-hour IOP exposure. By comparing this metric with the target IOP, one can determine the extent to which the target IOP is exceeded in individual patients. Whether this metric might facilitate early identification of so-called rapid progressors requires further prospective clinical study.[28,29] For instance, we hypothesize that MDM IOP correlates positively with the rate of visual field progression in glaucoma patients. If such a correlation were demonstrated prospectively, then performing home tonometry in newly diagnosed glaucoma patients could yield important prognostic data that would be useful to guide initial treatment recommendations.

We attempted to identify patient or ocular characteristics that predict deviations between clinic and home tonometry. Our generalized estimating equations found that younger age, male gender, and history of previous glaucoma filtering surgery predicted significant discrepancy between home and clinic tonometry. In contrast, ethnicity, glaucoma physician, glaucoma type, prior cataract surgery, number of glaucoma drops, central corneal thickness, and visual field mean deviation were not predictive of disagreement between home MDM IOP and either mean clinic IOP or target IOP. Whereas these characteristics (young men without prior glaucoma surgery) may help to identify patients at significantly greater risk of manifesting occult IOP elevation on home tonometry, the predictive value of these factors at present is insufficient to recommend their use for narrowing the potential pool of home tonometry candidates to any subset of patients.

We identified a significant association between male gender and a larger discrepancy between clinic and home tonometry. Several studies have examined potential associations between biological gender and IOP, with inconsistent results.[30,31] In the Barbados Eye Study and others, female gender was associated positively with IOP, whereas in the UK Biobank Study, male gender was associated positively with IOP.[32–35] Although no clear consensus exists on the role of biological sex in IOP, our study demographic included a high proportion of White patients, which is probably more similar to patients studied in the UK Biobank cohort. Our findings likely were not attributable to differences in central corneal thickness because no statistically significant difference was found in pachymetry between men and women in our study (542.0 μm and 537.3 μm, respectively; $P > 0.5$). Any potential association between biological sex and out-of-office IOP spikes awaits a prospective, adequately powered clinical study.

Clinic IOP measurements, although important, capture a limited snapshot of a dynamic variable. Home tonometry may be particularly beneficial in patients with evidence of progressive optic nerve damage, despite consistently low in-clinic IOP,[12] as was the case for many patients in this study. In the 2 illustrative patients highlighted in Figure 4, it is noteworthy that the highest peaks in home IOP occurred at times outside the standard clinic hours, and in both patients, the midday home IOP was closer to clinic IOP, demonstrating the limitation of isolated IOP measurements. Therefore in some patients, home tonometry can help to identify occult IOP elevation over target, thereby providing a supportive rationale for more aggressive IOP-lowering therapy, including surgery. In contrast, home tonometry consistently demonstrating IOP under target either may validate current therapy or should lead to a further reduction of the target IOP in patients with progressively worsening disease, with advancement of therapy as needed.[36]

Critically, our analyses do not assess whether these IOP fluctuations were predictive of worsening disease. Indeed, the retrospective nature of the study and the fact that most clinicians ordered the test out of concern for disease worsening precludes drawing such conclusions. Moreover, it is not surprising that a large difference in home IOP metrics was found when comparing patients whose therapy was advanced versus continued, because treating physicians were likely to respond to self-tonometry data, having ordered the test to aid in decision making. What is more interesting, however, is that none of the baseline characteristics or clinic IOP metrics were different between these groups. The lack of association between clinic IOP and management advancement suggests that, for this particular group of patients, home tonometry contributed independent IOP-based information on which the physician acted, a critical characteristic for home tonometry to be a meaningful adjunct to clinic tonometry. Previous retrospective studies

reported an association between large diurnal variation observed with self-tonometry and previous glaucoma progression[15,20]; however, prospective studies are needed to confirm this finding to guard against selection bias and to evaluate the predictive value of home tonometry. The clinical usefulness of home tonometry can be surmised only if it is demonstrated that home IOP measurements provide data that: (1) are distinct from in-clinic data for at least a subset of patients (as demonstrated herein), (2) are predictive of future disease worsening, and (3) alter treatment behavior in a way that improves clinical results. Ongoing prospective clinical studies therefore are warranted to assess the predictive power of home tonometry metrics for future glaucoma progression, and this study serves as a foundation for those efforts.

