Risk Factors for Poor Adherence to Eyedrops in Electronically Monitored Patients with Glaucoma

David S. Friedman, MD, PhD,[1,2] Constance O. Okeke, MD, MSCE,[3] Henry D. Jampel, MD, MHS,[1] Gui-shuang Ying, PhD,[3] Ryan J. Plyler, BA,[1] Yuzhen Jiang, MD, PhD,[4] Harry A. Quigley, MD[1]

Purpose: To identify risk factors for poor adherence to topical once daily therapy for glaucoma.

Design: Prospective, observational cohort study.

Participants: A total of 196 patients with glaucoma who were being treated with a prostaglandin analog in 1 or more eyes at the Scheie or Wilmer Eye Institutes between August 2006 and June 2007.

Methods: Demographics, ocular history, and responses to interview questions about glaucoma knowledge, health beliefs, and drop-taking behaviors were obtained from each patient. All patients used the Travatan Dosing Aid (DA; Alcon Laboratories Inc., Fort Worth, TX) to administer travoprost as prescribed. Devices were collected at 3 months, and the data of drop use were downloaded using software provided with the DA. Patients taking ≤75% doses during the 8-week period starting 2 weeks after the enrollment visit and ending 2 weeks before the 3-month visit were compared with those taking >75% of doses.

Main Outcome Measures: Risk factors for poor adherence.

Results: Eighty-seven patients (44.4% of the 196 subjects with evaluable data at 3 months) used the DA on 75% or less of the monitored days. In univariate analysis, poorer adherers were more likely to be <50 or ≥80 years of age, to be African American, to report less than excellent health, to report higher amounts of depression, to have lower income, and to be treated at the Scheie Eye Institute. Multivariate analysis (adjusting for education and income) found that age, race/ethnicity, and less than excellent health were associated with poor adherence.

Conclusions: Those who failed to take more than 75% of eyedrop doses were more likely to be African American and to report poor health. Those in the youngest and oldest age groups were less adherent, although this finding was not always statistically significant. Further research into the factors driving these associations and into developing predictive models to assist in screening for low adherence are warranted.

Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references.
Ophthalmology 2009;116:1097–1105 © 2009 by the American Academy of Ophthalmology.

Adherence to medical therapies for chronic diseases is known to be suboptimal, with approximately 70% of prescribed doses taken.[1–8] These findings are consistent across many disease states and have recently been documented in multiple studies to be similar for patients with glaucoma using topical ocular hypotensives.[9–11] Physicians cannot accurately predict who is complying with medical therapy,[12–14] and this failure frustrates effective intervention among the least adherent individuals. To improve the efficacy of glaucoma treatment, we must both identify patients who are poorly adherent and develop interventions that improve drop-taking behavior.

Becker and Maiman[15] reviewed social and psychologic factors associated with adherence to medical recommendations and medication use including motivators, such as concern about the illness, beliefs (e.g., likelihood of treatment success), and demographics, to create a model summarizing patient behaviors. A recent major review summarized the known associations with poor adherence, and these include psychologic problems (especially depression) and cognitive impairment.[16] Furthermore, the authors noted that adherence is worse when the following are present: asymptomatic diseases, barriers to obtaining medications, complex treatments, high cost of medications, and a poor doctor–patient relationship.

These analyses for systemic disease treatments are consistent with recent findings on patient adherence to topical glaucoma agents. Patient concern about glaucoma and cost of medications was associated with poor adherence in patients with glaucoma, calculated from pharmacy refill data and interviews.[17] Other factors associated with poor ocular adherence included ethnicity, traveling away from home, learning about glaucoma exclusively from the doctor, and not reporting medication side effects. Pharmacy claims are a surrogate for patient adherence with therapy;[18,19] electronic monitoring is a more accurate, direct measure.[20]

We report on the risk factors associated with poor adherence to topical ocular hypotensive agents as documented over 3 months with an electronic monitor attached to bottles of prostaglandin eyedrops.

Patients and Methods

The study protocol has been published.[14] In brief, patients 18 years of age or older taking a prostaglandin eyedrop for open-angle

ISSN 0161-6420/09/$–see front matter
doi:10.1016/j.ophtha.2009.01.021

glaucoma, angle-closure glaucoma, or ocular hypertension were recruited from the Glaucoma Services of the Wilmer Eye Institute and the Scheie Eye Institute. Institutional review boards at both centers approved the study protocol, and written informed consent was obtained from all study subjects. Subjects who underwent eye surgery during the study were censored at the time of surgery. Patients were excluded if they were unable to understand the study, did not instill their own drops, or were incapable of using the Travatan Dosing Aid (DA; Alcon Laboratories Inc., Fort Worth, TX) device despite a practical demonstration.

