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Systematic Review of Educational Interventions to Improve Glaucoma Medication Adherence

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Abstract

Adherence to prescribed glaucoma medications is often poor, and proper adherence can be challenging for patients. We systematically reviewed the literature and identified eight studies using educational interventions to improve glaucoma medication adherence. Overall, five of the eight studies found that educational interventions lead to a significant improvement in medication adherence, and the remaining studies found a trend towards improvement. Using information from this systematic review and Health Behavior Theory, we constructed a conceptual framework to illustrate how counseling and education can improve glaucoma medication adherence. More rigorous studies grounded in Health Behavior Theory with adequately powered samples and longer follow-up are needed.

Keywords

Adherence; Attitude; Barriers; Behavior; Belief; Compliance; Education; Glaucoma; Medications; Persistence

I. Introduction

A. Difficulties with adherence to glaucoma medications

Glaucoma medications have been shown to slow or halt the progression to blindness,[1–3] but their real-world effectiveness is often curtailed by poor adherence. Poor adherence has been shown to be correlated with disease progression.[4–6] Studies have demonstrated that at least 30% of glaucoma patients do not adhere to their medication regimen as measured by the gold standard of electronic medication monitoring,[7,8] and rates of poor adherence have been reported to be as high as 80%.[7] This high rate of poor adherence among glaucoma patients is

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not unusual compared to rates among patients with other chronic, asymptomatic diseases such as dyslipidemia[9] and hypertension.[10] Several qualitative studies have revealed that poor adherence rates are associated with inadequate education about glaucoma.[11–13] Since limited patient knowledge about glaucoma can be modified, there have been a number of educational interventions conducted aiming to improve glaucoma medication adherence.[14–21] The purpose of this systematic review is to describe published educational interventions in the peer-reviewed literature designed to improve glaucoma medication adherence and examine the success of these different approaches. A conceptual model will be presented describing how each of these interventions can operate within a part of a modified Health Belief Model[22] to affect behavior change.

B. Models of Health Behavior Change

The National Institute of Health recommends basing new educational interventions in Health Behavior Theory. There are a number of theoretical models of health behavior change within Health Behavior Theory that have been tested and found to be useful in improving health behaviors and adherence to prescribed regimen for a wide variety of medical conditions. [22] A few prominent models in treatment adherence include the Health Belief Model, the Theory of Planned Behavior/Reasoned Action, and the Theory of Self-Efficacy.[23] The Health Belief Model[24] was developed in the 1950s by the United States Public Health Service to explain why individuals did not participate in screening tests for asymptomatic diseases. It postulates that individual health behavior change is influenced by an individual's *perceived susceptibility* to the disease of interest, *perceived severity* of the disease, *perceived benefits* to screening or treatment, *perceived barriers* to action, or "cues to action" (or any stimuli that could trigger the desired behavior). For example, a patient's willingness to take eye drops for glaucoma twice a day will be influenced by whether or not the patient thinks he/she could go blind or lose vision from glaucoma and whether or not the drops will mitigate that risk. Actualizing the desire to take the drops twice a day would depend both on overcoming barriers to treatment, such as medication cost, and remembering to take the medication. The Theory of Planned Behavior added a cultural component to the Health Belief Model by proposing that a person's willingness to change a health behavior depends on his own attitude towards the behavior as well as what he perceives the social norm to be regarding the new behavior. For example, if the newly diagnosed glaucoma patient's mother also has glaucoma and has been faithfully seeing the ophthalmologist and using eye drops for years, the patient is more likely to adhere to treatment. The Theory of Reasoned Action further builds on this by adding that a person's attitude towards a behavior is comprised of his intention to perform the behavior and his ability to perform it. A central belief in Bandura's Social Cognitive Theory is that of self-efficacy, which is an individual's belief about how likely he/she is to be able to carry out a specific behavior and obtain a specific desired outcome. This idea of self-efficacy was added to the Health Belief Model in 1980s as an additional predictor of health behavior.[25] Using the earlier example, even if our patient's mother maintained excellent adherence to treatment herself, if our patient does not feel both empowered and physically able to use drops twice a day, the patient will not adhere to the regimen.

The Health Belief Model applies well to a condition like open-angle glaucoma because glaucoma is mostly an asymptomatic, chronic disease. The patient would not otherwise be stimulated by symptoms to seek care until generally late in the course of disease and will need to continue with medical treatment for a lifetime as well as tolerate any side effects from the medications, seemingly without much overt benefit. Existing medications prevent vision loss but do not improve vision. Therefore, patients' perceptions of how likely they are to develop vision loss from glaucoma, what impact it may have on their future functioning, and how strongly they believe that taking the medications will prevent vision loss, will greatly impact their willingness to use glaucoma medications and to tolerate a potentially complex, uncomfortable and costly medication regimen. Some of the educational interventions that have been designed to improve glaucoma medication adherence are identified in this review and address components of the Health Belief Model, while many other components of the model have not been addressed by the majority of the interventions (Figure 1). The specific ways in which each intervention uses components of health behavior change theory are addressed in this review.

