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How glaucoma patient characteristics, self-efficacy, and patientprovider communication are associated with eye drop technique

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Authors' contributions

Declaration of Conflicting Interests

Drs Sayner, Blalock, Carpenter, Muir, Giangiacomo, Goldsmith and Sleath, and Ms Vitko indicate no conflict of interest. Dr Robin has been a consultant for Biolight, Lupin Pharmaceuticals and Sucampo, and does paid lectures for Merck and Allergan. Also, Dr Robin has been a consultant for and has stock options in Glaucos, and is on the board of Aerie Pharmaceuticals. Dr Hartnett is a consultant for Axikin Pharmaceuticals. Dr Lawrence does paid lectures for Alcon Laboratories. Dr Muir receives salary support from a VA HSR&D career development award.

Robyn Sayner, PharmD helped design the data collection instruments, coordinate and supervise data collection, did the data analysis, drafted the initial paper, and approved the final paper as submitted. Delesha M. Carpenter, PhD helped design the study, reviewed and revised the paper, and approved the final paper as submitted. Alan L. Robin, MD helped design the study and the coding tool, reviewed and revised the paper, and approved the final paper as submitted. Susan J. Blalock, PhD helped design the study, helped design the coding tool, revised the paper and approved the final paper as submitted. Kelly W. Muir, MD: Dr. Muir reviewed and revised the paper and approved the final paper as submitted. Kelly W. Muir, MD: Dr. Muir reviewed and revised the paper and approved the final paper as submitted. Kelly W. Muir, MD: Dr. Muir reviewed and revised the paper and approved the final paper as submitted. Societ the paper, and approved the final paper as submitted. Societ D. Lawrence, MD reviewed the paper and approved the final paper as submitted. Gail Tudor, PhD, helped design the study, reviewed the paper, and approved the final paper as submitted. Betsy Sleath, PhD: Dr. Sleath conceptualized and designed the study, designed the data collection instruments, designed the coding tool, reviewed and revised the paper, and approved the final paper as submitted. All authors had complete access to the study data.

Abstract

Objectives—The objective of this study was to examine the extent to which patient characteristics, eye drop technique self-efficacy, and ophthalmologist–patient communication about eye drop administration are associated with glaucoma patients' ability to instil a single drop, have the drop land in the eye, and avoid touching the applicator tip of the medication bottle to the eye or face while self-administering eye drops.

Methods—Glaucoma patients (n = 279) were recruited from six ophthalmology clinics. Medical visits were videotape-recorded. Afterwards, patients were interviewed and demonstrated administering an eye drop on a videotaped-recording. Generalized estimating equations were used to analyse the data.

Key findings—Ophthalmologists provided eye drop administration instruction to 40 patients. Patients with more years of education were significantly more likely to both instil a single drop (P = 0.017) and have the drop land in their eye (P = 0.017). Women were significantly more likely to touch the applicator tip to their eyes or face (P = 0.014). Patients with severe glaucoma (P = 0.016), women (P = 0.026), and patients who asked at least one eye drop administration question (P = 0.001) were significantly less likely to instil a single drop. Patients with arthritis were significantly less likely to have the drop land in their eye (P = 0.008). African American patients were significantly less likely to touch the applicator tip to their eyes or face (P = 0.008).

Conclusions—Some glaucoma patients have a difficult time self-administering eye drops. As so few patients received eye drop administration instruction from their providers, there is an opportunity for pharmacists to complement care.

Keywords

glaucoma; eye drop instillation; self-efficacy; patient question-asking; patient-provider communication

Introduction

Glaucoma, affecting approximately 60 million people worldwide, is a leading cause of irreversible blindness.[1] Visual impairment caused by glaucoma can be lessened if the intraocular pressure (IOP) can be adequately minimized.

Topical IOP-lowering medications are used to delay the progression of glaucoma; however, patients may not recognize any visual benefit from using these medications as glaucoma is an asymptomatic disease.[2–4] Additionally, poor eye drop instillation technique could result in a patient missing a dose, which could negatively impact a patient's response to therapy and could hasten disease progression.[5,6] Thus, it is imperative for patients to properly self-administer their eye drops.