Patient Recruitment and Follow-up

Consenting patients who were using latanoprost or bimatoprost were switched to travoprost during the study because only its bottle fits the electronic monitor. Sufficient travoprost bottles for the study period were provided at no charge to participants. Baseline demographic and medical information, including age, gender, self-reported ethnicity, presence of comorbid diseases, ocular medications and dosage, systemic medications and dosage, family history of glaucoma, baseline untreated intraocular pressure (IOP) of each eye (if available), length of past glaucoma treatment and types of past ocular medication, including allergies and severe side effects, and target IOP of each eye, were obtained from the chart. We recorded whether prostaglandin eyedrops were prescribed unilaterally or bilaterally. Income level was estimated from home address zip code. In addition, all IOP measures of each eye and medications for the preceding 2 years were summarized for comparison with IOP measured during the study. Data for each eye from the most recent visual fields and most recent evaluation of the optic disc by clinical assessment, laser imaging, or photography were also recorded.

Consenting patients responded to a brief self-administered questionnaire on attitudes about eyedrop taking, their own assessment of their adherence with topical ocular hypotensives, self-reported health,[21] and presence of depression (using the 10-item Center for Epidemiologic Studies Short Depression scale).[22] They were also asked about the impact of glaucoma on their vision and attitudes and understanding of glaucoma.

The DA device records the time and date when the lever that releases a drop of travoprost is depressed. Subjects were told that the device records when the lever is depressed. All patients were also told that the DA was being assessed for its ability to aid the patient in delivering the eyedrops. Patients were instructed to use the device to deliver their travoprost each night until the 3-month follow-up visit. A telephone call was made at 1 week to ask if the patient was having difficulty using the device. If there were problems, the patient was asked to return to the clinic to undergo repeat instruction in using the DA, and the 3-month follow-up period was restarted from that point. If the patient did not feel comfortable using the device after the repeat instruction, the patient was removed from the study.

Patients brought their DA device to the 3-month visit, the information was downloaded, the battery was changed as necessary, and a questionnaire was administered to estimate self-reported adherence and satisfaction with the device. At the 3-month visit, visual acuity and applanation IOP were measured. The downloaded data from the DA were used to identify patients taking 75% or less of the daily doses. Because it has been demonstrated that patient adherence is artificially higher just after and before doctor visits,[14,23] the adherence rate was calculated from 2 weeks after the baseline visit until 2 weeks before the follow-up visit. A dose was considered taken if the lever of the DA was depressed and recorded within 4 hours of the routine dosing hour for the appropriate number of eyes. For example, if 10 PM was the patient's median dosing hour and the prescribed medication was for unilateral use, then any dose taken between 8 PM and 12 AM was considered taken appropriately. Because we recognized from our previous study[24] that the device has the potential to make extra recordings when the lever is depressed, we did not count more than 1 dose taken per eye per day in our adherence rate calculation. When the lever was depressed outside the time window, it was assumed that a dose was not taken.

Statistical Analysis

Baseline characteristics were compared between the patient group who took more than 75% of the doses (defined as "adherent") and the group who took 75% or less of the doses ("poorly adherent"), using the Fisher exact test for comparison of proportions and the Student's *t* test for the comparison of means. Subjects with missing data were excluded from the analysis. The identification of risk factors for poor adherence started with the univariate logistic regression models, comparing those with adherence greater than and less than 75%, and with univariate linear regression models for adherence rate as a continuous variable.

The risk factors associated with $P<0.10$ were included in the multivariate models. Multivariate models were further simplified by using stepwise selection to keep only statistically significant or marginally significant risk factors ($P<0.10$). Because of the right-skewed distribution of the adherence rate (longer on the lower adherence side), it was first log-transformed to a normal distribution by using the formula: log adherence rate = log10 (1-adherence rate), and the log-transformed adherence rate was then used in linear regression models to identify significant risk factors associated with the adherence rate.

Results

A total of 282 patients were identified between the 2 sites, 86 (30%) withdrew before 3 months, leaving 196 subjects (70%) with complete data on drop-taking behavior at 3 months. Those who completed the study were more likely to be male and white, and to report "excellent" health than those who did not, but they did not differ in ocular characteristics.[14] Among demographic factors, those associated with poorer adherence in the models using continuous adherence rate included age, ethnicity, health, and other variables. Those aged younger than 50 years and older than 80 years had lower adherence rates than those between 50 and 80 years of age in univariate analysis (Table 1). African Americans had lower mean adherence (0.64) than whites (0.77, $P<0.001$). Furthermore, lower educational achievement and lower family income were associated with lower mean adherence in univariate analysis ($P<0.05$). Participants with a higher depression score or worse self-reported overall health also had lower mean adherence ($P<0.01$ for both). Attendees of the University of Pennsylvania Scheie Glaucoma Service had lower adherence than those attending Johns Hopkins Wilmer Glaucoma Service. Similar associations were seen when defining poor adherence categorically as taking ≤75% of doses (Table 1).