C. Quantifying Medication Adherence

1. Characteristics of Adherence—The terms "adherence," "compliance," and "persistence" are often used interchangeably to describe how well a patient takes medications, but each term has its own specific nuances and technical considerations. "Adherence" is often used as a more patient-centered way to express how a patient is actively engaged in using the medications as prescribed, whereas "compliance" has often been used as a physician-centered approach. A non-compliant patient is described as a patient who is not following the doctor's orders. Kulkarni and colleagues reviewed the literature and offered the following definition of compliance: "the extent to which the patient acts in accordance with the prescribed interval and dose of a dosing regimen."[26] They further noted that "'compliance' has more to do with the *accuracy* with which a patient follows the treatment plan as opposed to the *extent* to which he/she continues the treatment, which is what 'adherence' stands for." Therefore, adherence is a quantifiable measure of how often a patient follows prescription instructions, and it accounts for gaps in use. For example, a patient who is prescribed brimonidine twice daily in both eyes for 28 days (112 drops/28 days) and uses it once daily in both eyes for the first week (14 drops/7 days), then uses it twice daily in both eyes for two weeks (56 drops/14 days), and then stops using it for the last week (0 drops/7 days) would be 62.5% adherent (70 drops/28 days divided by 112 drops/28 days). Persistence is the duration of continuous use of a prescribed medication. In the United Sates, persistence with a newly-prescribed glaucoma medication has been shown to range from 20%–64%,[27] meaning that on average, patients took their medication for about 5 months continuously prior to stopping their medication or using it intermittently for a total of 5 months usage over a year.

2. Methods to Measure Adherence—There are several ways to monitor adherence and persistence with glaucoma medications, and each has unique benefits and limitations.[28] Some studies have quantified adherence using self-reported measures. Kass and colleagues compared patient self-reported glaucoma medication adherence with an electronic eye drop monitor and found that patients reported they were 97% adherent with their medications

while the monitor revealed only a 76% rate of adherence.[29] Thus, self-reported adherence will likely overestimate true adherence. Since then, several studies have used Medication Events Monitoring Systems (MEMS) devices for studying adherence.[6,30,31] The MEMS cap is an electronic device that fits over a bottle of eye drops and records each time a drop is dispensed, although it cannot tell if the drop was instilled into the patient's eye or wasted on the cheek. Furthermore, the MEMS cap is subject to observation bias as subjects often improve their adherence when they are aware that their behavior is being recorded.[28] Despite the known limitations of using MEMS to quantify adherence, this measure is often viewed as the gold standard relative to other measures.

Another way to measure adherence and persistence is by analyzing health care claims data. Pharmacy refill data can be used to calculate the Medication Possession Ratio (MPR), which is defined as the number of days during a set time period when a patient had an adequate supply of medication to use at the prescribed frequency. Using Medicaid claims data, Gurwitz and colleagues calculated a 69% MPR for seniors prescribed a single glaucoma medication, meaning that these seniors possessed enough medication to take their glaucoma drops as prescribed 8.4 months out of the year.[32] Pharmacy data can also be used to calculate persistence or the amount of time before a patient has a gap in recommended treatment, with Days Without Medication (DWM) quantifying this gap.[28] There are several limitations for using pharmacy data to measure adherence, including the uncertainty whether a medication was prescribed to be used in one eye or both eyes. The assumption is often made that the medication was prescribed for both eyes, but that would underestimate the MPR if the medication was prescribed for monocular use. Another major limitation is that MPR cannot account for free samples given to patients, and this may be another source of underestimating adherence. Table 1 describes the strengths and weaknesses of each type of metric designed to measure adherence based on the qualities established by Muir and Lee[28], including the description of outcome measurements used in the studies included in this review.

D. Purpose

In published reviews of the ophthalmic literature on glaucoma medication adherence, authors have called for trials of educational interventions aimed at improving adherence.[7, 27] This review focuses on published trials that tested educational interventions' effect on glaucoma medication adherence. Specifically, we will evaluate the interventions based on quality, efficacy, and the extent to which they are grounded in evidence-based Health Behavior Theory.

II. Materials and Methods

We used Pubmed, CINAHL, and Embase to systematically search the published literature[33] available on November 9, 2011 using the following terms and medical subject headings (MeSH): "glaucoma," and "education," and "compliance," or "adherence." We used no language restrictions. We generated searches to account for synonyms of these keywords and MESH headings as follows: 1. "glaucoma" AND ("patient education as topic," OR "health education," OR "consumer health," OR "patient education," or "motivational

interviewing," or "instruction"), 2. "glaucoma" AND ("patient acceptance of healthcare," OR "patient compliance," OR "treatment refusal," OR "self-efficacy," OR "self-care," OR "compliance," OR "adherence," OR "persistence," OR "self-management.")