Several studies have shown that glaucoma patients have difficulties administering their own topical ophthalmic medications.[7–11] In a study of glaucoma and ocular hypertension patients who self-administered eye drops, younger patients were significantly more likely to have a good eye drop technique, which was defined as delivering a drop to the eye while not contaminating the eye drop bottle.[8] In another study involving visually impaired glaucoma

ocular adnexae.[9,10]

Prior studies have shown that increased patient self-efficacy in eye drop administration is associated with better eye drop technique performance in glaucoma patients.[12–14] However, other studies have found that patients may not be aware of their poor performance with self-administering eye drops and may report not having any difficulty instilling drops. [10,11] Another study found that about one-third of patients who reported never missing their eye actually missed their eye during their videotaped eye drop technique demonstration; approximately one-fourth of those who denied touching the applicator tip of the medication bottle to the ocular surface did so in a videotaped eye drop technique demonstration.[10]

As glaucoma patients have difficulties in self-administering eye drops, providers should communicate with patients about proper eye drop technique. However, little is known about how patient–provider communication is associated with the ability of glaucoma patients to self-administer eye drops. In a previous study, patients who received prior instruction on eye drop instillation technique were significantly more likely to have good eye drop technique. [8] However, patients may not receive proper eye drop instillation education as this is often neglected by ophthalmologists when they prescribe topical IOP-lowering medications.[15] Patients may benefit from asking clarification questions about eye drop technique to their providers. Patient question-asking during medical visits is important because patients who ask more questions in medical visits tend to receive more information from their healthcare providers, leading to increased patient self-efficacy and an increased sense of involvement in their healthcare.[16] One factor that may prevent patients from asking questions is health literacy. Patients with lower health literacy may be interested in participating in medical visits; however, they tend to ask fewer questions about medical issues and are less likely to inquire about new information related to their condition.[16,17]

The objective of this study was to examine the extent to which (1) patient characteristics; (2) patient self-efficacy in administering glaucoma eye drops; and (3) ophthalmologist–patient communication about eye drop administration (including patient question-asking about eye drop administration, ophthalmologist-provided education on eye drop administration, and provider showing a video about eye drop administration) are associated with glaucoma patients' correctly performing the following critical steps when instilling eye drops: administering a single drop into the eye, having the drop land in the eye on the first attempt, and not touching the applicator tip to the eye, ocular adnexae, or face.

Methods

This study was approved by the Institutional Review Boards at the University of North Carolina, Duke University, Emory University, and the University of Utah. This study (#08-1208) was initially approved by the University of North Carolina – Chapel Hill Institutional Review Board on 1 August 2008 and mostly recently on 15 Jan 2015. Providers were recruited at six ophthalmology clinics located in four states in the United States. The

principal investigator presented the project to the ophthalmologists at each clinic during lunch hours and obtained ophthalmologist consent. Ophthalmologists also completed a demographic questionnaire. Patients of these participating ophthalmologists were recruited between 2009 and 2012 by a research assistant. Patients were eligible if they were: (a) at least 18 years old; (b) able to speak English; and (c) considered as being either a glaucoma patient or a glaucoma suspect patient.

Clinic staff referred potentially eligible patients to a clinic-based research assistant. The research assistant explained the study, obtained patient consent and screened the patient for eligibility. The patient's medical visit was videotape-recorded. Afterwards, a research assistant interviewed the patient. Then, the research assistant asked the patient to demonstrate administering a single drop of artificial tears into their eye on a videotaped-recording. At a later time, the research assistant abstracted information from the patient's medical record.

Patient characteristics

The research assistant collected patient demographical information during the interview. Patient age and years of education were measured as continuous variables. Gender was measured as a dichotomous variable. Self-reported patient race was measured as a categorical variable (white, African American, Asian, Native American and Hispanic). The number of years of using glaucoma medications was measured as a categorical variable (less than 6 months, 6 months to less than 1 year, and 1 year or more). Whether the patient was newly prescribed glaucoma medications was measured as a dichotomous variable (new to or already using).

The Rapid Estimate of Adult Literacy in Medicine (REALM) was administered as part of the interview. This is a validated, rapid screening instrument that is designed to identify the health literacy of patients. Patients were asked to read a list of common medical and lay terms that are routinely used in patient education materials from a laminated card.[18] The research assistant noted which words the patient could not read. Patient scores on the REALM correspond to reading levels (score of 0-60 = eighth grade and below, 61-66 = ninth grade and above).