Among ocular factors, those with higher visual field mean deviation had a lower mean adherence ($P = 0.06$, test for trend) and were more likely to have an overall adherence rate ≤0.75 ($P = 0.03$, test for trend, Table 2). Other ocular risk factors, including the cup:disc ratio, the IOP, and the use of medication in 1 eye compared with both eyes, were not associated with the mean adherence rate.

Patients' attitudes and knowledge of glaucoma and their self-reported use of topical ocular hypotensive agents were associated with adherence rates in univariate analysis. Those who stated that they used their eyedrops "every day" or "all but 1 or 2 days" in the last 3 months at baseline had higher adherence rates (mean of 0.73

Table 1. Univariate Baseline Factors Associated with Adherence

Risk Factors	N	Adherence ≤75%; n (%)	*P* Value* (Trend *P* Value)	Adherence Rate Mean (SE)	*P* Value* (Trend *P* Value)
Age (yrs)			0.01		0.005
<50	22	15 (68.2%)		0.60 (0.05)	
50–59	49	15 (30.6%)		0.77 (0.03)	
60–69	53	23 (43.4%)		0.73 (0.03)	
70–79	52	21 (40.4%)		0.72 (0.03)	
≥80	20	13 (65.0%)		0.60 (0.05)	
Sex			0.47		0.08
Female	82	39 (42.6%)		0.67 (0.03)	
Male	114	48 (42.1%)		0.74 (0.02)	
Race			0.0005		0.0005
Black	90	53 (58.9%)		0.64 (0.02)	
White	100	32 (32.0%)		0.77 (0.02)	
Asian	6	2 (33.3%)		0.80 (0.09)	
Education			0.20 (0.07)		0.15 (0.03)
Less than high school	18	12 (66.7%)		0.56 (0.05)	
High school	49	22 (44.9%)		0.69 (0.03)	
College	77	32 (41.6%)		0.73 (0.03)	
Graduate school	50	19 (38.0%)		0.76 (0.03)	
General health			0.07 (0.03)		0.01 (0.007)
Excellent	51	16 (31.4%)		0.78 (0.03)	
Good	116	55 (47.4%)		0.70 (0.02)	
Fair/poor	29	16 (55.2%)		0.62 (0.04)	
Depression score			0.16 (0.04)		0.07 (0.008)
≤0.1	72	26 (36.1)		0.76 (0.03)	
0.1–0.3	44	18 (40.9)		0.73 (0.03)	
0.3–0.7	38	21 (55.3)		0.70 (0.04)	
0.7–2.5	42	22 (52.4)		0.61 (0.04)	
Family income†			0.12 (0.07)		0.02 (0.02)
≤35 K	48	29 (60.4)		0.61 (0.03)	
35–50 K	47	19 (40.4)		0.74 (0.03)	
50–75 K	42	17 (40.5)		0.74 (0.04)	
>75K	53	21 (39.6)		0.74 (0.03)	
Institute					
Johns Hopkins	161	66 (41.0)	0.04	0.74 (0.02)	0.006
UPenn	35	21 (60.0)		0.59 (0.04)	

SE = standard error; UPenn = University of Pennsylvania Scheie Eye Institute.
Patients who did not complete the first 3 months of study were excluded; patients (n = 15) who used Travatan (Alcon Laboratories Inc., Fort Worth, TX) without using the device during the study at least once per week were also excluded.
*From the Fisher exact test.
†Based on zip code.

and 0.74, respectively) than those who reported missing their drops more often than this (mean adherence 0.50, Table 3). Similarly, those who somewhat or strongly disagreed with the statement "some days I forget to take one of my doses of glaucoma medicines" had higher mean adherence rates than those who reported otherwise (0.75 vs. 0.62, $P<0.001$, Table 3). Patients reporting side effects had equal adherence rates to those not reporting them.

A correct understanding of glaucoma's effects on vision and glaucoma therapy was associated with better adherence. For example, patients who agreed with the statement that glaucoma treatment, "will keep my vision from getting worse" had a significantly higher mean adherence rate (0.73) than those who thought that glaucoma treatment would "improve vision" or "not do much" (0.54, $P<0.01$). Further evidence for the association between knowledge and adherence was the finding of poorer adherence among those who 1) did not know that topical ocular hypotensive agents work by decreasing eye pressure ($P<0.05$) or 2) thought that prostaglandins could be taken more than once per day or were unsure of how often prostaglandins should be taken ($P = 0.10$). The number with such poor understanding on how often to take drops was small, however, and the result was not statistically significant.