The searches generated 361 unique references. Abstracts from meetings were not included in the search as they generally do not contain sufficient information to adequately evaluate the intervention. Two independent researchers (PANC, JSW) evaluated the titles and abstracts of the articles to determine their eligibility for inclusion criteria. The trials had to include an educational intervention for patients taking glaucoma medications and glaucoma medication adherence as an outcome measure. We excluded any interventions targeted towards children or juvenile glaucoma. We included interventions that were not randomized controlled trials due to the limited number of interventions which met the inclusion criteria.

Two researchers (PANC, JSW) identified 44 published studies that were thought to meet the inclusion criteria. After reviewing and discussing the articles, the two researchers agreed that only 8 of the 44 articles met the inclusion criteria. There was disagreement about whether an additional three articles met the inclusion criteria;therefore, decision about those articles was adjudicated by an independent researcher (JDS). Ultimately eight articles were included in the analysis. A hand-search of the references of each of the eight articles did not reveal any additional relevant articles[33]. The data was abstracted from the articles by one researcher (PANC) and independently verified by a second researcher (JSW).

III. Results

A. Randomized Controlled Trials

Four of the eight studies which met the inclusion criteria were randomized controlled trials (RCTs), and the other four were observational studies. A Jadad score was calculated to evaluate the quality of each study. The Jadad score[34] is a five-point scale that awards one point for each of the following:

- Was the study randomized?
- Was the method of randomization appropriate?
- Was the study described as double-blind (the provider and the patient were both blinded to the intervention)?
- Was the method of double-blinding appropriate?
- Was there a description of withdrawals and dropouts?

The Jadad score has been widely used in the meta-analysis literature to judge the quality of RCTs, and we wanted to use a score that would be standardized across the literature. However, since double-blinding is not possible in these types of behavioral interventions, we assigned one point if the study was described as single-blinded and a second point if the assessors of the study outcomes were blinded specifically to whether or not the participant received the intervention. If adherence was measured by pharmacy claims data (as opposed to MEMS or self-report) and the outcome was out of the control of the assessor, the study was awarded two points.

1. RCT #1: Glaucoma education, addressing barriers to adherence, reminder systems vs. standard care[19]—Okeke and colleagues[19] (2009) conducted a RCT in which they randomized patients who had a baseline level of medication adherence < 75% to either a behavioral intervention or usual care. In the 3-month period before initiating the intervention, they measured medication adherence with MEMS to identify poorly-adherent patients (Table 1). The trial included 66 glaucoma patients and took place at US academic medical centers (Table 2). The intervention consisted of a ten-minute educational video on the importance of taking glaucoma medication consistently, and a structured individual discussion with a study coordinator was conducted to discuss any barriers that the patients had taking their medication and strategies to link eye drops administration to other daily activities. The study coordinator also distributed a blank calendar and taught patients how to keep a medication log. The training system for the study coordinator was not recorded. Patients received reminder phone calls to take their medications once a week for one month and then once every 2 weeks for two months. The particular MEMS device used in this trial, the Travatan Dosing Aid, was used to measure adherence and to serve as an alarm to remind patients to take their medication. A significant improvement over baseline medication adherence was found in the intervention group (54% to 73%) compared to the usual care group (46% to 51%) at 6 months ($P<0.001$). The Jadad Score for this trial was 2/5 as there was no description of those not completing follow-up or how the assessors of the outcome were masked to the treatment arm.

2. RCT #2: Nurse-led glaucoma education vs. standard care[21]—Sheppard and colleagues[21] (2003) randomized glaucoma patients with stable visual fields for a single visit either for standard care with an ophthalmologist or for a semi-structured educational session with an ophthalmic nurse. This trial took place in the United Kingdom and included 73 patients (Table 2). Adherence was classified by self-report on a scale where a score of 0 meant “I never use my eye drops,” and a score of 10 meant “I always use my eye drops” (Table 1). All patients reported their adherence at baseline to be approximately 9/10; there were no significant differences in baseline adherence between the nurse-led (8.92 ± 1.5) or physician-led groups (8.89 ± 1.8).The physician visit was scheduled for 10 minutes, and the content of the visit was at the discretion of the physician. The nurse visit was scheduled for 15 minutes, and 50% of the time was spent educating the patient on their type of glaucoma, test results, and addressing any problems with adherence. Educational brochures were given in the nurse-led session only. The nurses’ training to conduct the educational sessions was not reported. Patients completed pre- and post- questionnaires about their medication adherence, satisfaction with their glaucoma care, and questions related to their knowledge about glaucoma. Adherence was measured by self-report. Overall, adherence improved in both groups compared to baseline (p=0.004), but significantly fewer patients in the nurse-led group reported any specific problems with adherence (p=0.04). Patient satisfaction scores were significantly higher in the nurse-led group (p=0.03) but there was no effect of the nursing intervention on glaucoma knowledge. The Jadad Score for this trial was 2/5 as there was no description of those not completing follow-up or how the assessors of the outcome were masked to the treatment arm.