Additionally, a 6-item eye drop technique self-efficacy questionnaire was administered as part of the interview. This is a validated instrument that is strongly associated with a videotaped eye drop technique[14] and has strong psychometric properties.[12,19] Responses for each item are not at all confident (coded as 1), somewhat confident (coded as 2) and very confident (coded as 3). The responses from each item were added together to form a summary score, ranging from 6 (lower self-efficacy) to 18 (higher self-efficacy).

The research assistant abstracted specific information from the patient's medical record. The research assistant recorded the mean deviation, in decibels (dB), from the patient's most recent reliable visual field test for each eye. We classified the severity of glaucoma using the mean deviation of the worse eye, and coded it as mild (-6 dB), moderate (between -12 dB and -6 dB), or severe (-12 dB) according to the Hodapp-Parrish-Anderson criteria.[20]

Poor vision (i.e. glaucoma severity) has been associated with poor eye drop technique.[12] Additionally, the research assistant documented whether there was a diagnosis of arthritis listed in the patient's medical record since conditions that affect manual dexterity, such as arthritis, may also negatively impact eye drop administration.[9]

Patient-provider communication

Each medical visit was videotape-recorded, and was transcribed verbatim with identifiers removed. Three research assistants coded whether ophthalmologists provided instruction on eye drop administration and whether patients were shown a video about eye drop administration during the medical visit. The three coders coded the same 25 transcripts throughout the study to assess inter-rater reliability. A single research assistant coded whether the patient asked one or more questions about eye drop administration during the medical visit.

In a private examination room where the interview occurred, patients demonstrated their eye drop technique using a bottle of artificial tears (5 ml Systane® lubricant eye drops, Alcon Laboratories, Inc., Ft. Worth, Texas, USA) while a research assistant videotape-recorded. The research assistant positioned the camera close enough to the patient to view the eye drop administration demonstration. Patients were asked to instil a single drop of the artificial tears into their eye as they normally would with their glaucoma medications at home. If the patient instilled glaucoma eye drops into both eyes, the patient was asked to administer a single eye drop into the right eye. A checklist to assess eye drop technique was developed with input from the ophthalmologists on the study team. [21,22] Using this checklist, a single coder noted whether the patient performed the following steps during the eye drop administration demonstration (yes/no): (a) tilts head backward, (b) directs bottle to eye, (c) able to squeeze the bottle to produce at least one drop, (d) the produced drop(s) do not miss eye on first attempt, (e) instils a single drop, (f) does not touch applicator tip to eye or face, and (g) whether the patient performed punctual occlusion afterwards. If a patient made multiple attempts to instil eye drop into his/her eyes, the coder was instructed to mark the checklist using only the first attempt and to note how many attempts the patient made to instil the eye drops. Direct observations of eye drop technique demonstrations were not done by the study team. Ophthalmologists on the study team determined the three critical steps of administering eye drops to be: (1) drop(s) do not miss eye, (2) instils a single drop, and (3) does not touch applicator tip to eye or face.

Analysis

Any patient who did not self-administer eye drops on videotape was excluded from this analysis. All analyses were performed using IBM SPSS Statistics version 19 (Armonk, New York, USA). We set the a priori level of statistical significance at P < 0.05. Descriptive statistics were calculated. The number and percentage of the patients performing each step correctly was presented. We used generalized estimation equations to examine how patient characteristics (age, race, gender, health literacy, years of education, arthritis, severity of glaucoma, and length of time using glaucoma medications), eye drop technique self-efficacy, and patient–provider communication were associated with the patient instilling a single

drop, the eye drop landing in the eye on the first attempt, and the bottle applicator tip touching the ocular surface, eye adnexae, or face during the eye drop administration. The following were not included in the multivariable analysis: (1) physician race since we only had one non-white physician; (2) physicians showing a video about how to administer eye drops since none did; and (3) physicians providing education on eye drop administration as two physicians performed the majority (53%) of the education, and physicians providing education on eye drop administration was highly correlated with patient question-asking leading to collinearity issues.

We used Cronbach's alpha to measure the internal consistency of the 6-item eye drop technique self-efficacy scale in this study. Additionally, we used intra-class correlation to measure the inter-rater reliability among the three coders who evaluated patient-provider communication.