In a multivariate analysis looking at mean adherence rate as a continuous variable, those baseline variables associated with better adherence were middle-aged group (50–79 years), white race, and better general health (Table 4). In a logistic regression model with poor adherence judged categorically as taking ≤75% of doses, the same variables were associated with higher adherence: middle-aged group ($P<0.05$), white race ($P<0.05$), and self-reported excellent health ($P = 0.06$) (Table 5). A more extensive multivariate model was constructed to include 3-month interview data as independent variables with mean adherence rate as the dependent variable. This model found that better adherence was associated with age group 50 to 79 years, white race, excellent general health, reporting taking drops either "every day" or "all but 1 or 2 days" in the past 2 weeks, and reporting that glaucoma treatment will "keep my vision from getting worse" as opposed to "improve vision" or "not do much" (Table 6). Findings were similar when the model including interview data was constructed with adherence dichotomously as ≤75% of drops taken, except that 2 vari-

Table 2. Univariate Baseline Glaucoma-related Factors Associated with Adherence

Risk Factors	N	Adherence ≤75%; n (%)	*P* Value* (Trend *P* Value)	Adherence Rate Mean (SE)	*P* Value* (Trend *P* Value)
Worse Eye CDR			0.77 (0.48)		0.77 (0.54)
≤0.7	55	26 (47.3)		0.70 (0.03)	
0.7–0.9	112	51 (44.6)		0.70 (0.02)	
>0.9	26	10 (38.5)		0.74 (0.05)	
Mean deviation of worse eye			0.06 (0.03)		0.14 (0.06)
≤5 db	83	32 (38.6)		0.75 (0.03)	
5–15 db	50	20 (40.0)		0.67 (0.03)	
>15 db	57	33 (57.9)		0.69 (0.03)	
IOP of worse eye			0.26 (0.30)		0.38 (0.83)
≤15	68	29 (42.7)		0.72 (0.03)	
15–17	42	18 (42.9)		0.69 (0.04)	
17–20	44	16 (36.4)		0.76 (0.04)	
>20	42	24 (57.1)		0.67 (0.04)	
Time using glaucoma medications			0.70		0.13
≤1 yr	31	15 (48.4)		0.64 (0.04)	
>1 yr	162	71 (43.8)		0.72 (0.02)	
Use of medicine			1.00		0.32
Unilateral	49	22 (44.9)		0.69 (0.03)	
Bilateral	147	65 (44.2)		0.72 (0.02)	
Glaucoma Medications			0.96		0.34 (0.19)
Travoprost only	97	44 (45.4)		0.68 (0.02)	
2 agents	66	29 (43.9)		0.73 (0.03)	
>2 agents	33	14 (42.4)		0.74 (0.04)	

CDR = cup:disc ratio; IOP = intraocular pressure; SE = standard error.
Patients who did not complete the first 3 months of study were excluded; patients (n = 15) who used Travatan without using the device during the study at least once per week were also excluded.
*From the Fisher exact test.

ables were no longer significant: self-reported health and the reporting that glaucoma treatment will "keep my vision from getting worse" (Table 7). Finally, patients were more likely to be adherent if they somewhat or strongly disagreed with the statement "some days I forget to take one of my doses of glaucoma medicines" (odds ratio = 2.08; 95% confidence interval, 0.96–4.55), but this result did not reach statistical significance.

Identical multivariate linear and logistic regression models were constructed to assess our 90 African American participants alone. In these, age <50 years and ≥80 years, worse general health ($P = 0.06$), higher depression score, and clinic location were associated with lower adherence in univariate analysis, as in the larger study group. In addition, those taking medications for ≤1 year were less adherent (0.53 vs. 0.67, $P = 0.06$). In a multivariate model, age, general health, and clinic location remained statistically significant for this subgroup.

Discussion

The current study adds substantially to previous work by Kass et al[12,25] that assessed predictors of adherence among subjects taking pilocarpine eyedrops. We now have identified additional factors associated with lower adherence to topical therapy, including African American ethnicity, poor self-reported drop taking, poor patient knowledge about glaucoma and its eyedrop treatment, and, in some analyses, the extremes of age. In a previous study, patient self-report was weakly but significantly correlated with actual adherence as measured by an electronic monitor (R = 0.2).[12] However, the only predictors of adherence in a final multivariate model in that study were the weight of the bottle at the end of the study, the size of the pupil on examination (for patients taking pilocarpine), and physician estimate of patient compliance. We have reported previously that physician estimates are correlated with patient adherence rates, but poorly so, and they add little to the overall identification of patients who are poorly adherent.[14]