3. RCT #3: Tailored glaucoma education vs. standard care[18]—Norell[18] (1979) randomized 73 patients from an academic hospital in Sweden with high-tension glaucoma who were already taking pilocarpine three times per day to an educational intervention with an ophthalmic assistant or standard care with an ophthalmologist (Table 2). The patients were monitored with an electronic medication monitoring device for 20 days before and after the educational intervention. The length of time between each dose of medication was also measured (Table 1). The educational intervention consisted of a slideshow and leaflet about glaucoma and its treatment followed by an interview with the ophthalmic assistant who went over information from the slideshow that the patients may have not understood and discussed any problems patients were having with their medications. The assistant also created a plan with each patient to match the timing of their glaucoma drops to a daily activity, and they wrote this plan down together. The training program for the ophthalmic assistant was not reported. The intervention group had 9 ± 6.1% fewer missed doses of pilocarpine (p=0.0004) compared with the control group, and the intervention group also had 12.9 ± 5.5% fewer dosing intervals that were prolonged >8 hours (P<0.0001). The Jadad score for this trial was 3/5 as there was no description of how the assessors of the outcome were masked to the treatment arm.

4. RCT #4: Health literacy tailored glaucoma education vs. standard care[17]—Muir and colleagues[17] (2011) performed an RCT comparing an educational intervention tailored to each patient's health literacy level to others who received standard care with an ophthalmologist. The trial involved 127 patients from the Durham, North Carolina Veterans Administration Medical Center, VAMC (Table 2). An ophthalmic research assistant trained by an ophthalmologist administered an educational video about glaucoma at a 4th, 7th or 10th grade reading level depending on the health literacy of the patient. The research assistant reviewed eye diagrams about glaucoma and its treatment with participants who had a 4th or 7th grade reading level and gave the American Academy of Ophthalmology's brochure about glaucoma to patients who had at least a 10th grade reading level (the brochure is written at a 10th grade reading level). The research assistant then taught proper eye drop instillation techniques and observed the patients instill their own drops. The research assistant was observed by an ophthalmologist to ensure the quality and consistency of the intervention. VAMC pharmacy records were used to quantify the number of days that every participant went without medication (DWM) for the 6 months following the intervention (Table 1). Although there was no statistically significant difference between the treatment and control groups for DWM, there was an overall trend towards improved adherence in the groups of patients with 4th and 7th grade health literacy levels. The authors emphasized both the importance and need to tailor interventions based on the specific needs of each patient. The Jadad score for this trial was 5/5 as the study was appropriately randomized, the subjects lost to follow-up were appropriately described and the assessment of adherence utilized pharmacy claims data so the assessor was effectively masked to the measurement of the outcome. A limitation to this study was that it was 99% male.

B. Observational studies

There were four observational studies that took place between 2000 and 2011 which met our inclusion criteria.[14–16,20] All of the studies had a pre-post design in which baseline

adherence was measured prior to the implementation of an educational intervention, and then adherence was measured again after the intervention. Since this study design can bias the result away from the null hypothesis because of regression to the mean, we assessed each study for its use of a non-random control group or the use of a time-series analysis, as both methods can help account for regression to the mean.[35]

1. Observational Study #1: Motivational interviewing-based glaucoma education vs. standard care[16]—Cook and colleagues[16] (2010) assessed the feasibility of using motivational interviewing to improve glaucoma medication adherence. Motivational interviewing is a counseling style that identifies and mobilizes a patient's intrinsic values and goals to stimulate behavior change[36] and is based on several health-behavior theories, including the Health Belief Model and the Theory of Self-Efficacy. They identified 12 glaucoma patients from a US academic medical center (Table 2) who were ≤80% adherent as identified by MEMS monitoring for 2 months (mean adherence 36.7 ± 18.5%, Table 1). Eight out of these twelve study participants were randomly chosen to receive the educational intervention, and adherence for these participants was measured before and after the educational intervention. The intervention consisted of three 30–45 minute sessions and three 5–10 minute phone calls over a 6-month period in which an ophthalmic technician used a motivational interviewing technique to explore the patient's current adherence, barriers to taking medications, difficulties with medication side effects, or any questions the patient had about treatment. The ophthalmic technician also distributed American Academy of Ophthalmology brochures about glaucoma. Four participants completed all three in-person counseling sessions, and the other four completed two out of the three in-person counseling sessions. A significant (P=0.03) improvement in adherence was noted over the six month study period compared to the patients' baseline.