Results

Four of the participating ophthalmology clinics were affiliated with academic medical centres and two were private practices. Fifteen ophthalmologists who care for glaucoma patients agreed to participate in this study while one refused, resulting in a participation rate of 94%. Sixty-seven percent (n = 10) of the providers were male. Providers ranged in age from 26 to 66 years (mean 40.8 years, standard deviation 11.7 years).

Two hundred seventy-nine patients were enrolled into this study. For all 279 enrolled patients, we had both questionnaire and medical record data. Of the enrolled patients, 255 administered their own eye drops on a videotaped-recording. Twenty-four patients were excluded from analysis: three patients did not self-administer eye drops and 21 patients had missing videotaped-recordings. Table 1 presents the patient characteristics of those who administered their own eye drops. The self-reported patient race was re-coded into African American and non-African American as the majority of the study sample who were non-African American were white (91%). The number of years of using glaucoma medications was re-coded into a dichotomous variable (less than 1 year or 1 year or longer). The 6-item eye drop technique self- efficacy questionnaire scale has a Cronbach's of 0.835 in this study. Table 2 presents the results of whether the patients correctly performed each step in eye drop administration and if any steps were not clearly seen. In 130 (51%) videotaped-recordings, patients instilled a single drop. Two hundred thirty (90%) patients were able to get the drop to land into the eye on the first attempt. One hundred one (40%) patients avoided touching the applicator tip to any part of the eye or face.

Ophthalmologists provided instruction about eye drop administration to 40 patients, and did not show a video about eye drop administration to any patients. The inter-rater reliability for whether the ophthalmologist provided education on eye drop administration was 0.951 among the three coders. Inter-rater reliability could not be calculated for whether the patient was shown a video on eye drop administration since there were no occurrences of this; however, the coders agreed 100% of the time that this did not occur.

Page 7

Table 3 presents the generalized estimation equation results predicting whether patients instilled a single drop into the eye, had the drop land in the eye on the first attempt, and avoided touching the applicator to the eye or face. Patients with more years of education were significantly more likely to instil a single drop (P = 0.017). Women were significantly less likely to instil a single drop (P = 0.026), as were patients with more severe glaucomatous defect in their worse eye (P = 0.016). Patients with more years of education were significantly more likely to have the drop land in the eye on the first attempt (P =0.017). Patients with a diagnosis of arthritis listed in their medical records were significantly less likely to have the drop land in the eye on the first attempt (P = 0.008). African American patients were significantly less likely to touch the applicator tip of the bottle to their eyes or face (P = 0.006). Women were significantly more likely to touch the applicator tip to their eves or face (P = 0.014). Patients who asked at least one question about eye drop administration were significantly less likely to instil a single drop into their eye (P = 0.001). No other characteristics (health literacy, age, using glaucoma medications for longer than 1 year, or self-efficacy in administering eye drops) were significantly associated with the three critical steps in administering eye drops.

In this study, women were significantly more likely to have a diagnosis of arthritis listed in their medical records (chi-square = 9.827, P = 0.007). No other patient characteristics were significantly different between males and women.

Discussion

This study examined the extent to which patient characteristics, patient self-efficacy in administering glaucoma eye drops and patient–provider communication about eye drop administration are associated with glaucoma patients' ability to perform the three critical steps in self-administering eye drops. We found that 51% of glaucoma patients were able to instil a single drop, 90% had the drop land in their eyes on first attempt, and 40% avoided touching the applicator tip to their eyes or face. Also, we found several factors that were significantly associated with whether a glaucoma patient correctly performed each of these steps. Finally, we found that providers rarely instructed patients how to instil eye drops.

There were several limitations to this study. First, selection bias could be a limitation as ancillary staff did not track the characteristics of those who declined to speak with the research assistant to learn more about the study. The majority of the non-African American patients in this study were white. Many patients blocked the camera while demonstrating their eye drop technique and several videotape-recordings were not adequately focused – both of which prevented the coder to have a clear view for the evaluation of one or more steps in the patient's eye drop administration. Also, the shape and size of the Systane® bottle the patients used in their eye drop technique demonstration may have been different than what they were accustomed to, and may have influenced – either positively or negatively – patients' ability to instil eye drops. Some patients may have been affected by having to demonstrate their eye drop technique while being videotape-recorded. Finally, we did not assess if patients had received eye drop administration instruction prior to study enrolment.