The factors associated with adherence rate in this study are similar to those previously reported in studies of patients with other chronic diseases. In a literature review on systemic therapy, Osterberg and Blaschke[16] found that predictors of poor adherence included treatment of asymptomatic disease, lack of insight into the illness, and presence of depression. These factors affect many patients with glaucoma and were present in poor adherers in the current study. Similarly, African American ethnicity has been reported as a predictor of poor adherence in a recent study of lipid-lowering therapy[26] and was identified as a substantial risk factor for lower use of glaucoma medicines in a study of insured patients diagnosed with glaucoma in the United States.[17] African American ethnicity might appear as a risk factor if covariables such as income level, educational attainment, or general health status were systematically associated with ethnicity. However, in our data, ethnicity remained associated with poor adherence even after adjustment in multivariate analyses for these and other variables. Furthermore, we had substantial numbers of

Table 3. Univariate Analysis of Factors Associated with Adherence ≤75% and Overall Adherence Rate using the 3-Month Follow-Up Questionnaire[‡]

Risk Factors	N	Adherence Rate ≤0.75 n (%)	P Value*	Adherence Rate Mean (SE)	P Value[†]
Past 3-mo glaucoma drop use			0.003		0.0006
Every day	114	41 (36.0%)		0.73 (0.02)	
All but 1 or 2 days	61	30 (49.2%)		0.74 (0.03)	
Not for >2 days	20	15 (75.0%)		0.50 (0.05)	
Some days forget to take one of my doses of glaucoma medicines			0.0009		<0.0001
Strongly/somewhat/neither agree	59	38 (64.4%)		0.62 (0.03)	
Somewhat/strongly disagree	136	48 (35.3%)		0.75 (0.02)	
Experienced any side effect			0.87		0.71
Yes	53	24 (45.3%)		0.68 (0.03)	
No	141	62 (44.0%)		0.72 (0.02)	
The most drops taken in 1 day for each treated eye is			0.07		0.10
1	181	77 (42.5%)		0.72 (0.02)	
2 or "don't know"	15	10 (66.7%)		0.60 (0.06)	
These drops work primarily by			0.48		0.08
Lower eye pressure	164	71 (43.3%)		0.72 (0.02)	
Other/don't know	32	16 (50.0%)		0.66 (0.04)	
Glaucoma treatment will			0.051		0.003
keep my vision from getting worse	169	70 (41.4%)		0.73 (0.02)	
improve vision or not do much	25	16 (64.0%)		0.54 (0.05)	
Use the glaucoma drops in past 2 wks			0.02		0.002
Every day	140	54 (38.6%)		0.74 (0.02)	
All but 1 or 2 days	36	19 (52.8%)		0.71 (0.04)	
Not >2 days	20	10 (70.0%)		0.48 (0.06)	
Some days I forgot to take one of my doses of glaucoma medicines			0.03		0.01
Strongly/somewhat agree	63	35 (55.6%)		0.67 (0.03)	
Neither/somewhat/strongly disagree	127	48 (37.8%)		0.74 (0.02)	
I am the sort of person who follows doctor's orders exactly			0.22		0.13
Strongly agree	148	62 (41.9%)		0.73 (0.02)	
Others	48	25 (52.1%)		0.66 (0.03)	
Using glaucoma medications every day may cause long-term problems			0.34		0.21
Strongly/somewhat/neither agree	55	28 (50.9%)		0.68 (0.03)	
Somewhat/strongly disagree	140	59 (42.1%)		0.72 (0.02)	
I have an easy time remembering to take my Travatan once per day			0.24		0.04
Strongly agree	146	60 (41.1%)		0.73 (0.02)	
Others	45	23 (51.1%)		0.66 (0.04)	
I don't like the idea of using glaucoma drops			0.08		0.13
Strongly agree	29	12 (41.4%)		0.69 (0.04)	
Somewhat agree	20	11 (55.0%)		0.66 (0.05)	
Agree	12	1 (8.33%)		0.84 (0.07)	
Somewhat disagree	24	12 (50.0%)		0.65 (0.05)	
Strongly disagree	109	51 (46.8%)		0.72 (0.02)	

SE = standard error.
*From Fisher exact test.
[†]From the 1-way analysis of variance.

persons of both European and African derivation to compare in these data. Adjustment may have been inexact for income, because this was based on zip code alone. Note that access to health care and cost of medications were not possible factors in this study, because drugs were provided free and participants were patients with insurance coverage for visits.