The technician was trained in motivational interviewing using a motivational interviewing instruction manual for 5.5 hours of self-study along with 6 hours of teaching by a behavioral psychologist (who had expertise in motivational interviewing). The technician also received training from an ophthalmologist about glaucoma medications and their side effects. The technician was observed by the psychologist while he was counseling the patients, and the psychologist assessed his fidelity to the motivational interviewing technique.

Study strengths include the rigorous training of the ophthalmic technician administering the intervention and multiple measurements of adherence with MEMS prior to selecting poorly adherent patients for inclusion in the study to reduce regression to the mean. Limitations included a small sample size.

2. Observational Study #2: Glaucoma knowledge and adherence[20]—Rendell[20] (2000) conducted a study to assess the relationship between knowledge about glaucoma and medication adherence. They measured knowledge about glaucoma, health motivation, health locus of control and self-reported adherence in theoretical vignettes in 100 glaucoma patients in the United Kingdom (Table 2). Knowledge and adherence before and after participation in one of two types of educational interventions were measured (Table 1). The first intervention utilized a didactic approach in which the patient was shown a disassembled model eye and the researcher drew the effect of glaucoma on the model eye and listed risk

factors for glaucoma and times for drop instillation. The second intervention utilized a participatory method in which the patients took the model eye apart and were encouraged to point out relevant structures and label the structures affected by glaucoma. Study participants were given leaflets with illustrations of risk factors for glaucoma, and they were asked to place a glaucoma medication bottle onto the appropriate dosing times on a chart of drop instillation times. There were no significant differences in knowledge or beliefs about adherence between the two groups. However, for all study participants, post-test knowledge scores were significantly higher than pre-test knowledge scores ($P<0.0001$), and an improvement in knowledge was correlated with an improved belief about adherence ($P<0.0001$). The major limitation was that adherence was only measured as "a belief about adherence" through self-report.

3. Observational Study #3: Group glaucoma education and adherence[15]—The Shanghai Glaucoma Club[15] was started in 1998 and met every two months for lectures by ophthalmologists; its goal was to provide an informal group setting in which ophthalmologists and their patients could interact and learn about glaucoma from each other. In this study, a survey was given to 301 glaucoma patients who were randomly selected from the Shanghai Glaucoma Club membership roster and to 314 consecutive non-club patients seen in the Shanghai glaucoma clinic. Knowledge about glaucoma was found to be significantly higher among club members than in clinic patients who were not in the club ($P<0.01$), and there was a trend towards improved self-reported adherence among club members ($P=0.08$) (Table 1). The major strengths of this study included its relatively large sample size and inclusion of a non-random control group. A major limitation is that adherence was measured by self-report through a non-standardized instrument.

4. Observational Study #4: Glaucoma knowledge and persistence[14]—Blondeau and colleagues[14] (2011) measured the change in patient persistence with glaucoma medication before and after a two-hour educational session among 342 glaucoma patients from a solo practice (Table 2). The participants had glaucoma for a mean of 10 years, had a mean baseline persistence of 78.9%, and opted to participate in the educational session. The session included a presentation about glaucoma given by a nurse, and the nurse also observed each participant as he or she practiced instilling eye drops. The sessions were limited to 15 people and included patients' family members. Patients were given a handout about glaucoma after the session. They were contacted by the nurse at 1, 4, and 10 months after the session to address any general concerns, encourage adherence, and schedule follow-up visits. Pharmacy data was used to measure persistence for two years prior to the session and one year after the session; persistence was unchanged after the intervention ($P>0.05$) (Table 1). However, compared to a non-random control group of 1187 glaucoma patients from the same practice who did not choose to attend the educational sessions, the patients who attended the session were 6.0% more persistent than those who did not attend the session ($P<0.05$). Strengths of this study included its relatively large sample size, inclusion of a non-random control group, and time-series analysis where multiple measurements of persistence were taken before and after the intervention. A limitation of this study was the high level of baseline persistence in the patients who chose to participate

in the educational session; the “healthy volunteer effect” may have significantly impacted this study.

IV. Discussion

Overall, five out of eight (63%)[16,18–21] of the reviewed studies revealed a statistically significant improvement in glaucoma medication adherence after educational interventions, and two others (25%)[14,15,17] demonstrated a trend towards an improvement in adherence that was not statistically significant. One study (12%)[14] of patients who already had a relatively high baseline adherence level showed no improvement after an educational intervention. The types of educational interventions utilized in each study were very different from one another; therefore, it is difficult to determine which specific aspects of the educational interventions had the most impact on medication adherence.