Prior studies evaluating eye drop technique in glaucoma patients found high rates of poor technique because of patient characteristics. [7-11] Similar to what prior studies found, we found that those patients who had the greatest severity of glaucomatous defect were significantly less likely to instil a single drop.[9,10] This further strengthens the need for physicians to routinely evaluate their patients' eye drop technique and discuss the importance of consistently and correctly using eye drops with all of their patients, especially with those patients with severe glaucoma. Also, we found that women were significantly less likely to instil a single drop into their eyes, which is similar to what Stone and colleagues found.[11] This result may be due to more women in this study having a diagnosis of arthritis listed in their medical record. We found that patients with a diagnosis of arthritis were significantly less likely to instil a single drop, which is similar to the results from a previous study.[10] Perhaps this is due to the patient's limited dexterity with manipulating the bottle. Extrapolating this further, it may be possible that other health conditions, such as Parkinson's, could also negatively impact a patient's ability to instil eye drops. Additionally, we found that years of formal education, but not health literacy, was significantly associated with being more likely to being able to instil a single drop and having that drop land in the eye on first attempt. This could be due, in part, with how health literacy was assessed in this study. We used the REALM, which evaluates a person's ability to read common medical terms. This study found that women were significantly more likely to touch the applicator tip to their eyes or face, which could potentially contaminate the bottle. This is an important finding as a patient may be more likely to suffer from eye infections, abrasions, or ulcerations if they contaminate the bottle containing their eye drops. [23,24] Additionally, we found that African American patients were significantly less likely to touch the applicator tip to their eyes or face. Other patient characteristics, such as patient age, were not associated with predicting whether patients correctly instilled eye drops, contrasting the results from previous studies.[9,10]

Previous studies have shown that self-efficacy of administering eye drops is strongly associated with videotaped eye drop technique.[12–14] However, in this study, the 6-item eye drop technique self-efficacy measure – or self-efficacy in administering eye drops – was not significantly associated with correctly performing any of the three key steps in self-administering eye drops. This unexpected result may be due to patients being overconfident in their ability to instil eye drops, patients being unaware of their poor performance, patients not being able to feel the drop land onto their eyes due to poor corneal sensitivity, or the amount of steps that were not clearly visible on the videotaped-recordings.

Interestingly, patients who asked at least one question to their physician about eye drop administration were significantly less likely to instil a single drop into the eye. This may be due to patients asking more questions when they are not confident with self-administering eye drops. Also, only a few patients received instruction on how to administer eye drops from their physicians, and none were shown a video about eye drop administration. This may be due to the limited time that glaucoma patients have with their ophthalmologists, who likely tailor conversations to the points that they believe will benefit their patients the most. Previous studies suggest that there should be more education of eye drop technique in patients.[8,15,24] Tatham and colleagues found that prior instruction on how to administer

eye drops was significantly associated with a better overall eye drop instillation technique. [8]

Proper use of topical IOP-lowering medications is a complex issue. Certain patient-level factors may influence a patient's ability to administer their own eye drop medication. There is an opportunity for pharmacists to positively impact the care of glaucoma patients since glaucoma patients rarely receive ongoing instruction on how to administer eye drops from their physicians and as some glaucoma patients find it difficult to self-administer eye drops. When glaucoma patients pick up their medications, pharmacists could assess whether they have any questions regarding self-administering eye drops by asking questions such as, 'Some people find it difficult to consistently administer their own eye drops, what concerns do you have with administering your glaucoma eye drops?' Additionally, pharmacists could offer to demonstrate how to administer eye drops or to evaluate the patient's eye drop technique. If time is limited in patient consultations, pharmacists could provide a link to a videotaped-recording of how to correctly administer eye drops.

Conclusion

This study provided insight on how glaucoma patients from several geographically distinct clinics performed when self-administering eye drops, and how certain characteristics, such as gender, glaucoma severity, and patient question-asking, were significantly associated with poor eye drop technique. As glaucoma patients may find it difficult to self-administer eye drops and rarely receive instruction on eye drop administration, physicians and pharmacists should assess if glaucoma patients have questions about self-administering eye drops, and should offer a demonstration of eye drop instillation. Future research should focus on whether targeted instruction – both during medical visits and between medical visits – has an impact on a patient's eye drop administration performance. Additionally, future research should evaluate the effectiveness of different methods of educating eye drop technique.