In a recent prospective study using the iCare HOME tonometer in a cohort of patients after medication washout, Tatham et al[27] demonstrated the ability of home tonometry to capture more IOP events and identified a larger peak and SD in IOP in home measurements compared with clinic-based measurements. McGarva et al[22] showed in 18 patients that iCare HOME tonometry yields a progressively greater range in IOP as the duration of monitoring is extended. Thus, prior work supports the imprecise nature of relying on in-clinic tonometry for establishing a target IOP based on the maximum recorded IOP and judging responses to advance therapy. Of note, Tatham et al examined only eyes with "low-tension glaucoma" after washout, which limits the broader application of those findings. In our study, we characterize IOP for any patients who were receiving active treatment for primary or secondary glaucoma. Our study reiterates the importance of viewing IOP as a dynamic variable and highlights the potential incomplete characterization of untreated IOP using clinic-based measurements alone. This notion alone is not new. More than half a century ago, Drance[37] reported findings on diurnal variation in IOP showing larger fluctuation in patients with untreated glaucoma compared with nonglaucomatous eyes. However, the historic motivation for 24-hour IOP monitoring has been to identify latent high IOP (i.e., more than 21 mmHg). Herein, we propose a paradigm shift in searching for IOP elevation at more than a target IOP rather than an arbitrary threshold value.

Besides capturing occult IOP elevation, home tonometry has been used as a potential adjunctive source of clinical data in the management of childhood glaucoma. A previous studying using the iCare model TA01 rebound tonometer in children with glaucoma reported that IOP, obtained by the child's guardian in the home setting, led to a change in medical therapy in 76% of participants and prompted or validated the decision for surgery in 55% of participants.[38] Our study of adults performing self-tonometry suggests that relatively fewer patients exhibit clinically significant out-of-office IOP fluctuation, even in a selected sample in which such fluctuations were suspected by the ordering clinician. Data also are building to support the implementation of home tonometry in specific clinical situations. iCare rebound tonometry was useful for identifying a luminal tube opening in a group of pediatric patients after tube shunt implantation, guiding postoperative management in real time.[24] In a group of patients starting latanoprost, iCare HOME measurements demonstrated a significant response to therapy beginning 24 hours after drop initiation.[23] Self-tonometry in patients for 1 week before and 1 week after selective laser trabeculoplasty can confirm overall reduction in IOP as well as absence of IOP spikes after laser treatment.[25]

Other devices that permit remote monitoring of IOP may enable a more complete understanding of glaucoma patients' overall IOP exist or are under development. The Sensimed Triggerfish (Sensimed AG, Lausanne, Switzerland) contact lens is a wearable sensor that provides real-time information about IOP-related ocular dimensions and has been used extensively in the research setting to elucidate 24-hour IOP profiles and to discern the effects of IOP-lowering therapies.[39–42] However, its output is an indirect approximation of IOP as measured in millivolt equivalents rather than millimeters of mercury. An intraocular IOP sensor (EYEMATE-IO; Implandata Ophthalmic Products) is under development,[43] but requires implantation during cataract surgery, making its usefulness reasonable likely for only a subset of patients. Further work is underway in the development of an injectable IOP sensor (Injectsense; Injectsense, Inc); however, this technology is not yet available for clinical use. Therefore, for the time being, home self-administered rebound tonometry represents a particularly accessible approach to identifying occult IOP elevation.

Study limitations include the retrospective study design and selection bias as previously described. In addition, clinic IOP was measured using GAT in the vast majority of patients, and occasionally iCare rebound tonometry, whereas all home IOP measurements were obtained with the iCare HOME tonometer. Importantly, however, certification trials before home self-tonometry confirmed reasonable agreement between iCare HOME measurements and in-clinic GAT. In addition, although comparison of IOP using 2 different devices could introduce systematic bias, the mean difference between concurrent applanation and iCare HOME tonometry is less than 0.5 mmHg, with more than 91% of individuals achieving iCare values within 5 mmHg of GAT measurements.[16]

In summary, our findings suggest that home tonometry can identify a substantial subset of at-risk glaucoma patients whose IOP during clinic visits does not capture manifest large IOP deviations outside of office hours. Further prospective studies are needed to confirm the validity of home tonometry to aid in glaucoma decision making by assessing whether home tonometry is independently predictive of future glaucoma disease worsening.

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Author Contributions:

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Analysis and interpretation: McGlumphy, Mihailovic, Ramulu, Johnson

Data collection: McGlumphy, Ramulu, Johnson

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Abbreviations and Acronyms:
GAT = Goldmann applanation tonometry; **IOP** = intraocular pressure; **MDM** = mean daily maximum; **MDR** = mean daily range; **SD** = standard deviation.

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