All eight studies focused on improving knowledge in order to improve glaucoma medication adherence. We developed a conceptual model (Figure 1) based on the Health Belief Model and the Theory of Self-Efficacy to frame the various aspects of knowledge about glaucoma that could affect adherence as well as the various barriers to adherence that have been identified. Knowledge about glaucoma can be broken down into four categories (Figure 1, Components of Knowledge): 1) a patient’s perceived susceptibility to glaucoma, 2) perceived severity of disease, 3) perceived benefits of treatment or 4) ability to instill eye drops correctly. A patient’s perceived susceptibility to glaucoma and perceived severity of disease is also linked to acceptance of diagnosis: does the patient believe that he/she has a potentially vision-threatening condition that is important to treat to prevent blindness? While all of the educational interventions included in our analysis addressed overall knowledge about the pathophysiology and treatment of glaucoma, only the study by Cook and colleagues addressed individual *perceptions* of how glaucoma affected them through motivational interviewing.

The second part of our conceptual framework (Figure 1, Types of Barriers to Adherence) attempts to classify barriers to glaucoma medication adherence that have been identified in the literature. Reasons for poor adherence include: a limited knowledge about glaucoma,[11,12,37] forgetfulness,[12,37,38] medication cost,[12,37] side effects,[11,37,38] difficulty with drop administration,[11,12,37,38] or complexity of the regimen.[37,38] There have been a number of in-depth qualitative studies undertaken to better understand reasons for non-adherence in glaucoma patients. One of the largest studies assessing adherence, the Glaucoma Adherence and Persistency Study, found patients to be less adherent if they did not understand that not taking their medicine increased their risk for vision loss.[39] Stryker and colleagues[11] conducted 80 in-depth interviews and found that non-adherent patients did not know what the benefit was to taking their glaucoma medications regularly and were not likely to question their doctor. Interviews with adherent glaucoma patients revealed that keys to their success were education and social support.[13] Lacey and colleagues conducted a combination of focus groups and semi-structured interviews with glaucoma patients and found that a fear of blindness and a belief in effective glaucoma medications were key motivators for adherence.[12]

In our model, we divided barriers to adherence into two categories: “patient and situational factors” and “regimen factors.” Tsai and colleagues developed a taxonomy of barriers to glaucoma medication adherence, and they found that patient and situational factors and regimen factors accounted for >95% of barriers to adherence.[37] “Regimen factors” are barriers that cannot be fundamentally changed with education, such as medication cost, side effects or the complexity of the medication regimen. These barriers can be addressed by providing the patient a longer opportunity with either a physician or a physician-extender to discuss their issues with these external factors. “Patient and situational factors” are barriers identified in the literature that *can* be improved by education and motivation. Forgetfulness, difficulty instilling drops, self-efficacy, or lack of understanding of the disease process can all be affected by educational interventions. All eight studies addressed a lack of understanding of the disease process. Three studies addressed forgetfulness;[16,18,19] three studies addressed eye drop instillation;[14,17,19] one study addressed self-efficacy.[16]

While only one study addressed patients’ perceptions of their susceptibility to losing vision from glaucoma, a number of the interventions were personalized in other ways. Four out of the five[16,18,19,21] studies which showed a significant improvement in glaucoma medication adherence personalized the educational information provided to the specific needs of their patients. All of these interventions had a member of the study team sit down with the patient and discuss the various barriers to adherence or answer questions about his or her disease individually. Muir and colleagues[17] tailored their intervention more formally based on their patients’ levels of health literacy, and their approach was more effective for patients with low and marginal health literacy compared to patients with at least a 10th grade health literacy level. “Tailoring” refers to creating educational material that is individualized. Tailored information has been shown to be more effective than non-tailored educational materials in other areas of health prevention as well, such as in improving rates of smoking cessation, fruit and vegetable consumption and obtaining mammograms.[40,41] The fact that the majority of the effective educational interventions to improve glaucoma knowledge used a personalized educational approach further reinforces the effectiveness of tailored educational material.

In order to build upon existing knowledge, the National Health Institute recommends utilizing health-behavior theory to design new educational interventions.[22] In our systematic review of the literature on educational interventions targeting improving glaucoma medication adherence, the majority of the studies utilized some aspects of different behavior change theories in their interventions, but only two out of eight[16,20] interventions formally defined exactly which theories they were using, how providers were trained in these approaches, and how they applied the theories to their interventions. Cook and colleagues focused specifically on using motivational interviewing to improve self-efficacy in order to improve glaucoma medication adherence. Rendell and colleagues focused on different aspects of adult learning theory and health motivation theory to inform their intervention, and they found that more knowledge, regardless of their particular educational technique, was associated with better glaucoma medication adherence.

The majority of the studies in this systematic review revealed either a significant improvement in glaucoma medication adherence with an educational intervention or a trend

towards improvement. The most multifaceted intervention targeted towards patients with poor adherence undertaken by Okeke and colleagues had a statistically significant improvement in medication adherence at 6 months. The nurse-led educational session in fairly persistent patients by Blondeau did not show any improvement in persistence at one year. The diabetes literature has shown that the effect of educational interventions on disease self-management and medication adherence tends to wane over time and may need to be repeated to sustain an effect.[42] Studies with additional data and longer follow-up are needed to evaluate the impact of educational interventions on maintenance of adherence in order to determine the optimal way to structure educational sessions in the ophthalmologists' office.