The ethnic association with adherence is potentially explained by factors unmeasured here that are associated with ethnicity and that could influence patient decisions regarding medication use. In a detailed review of patient–doctor interactions, Cooper et al[27] summarized a body of publications that show that patient–doctor dynamics may vary depending on the ethnicity of the physician and the patient. This article points out that studies of interactions with African American patients have shown that physicians demonstrate less nonverbal attention, empathy, courtesy, and information giving; are more technical in their communications; spend less of the total time educating African American patients, carrying on small

Table 4. Multivariate Analysis of Baseline Factors Associated with Adherence Rate

Risk Factors	N	Mean Adherence Rate (SE)*	*P* Value† (*P* Value for Linear Trend‡)
Age (yrs)			0.002
<50	22	0.60 (0.06)	
50–59	49	0.78 (0.04)	
60–69	53	0.76 (0.05)	
70–79	52	0.75 (0.05)	
≥80	20	0.65 (0.06)	
Race			0.002
Black	90	0.62 (0.03)	
White	100	0.73 (0.03)	
Asian	6	0.77 (0.09)	
General health			0.03 (0.02)
Excellent	51	0.77 (0.04)	
Good	116	0.70 (0.03)	
Fair/poor	29	0.65 (0.05)	

SE = standard error.
*From least square means.
†For the test of any difference among levels of a risk factor.
‡From test of linear trend.

Table 6. Multivariate Analysis of Factors Associated with Adherence Rate

Risk Factors	N‡	Mean Adherence Rate (SE)*	*P* Value†
Age (yrs)			0.005
<50	21	0.55 (0.06)	
50–59	49	0.69 (0.04)	
60–69	53	0.68 (0.05)	
70–79	51	0.66 (0.05)	
≥80	20	0.55 (0.06)	
Race			0.01
Black	89	0.54 (0.03)	
White	99	0.62 (0.04)	
Asian	6	0.72 (0.09)	
General health			0.007
Excellent	49	0.67 (0.05)	
Good/fair/poor	145	0.59 (0.04)	
In past 2 wks I used my glaucoma drops			0.0002
Every day	138	0.72 (0.04)	
All but 1 or 2 days	36	0.67 (0.05)	
Not for >2 days	20	0.48 (0.06)	
Glaucoma treatment will			0.03
keep my vision from getting worse	169	0.70 (0.04)	
improve vision, or not do much	25	0.55 (0.05)	

SE = standard error.
*From least square means with all listed covariates in the multivariate model.
†For the test of any difference among levels of a risk factor.
‡Two patients were excluded because of missing data in the question on glaucoma treatment.

talk, and answering questions; and are more verbally dominant and exhibit more negative emotional tone than with white patients.

In the present research, one physician was African American, but the African American patients attending her clinic were less well educated, more often depressed, and had been taking medications for 1 year or less more frequently than those treated by the European-derived physicians at the other glaucoma service. It is not possible to draw firm conclusions about the effect of the race of the physician on patient adherence. Further research is needed to understand more clearly what factors produce the lower adherence rate seen among African Americans in the current study.

Some variables were present in the univariate analysis but not in multivariate regression. Depressive symptoms as measured using the 10-item Center for Epidemiologic Studies Short Depression scale were associated with lower adherence rates, but this association was not statistically significant after adjusting for other factors. Others have found that depression is associated with lower adherence.[26,28,29] In one study, patients who had myocardial infarction were interviewed before discharge,

Table 5. Multivariate Analysis of Baseline Factors Associated with Adherence ≤75%

Risk Factors	N	Adherence ≤75%; n (%)	Odds Ratio (95% CI)*	*P* Value	Overall *P* Value
Age (yrs)					0.01
<50	22	15 (68.2%)	3.87 (1.25–12.0)	0.02	
50–59	49	15 (30.6%)	0.64 (0.27–1.52)	0.31	
60–69	53	23 (43.4%)	1.00		
70–79	52	21 (40.4%)	0.88 (0.39–2.00)	0.76	
≥80	20	13 (65.0%)	2.46 (0.80–7.58)	0.12	
Race					0.003
Black	90	53 (58.9%)	1.00		
White	100	32 (32.0%)	0.34 (0.17–0.63)	0.0008	
Asian	6	2 (33.3%)	0.38 (0.06–2.39)	0.30	
General health					0.06
Excellent	51	16 (31.4%)	1.00		
Good/fair/poor	145	71 (49.0%)	2.11 (0.99–4.53)	0.06	

CI = confidence interval.
*From multivariate logistic regression with the listed risk factors (ie, age, race, general health) in the same model.

Table 7. Multivariate Analysis of Baseline and Follow-Up Factors Associated with Adherence ≤75%