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Table 1

Patient Characteristics of patients who self-administered eye drops on videotape-recording (n = 255)

	Percentage (n)
Gender	
Male	40.4 (103)
Female	59.6 (152)
Race	
African American	34.9 (89)
Non-African American	64.7 (165)
Number of years taking glaucoma medications	
Newly prescribed	15.7 (40)
One year or less	27.8 (71)
More than one year	56.5 (144)
Glaucoma Severity (worse eye)	
Mild	57.3 (146)
Moderate	20.4 (52)
Severe	16.5 (42)
Diagnosis of arthritis found in medical record	23.9 (61)
REALM	
Eighth grade or lower	14.1 (36)
Ninth grade or higher	83.9 (214)
Patient asked one or more questions about how to administer eye drops during medical visit	11.8 (30)
Patient received education about eye drop administration from ophthalmologist during medical visit	14.6 (40)
Patient was shown a video about eye drop administration during medical visit	0 (0)
	Mean (standard deviation); rang
Age (in years)	66.2 (12.5); 21 – 93
Years of Education	15.1 (3.4); 5 – 26
Glaucoma Eye Drop Self-Efficacy	16.7 (2.0); 6 – 18

Page 12

Table 2

Number and percentage of glaucoma patients who performed each step (n = 255).

	Percent (n
Does patient tilt head back while sitting, standi	ng, or lying down?
Yes	99.6 (254)
No	0.4 (1)
Unclear	0.0 (0)
Does patient direct bottle towards eye?	
Yes	100.0 (255
No	0.0 (0)
Unclear	0.0 (0)
Does patient squeeze bottle to produce a single	drop?
Yes	64.3 (164)
No	0.8 (2)
Unclear	34.9 (89)
Does drop land in eye on first attempt?	
Yes	90.2 (230)
No	5.9 (15)
Unclear	3.9 (10)
Does patient instil a single drop?	
Yes	51.0 (130)
No	18.4 (47)
Unclear	30.6 (78)
Does patient touch any part of eye or face with	bottle applicator tip?
Yes	38.8 (99)
No	39.6 (101)
Unclear	21.6 (55)
Does patient perform nasolacrimal occlusion?	
Yes	4.3 (11)
No	95.7 (244)

Table 3

Generalized estimating equations predicting whether patients performed each of the critical steps in eye drop technique.

	Patient instills a single drop into eye OR (95% CI) n = 177	Drop lands in eye on first attempt OR (95% CI) n = 245	Bottle touches eyes or face OR (95% CI) n = 200
Age	1.01 (0.98 – 1.04)	0.94 (0.88 - 1.00)	1.02 (0.99 – 1.04)
Gender – women	0.36 (0.14 – 0.93)*	1.45 (0.22 – 9.45)	2.24 (1.17 – 4.26)*
Race – African American	2.23 (0.87 - 5.68)	0.53 (0.12 – 2.42)	0.42 (0.23 – 0.78)**
Health literacy < 8 th grade	0.86 (0.27 – 2.76)	0.73 (0.23 – 2.36)	2.68 (0.93 - 7.72)
Years of education	1.18 (1.03 – 1.35)*	1.17 (1.04 – 1.32)*	0.92 (0.82 - 1.03)
Arthritis listed on patient's medical record	0.50 (0.14 - 1.82)	0.25 (0.09 - 0.70) **	1.06 (0.63 – 1.80)
Patient used glaucoma medications for longer than 1 year	0.83 (0.35 – 1.97)	3.42 (0.71 – 16.53)	0.90 (0.47 – 1.73)
Severity of defect of worse eye (severe compared to mild)	0.53 (0.32 – 0.89)*	2.47 (0.99 - 6.16)	0.86 (0.68 - 1.08)
Self-efficacy in administering eye drops	1.10 (0.95 – 1.27)	1.10 (0.76 – 1.59)	0.89 (0.77 – 1.04)
Patient asked at least one question about eye drop administration	0.21 (0.08 – 0.57) **	0.92 (0.109 – 9.51)	1.21 (0.61 – 2.43)
Ophthalmologist Age	1.02 (0.98 – 1.06)	1.03 (0.98 – 1.09)	0.99 (0.95 - 1.04)
Ophthalmologist Gender - women	1.08 (0.45 - 2.58)	0.85 (0.18 - 3.92)	2.12 (0.88 - 5.14)

CI, confidence interval; OR, odds ratio.

*P<0.05;

** P<0.01.