A limitation to this study is that of publication bias; studies that have negative results are less likely to be published than studies with positive results. This review cannot comment on studies that have not been published and may give a more favorable impression of the efficacy of educational interventions' effect on glaucoma medication adherence than is warranted.

Conclusion

The challenges of glaucoma medication adherence and health-behavior change require continuing efforts to define useful educational interventions based on the framework of health-behavior theory. At present, there are a few high-quality studies grounded in Health Behavior Theory that address glaucoma medication adherence through educational and counseling interventions with adequate sample size and follow up. We propose that future educational interventions should attempt to focus on: 1) improving knowledge about glaucoma by addressing patient perceptions of glaucoma severity, their susceptibility to glaucoma, and how effective the treatment would be for a particular patient, 2) addressing both types of barriers, "patient and situational factors" and "regimen factors," which include patient self-efficacy, as presented in our model, 3) evaluating long-term effects of educational interventions on maintenance of good adherence beyond 1 year, 4) utilizing multiple measures of adherence to more precisely and accurately quantify adherence, 5) conducting trials of educational interventions in which the assessors of adherence are adequately masked, and 6) describing the technique used to train the staff administering the intervention in enough detail that it could be easily taught to ophthalmic nurses or technicians.

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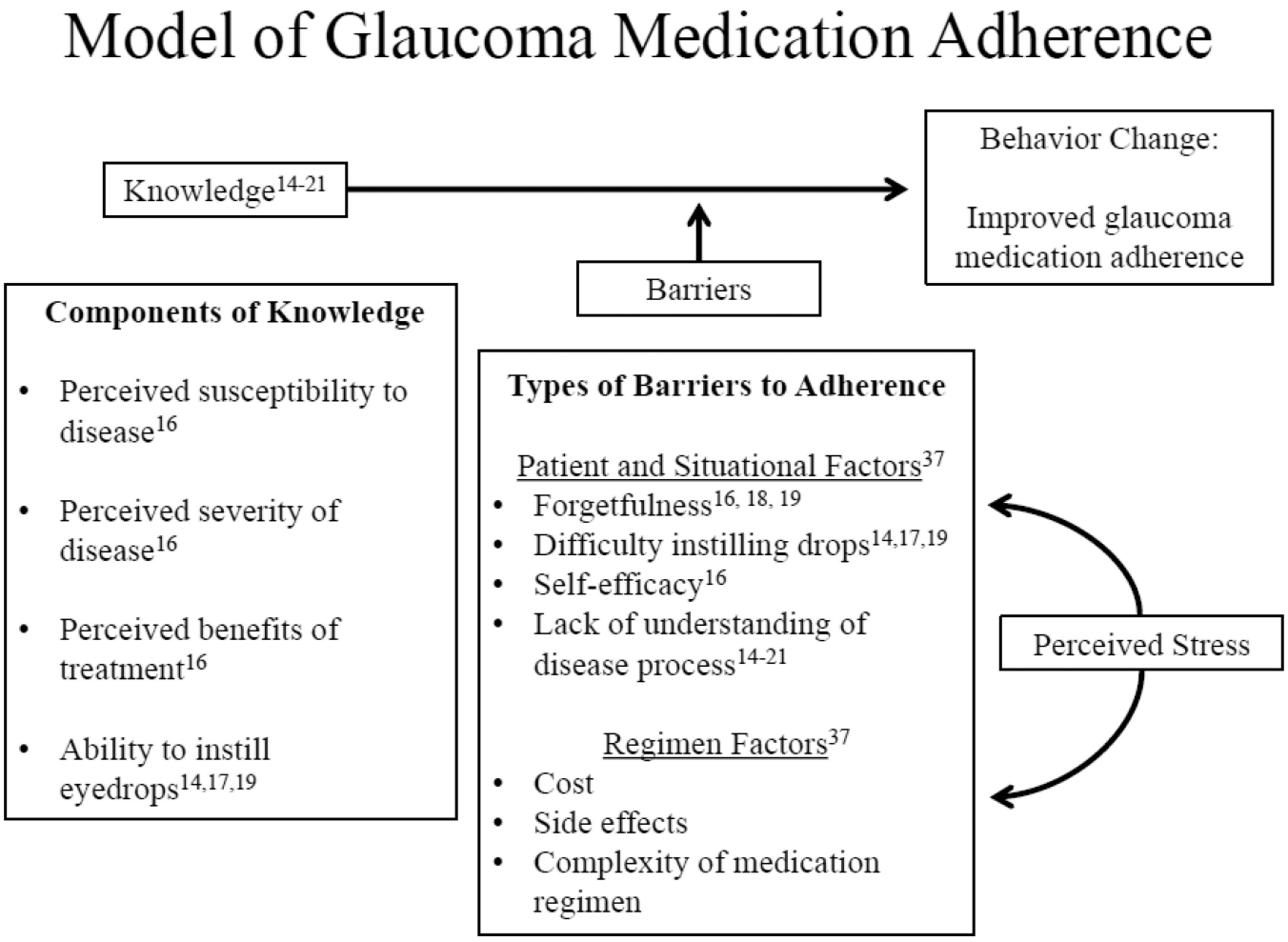