Risk Factors	N†	Adherence ≤75%; n (%)	Odds Ratio (95% CI)*	*P* Value	Overall *P* Value
Age (yrs)					0.06
<50	21	14 (66.7%)	1.55 (0.46–5.22)	0.48	
50–59	49	15 (30.6%)	0.51 (0.21–1.27)	0.15	
60–69	53	23 (43.4%)	1.00		
70–79	52	21 (40.4%)	1.01 (0.44–2.34)	0.97	
≥80	20	13 (65.0%)	2.88 (0.91–9.09)	0.07	
Race					0.004
Black	90	53 (58.9%)	1.00		
White	99	31 (31.3%)	0.33 (0.17–0.64)	0.0009	
Asian	6	2 (33.3%)	0.55 (0.08–3.52)	0.52	
In past 2 wks I used my glaucoma drops					0.07
Every day	139	53 (38.1%)	1.00		
All but 1 or 2 days	36	19 (52.8%)	1.35 (0.64–2.83)	0.43	
Not for >2 days	20	14 (70.0%)	4.18 (1.22–14.2)	0.02	
Some days I forgot to take one of my doses of glaucoma medicines					0.06
Strongly/somewhat/neither agree	59	38 (64.4%)	1.00		
Somewhat/strongly disagree	136	48 (35.3%)	0.48 (0.22–1.04)	0.06	

CI = confidence interval.
*From multivariate logistic regression with the listed risk factors in the same model.
†One patient was excluded because of missing data in the question on use of drops in past 2 wks.

and those who had higher scores on a depression inventory were more likely to be poorly adherent to post-hospitalization medical therapy.[28] A recent meta-analysis found that patients with depression are 3 times as likely to fail to adhere to medical therapy or treatment recommendations.[5] The fact that depression was not statistically significant in the adjusted analysis may be due to small sample size or a relatively limited range of reported depressive symptoms in this clinic-based population of patients willing to participate in clinical research. It seems plausible that those who are depressed might be less likely to take their glaucoma medicines. Future studies should assess this plausible hypotheses in greater depth.

Lower adherence was found among patients with poor knowledge of glaucoma treatments and those unaware of what eyedrops do, how often they are taken, or what their purpose is. Higher adherence has been demonstrated among Korean hypertensive patients who were better informed,[30] but this was not found to be the case in a Veterans Administration cohort studied in the United States.[29] We previously found that patients who derive all their glaucoma information from physicians have lower adherence than those who seek additional knowledge on their own.[17] Perhaps knowledge seeking beyond the office is a surrogate for a more proactive approach to one's own health care. We have also reported greater adherence among those who were concerned about vision loss from glaucoma.[17] It may be that lack of knowledge and lack of concern are synergistic factors leading to poor adherence.

Patients who admit to less than ideal use of medications indeed had lower adherence rates, even after adjustment for other factors. Admitting to missing the prescribed dose on 2 or more days in the past 2 weeks was associated with a substantial decrease in mean adherence, but few patients confessed to this behavior. From this we can speculate that asking patients in a nonjudgmental way whether or not they are taking their medications and how often they fail to take them might help to identify those at risk. In fact, a predictive model based on the findings from the present study had 46% sensitivity and 87% specificity for identifying those with adherence rates ≤0.75. This means that administering a brief questionnaire to patients in the waiting room might be a potential approach for identifying patients who are at substantial risk of poor adherence.

Study Limitations

Limitations of our study include the fact that 85 study participants (30%) failed to complete follow-up. Although these persons were similar to those who completed the study, they were more likely to be African American and female, and to report worse general health.[14] It is possible that the associations may have been weaker or nonexistent if the entire cohort had completed the study. In addition, patients knew they were being monitored and may have altered their behavior as a result, although this would be expected to have made it more difficult for us to detect certain risk factors. If some groups were more influenced by this than others, associations may have occurred on this basis. Finally, the sample size was modest such that some weaker, but clinically important, associations may have been missed.

This study of patients with glaucoma using eyedrops with an electronic monitor shows that younger and older patients, African Americans, and those in poor health have lower adherence. Furthermore, those who admit to missing doses are also taking less medication. A simple survey of

demographic factors and self-reported health may help to identify many of those who are taking less than 75% of their drops.