Figure 1.
Conceptual Model of Glaucoma Medication Adherence

Table 1

Outcome Measurements

	Electronic Medication Monitoring	Pharmacy Claims Data	Self-Report
How well does the measurement capture adherence?[28]	✓ Obtaining medication ✓ Using medication daily ✓ Timing medication dosages appropriately	✓ Obtaining medication	➢ Low reliability for all 3 measures
Outcome Measurements by Study			
Blondeau et al.[14]		Persistence with Medication	
Chen et al.[15]			Questionnaire, “do you use your medications on time?” “do you occasionally forget?”
Cook et al.[16]	Used MEMS but no details of measurement methodology		
Muir et al.[17]		Days Without Medication & Medication Possession Ratio	
Norell[18]	# missed doses and # doses outside the every 8 hour time window		
Okeke et al.[19]	Drop taken within ±4 hours of prescribed time		
Rendell et al.[20]			Vignettes addressing persistence, adherence to prescribed timing and # of doses, and no un-prescribed treatments
Sheppard et al.[21]			11 point scale “I never use my drops” to “I always use my drops”

MEMS, Medication Events Monitoring System

Table 2

Study Characteristics

Study	RCT (Yes/No)	Type of Glaucoma	Age, years (mean±SD)	Sex (%)	Race (%)	Funding
1. Okeke C et al.[19]	Yes	OAG, ACG, OHTN, Glaucoma Suspect using Travatan	1. Treatment Group: 66.2±13.1 2. Control Group: 63.8±13.4	1. Treatment Group: Male, 51.4% ; Female, 48.6% 2. Control Group: Male, 58.1%; Female, 41.9%	1. Treatment Group: White, 34.3%; Black, 65.7% 2. Control Group: White 41.9%; Black, 54.8%	NIH, Alcon, Wilmer Eye Institute, Bell Foundation Trust
2. Sheppard J et al.[21]	Yes	POAG, NTG, OHTN, PEX, Glaucoma Suspect with stable vision, fields and IOP for 1 year & ≤2 glaucoma meds	Total population: 73±11.3	Not recorded	Not recorded	Not Recorded
3. Norell SE.[18]	Yes	Simple Chronic Glaucoma with elevated IOP, vision ≥20/60 & on pilocarpine tid	Total population: 73	Total population: Male, 55%; Female 45%	Not recorded	Not Recorded
4. Muir KW et al.[17]	Yes	Any Type of Glaucoma with vision ≥20/200, without eye surgery in the last month and with a Mini-Mental Status Score ≥18	1. Treatment Group: 66±9.2 2. Control Group: 66±10.1	1. Treatment Group: Male, 100% 2. Control Group: Male, 99%; Female, 1%	1. Treatment Group: White, 25%, Black 74%, Other, 1% 2. Control Group: White 33%, Black 64%	NIH/NEI, Prevent Blindness America
5. Cook PF et al.[16]	No	Primary or Secondary Open-Angle Glaucoma on monotherapy with ≤80% adherence	Total population: 57.9±8.5	Total population: Male, 50%; Female, 50%	Total population: White, 50%; Black, 50%	American Glaucoma Society, Pfizer
6. Rendell J[20]	No	POAG ≥40 years old	Total population: 68.5	Total population: Male, 61%; Female, 39%	Total population: White, 70%; Black 30%	Not recorded
7. Chen X et al.[15]	No	Any Shanghai Glaucoma Club member or patient in Shanghai Glaucoma clinic	Glaucoma Club: 67 (median) Glaucoma Clinic: 57 (median)	Glaucoma Club: Male, 48%; Female, 52% Glaucoma Clinic: Male, 47%; Female, 53%	Not recorded	Not recorded
8. Blondeau P et al.[14]	No	Any patient in Dr. Blondeau's glaucoma practice taking a glaucoma medication	Educational session: 67.1 Did not attend session: 69.2	Not recorded	Not recorded	Allergan

OAG=open-angle glaucoma, ACG= angle-closure glaucoma, OHTN=ocular hypertension, glc suspect = glaucoma suspect, POAG= primary open-angle glaucoma, NTG= normal-tension glaucoma, PEX=exfoliation syndrome glaucoma, IOP=intraocular pressure, NIH= National Institute of Health, NEI = National Eye Institute