References

1. Cramer JA, Mattson RH, Prevey ML, et al. How often is medication taken as prescribed? A novel assessment technique. JAMA 1989;261:3273–7.
2. Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: clinical applications. JAMA 2002;288: 2880–3.
3. Haynes RB, Yao X, Degani A, et al. Interventions to enhance medication adherence. Cochrane Database Syst Rev 2005;(4): CD000011.
4. Haynes RB, McDonald HP, Garg AX, Montague P. Interventions for helping patients to follow prescriptions for medications. Cochrane Database Syst Rev 2002;(2):CD000011.
5. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40:794–811.
6. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. Med Care 2004;42:200–9.
7. Knight KM, McGowan L, Dickens C, Bundy C. A systematic review of motivational interviewing in physical health care settings. Br J Health Psychol 2006;11:319–32.
8. Sabate E, ed. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003:48–89. Available at: http://whqlibdoc.who.int/publications/2003/9241545992.pdf. Accessed August 1, 2008.
9. Olthoff CM, Schouten JS, van de Borne BW, Webers CA. Noncompliance with ocular hypotensive treatment in patients with glaucoma or ocular hypertension: an evidence-based review. Ophthalmology 2005;112:953–61.
10. Nordstrom BL, Friedman DS, Mozaffari E, et al. Persistence and adherence with topical glaucoma therapy. Am J Ophthalmol 2005;140:598–606.
11. Schwartz GF, Reardon G, Mozaffari E. Persistency with latanoprost or timolol in primary open-angle glaucoma suspects. Am J Ophthalmol 2004;137(suppl):S13–6.
12. Kass MA, Gordon M, Meltzer DW. Can ophthalmologists correctly identify patients defaulting from pilocarpine therapy? Am J Ophthalmol 1986;101:524–30.
13. Norell SE. Accuracy of patient interviews and estimates by clinical staff in determining medication compliance. Soc Sci Med [E] 1981;15:57–61.
14. Okeke CO, Quigley HA, Jampel HD, et al. Adherence with topical glaucoma medication monitored electronically: the travatan dosing aid study. Ophthalmology 2009;116:191-9.
15. Becker MH, Maiman LA. Sociobehavioral determinants of compliance with health and medical care recommendations. Med Care 1975;13:10–24.
16. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487–97.
17. Friedman DS, Hahn SR, Gelb L, et al. Doctor-patient communication, health-related beliefs, and adherence in glaucoma: results from the Glaucoma Adherence and Persistence Study. Ophthalmology 2008;115:1320–7, 1327.31–3.
18. Friedman DS, Quigley HA, Gelb L, et al. Using pharmacy claims data to study adherence to glaucoma medications: methodology and findings of the Glaucoma Adherence and Persistency Study (GAPS). Invest Ophthalmol Vis Sci 2007; 48:5052–7.
19. Quigley HA, Friedman DS, Hahn SR. Evaluation of practice patterns for the care of open-angle glaucoma compared with claims data: the Glaucoma Adherence and Persistency Study. Ophthalmology 2007;114:1599–606.
20. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. Clin Ther 1999;21:1074–90.
21. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–63.
22. Ross CE, Mirowsky J. Components of depressed mood in married men and women: the Center for Epidemiologic Studies' Depression Scale. Am J Epidemiol 1984;119:997–1004.
23. Feldman SR, Camacho FT, Krejci-Manwaring J, et al. Adherence to topical therapy increases around the time of office visits. J Am Acad Dermatol 2007;57:81–3.
24. Friedman DS, Jampel HD, Congdon NG, et al. The TRAVATAN dosing aid accurately records when drops are taken. Am J Ophthalmol 2007;143:699–701.
25. Kass MA, Meltzer DW, Gordon M, et al. Compliance with topical pilocarpine treatment. Am J Ophthalmol 1986;101: 515–23.
26. Kaplan RC, Bhalodkar NC, Brown EJ Jr, et al. Race, ethnicity, and sociocultural characteristics predict noncompliance with lipid-lowering medications. Prev Med 2004;39:1249–55.
27. Cooper LA, Beach MC, Johnson RL, Inui TS. Delving below the surface: understanding how race and ethnicity influence relationships in health care. J Gen Intern Med 2006;21(suppl): S21–7.
28. Ziegelstein RC, Fauerbach JA, Stevens SS, et al. Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction. Arch Intern Med 2000;160:1818–23.
29. Wang PS, Bohn RL, Knight E, et al. Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors. J Gen Intern Med 2002;17: 504–11.
30. Kim EY, Han HR, Jeong S, et al. Does knowledge matter? Intentional medication nonadherence among middle-aged Korean Americans with high blood pressure. J Cardiovasc Nurs 2007;22:397–404.

Footnotes and Financial Disclosures

Originally received: August 11, 2008.
Final revision: January 14, 2009.
Accepted: January 20, 2009.
Available online: April 19, 2009. Manuscript no. 2008-964.

[1] Wilmer Eye Institute, Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

[2] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

[3] Scheie Eye Institute, Department of Ophthalmology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

[4] Department of Preventive Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China.

Financial Disclosure(s):
The author(s) have made the following disclosure(s):

Drs. Friedman and Quigley are paid consultants for and have received honoraria or research support from Alcon. Dr. Jampel is a consultant for Allengan, Ivantis, and Glaucos. No conflicting relationship exists for any other authors.

Supported in part by PHS Research Grants EY01765 (Core Facility Grant, Wilmer Institute), NIH K12 EY015398, (Dr. Okeke), a grant from The Paul and Evanina Bell Mackall Foundation Trust (Dr. Okeke), and an unrestricted gift from Alcon, Inc.

Correspondence:
David S. Friedman, MD, MPH, PhD, Wilmer Eye Institute, Wilmer 120, 600 North Wolfe Street, Baltimore, MD 21210. E-mail: david.friedman@jhu.edu.