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Patterns of Glaucoma Medication Adherence over Four Years of Follow-Up

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Abstract

Purpose—To assess longer-term patterns of glaucoma medication adherence and identify whether patterns of adherence established during the first year of medication use persist during three subsequent years of follow-up.

Design—Retrospective longitudinal cohort analysis.

Participants—Beneficiaries 40 years old enrolled in a U.S. managed care plan for 7 years between 2001–2012 newly diagnosed and treated for open-angle glaucoma.

Methods—For each enrollee, we quantified medication adherence using the medication possession ratio. Group-based trajectory modeling (GBTM) was applied to all enrollees to look for similar patterns of adherence for groups of enrollees. These patterns were described for 1 and 4 years of follow-up and analyses were performed to identify persons who experienced similar adherence patterns at 1 and 4 years and others who had dissimilar patterns. Factors impacting adherence at 1 and 4 years were identified using regression analyses.

Main Outcome Measure—Patterns of glaucoma medication adherence.

Results—Of the 1,234 eligible beneficiaries, GBTM identified five distinct glaucoma medication adherence patterns in both the one-year and four-year follow-up periods. These groups were: 1) *Never adherent* after their index prescription fill (7.5%, 15.6% of persons in the one and four-year

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models, respectively); 2) *Persistently very poor adherence* (14.9%, 23.4%); 3) *Declining adherence* (9.5%, 9.1%); 4) *Persistently moderate adherence* (48.1%, 37.0%); and 5) *Persistently good adherence* (20.0%, 15.0%). Over 90% of beneficiaries in the 4 groups with the worst and best adherence patterns (Groups 1, 2, 3, 5) maintained their patterns from their first year throughout their 4 years of follow-up while those with *Persistently moderate adherence* (Group 4) – the largest sized group – were most likely to change groups from 1 to 4 years of follow-up. Persons with the best adherence over 4 years were more likely to be white, older age, earn > \$60,000/year, and have more eye care visits ($p < 0.05$ for all comparisons). Those with a higher initial co-payment cost had lower adherence rates ($\beta = -0.06/\text{dollar}$, $p = 0.03$).

Conclusion—For most patients newly-started on glaucoma medications, adherence patterns observed in the first year of treatment reflect adherence patterns over the subsequent 3 years. Investing resources in both identifying and helping patients with suboptimal adherence patterns over the first year may have a large impact on longer-term adherence.

Introduction

Many patients with glaucoma struggle with medication adherence.^{1–3} Systematic reviews estimate medication non-adherence rates can be as high as 80%, though many studies cite rates closer to 30%.^{2–3} Only one-quarter (24.2%) of newly diagnosed glaucoma patients persisted with their medications for two years in a recent study in Taiwan.⁴ Since non-adherent patients are known to take their medications on the dates of clinic visits,⁵ physicians cannot easily discriminate which patients are taking glaucoma medications as prescribed by simply measuring their intraocular pressure during the clinic visit. Moreover, patient self-reported medication adherence is inflated compared with pharmacy refill records and electronically monitored adherence data.^{6–8} Patients who do not consistently take their medications risk periods of uncontrolled intraocular pressure which can result in glaucomatous progression; patients with poor adherence have more severe glaucomatous damage,^{9–11} and poor adherence is an important risk factor for blindness from glaucoma.^{12–15}

With widespread implementation of electronic medical records and electronic prescribing, clinicians are gaining access to pharmacy refill data for their patients. An established approach for quantifying adherence using pharmacy refill data is to calculate the medication possession ratio (MPR), or the number of days the patient had the correct amount of medication in-hand divided by the total number of days of surveillance.^{16,17} This provides a single number that can quantify a complex behavior, with “good adherence” usually defined as an MPR of 80%.^{18,19} Although this is a widely used measure of quantifying adherence, one problem with this mode of classification is that patients can have the same MPR but very different patterns of actual adherence. For example, three patients could all have an MPR of 75%. The first patient had excellent adherence for nine months, stopped taking the medication completely and then re-started two days before her one-year return visit. The second patient had intermittent use taking her drops 3 of every 4 days throughout year until her follow-up visit, and the third patient had poor use for 3 months but then integrated the medication better into her daily routine with excellent adherence for the remaining 9

months. Understanding these different patterns of medication use is important to inform how we should design health care delivery to best support glaucoma patients' self-management.

Group-based trajectory models (GBTM) have been used to capture longer-term medication use in other chronic disease states such as hyperlipidemia,²⁰ hypertension,²¹ psoriasis²² and epilepsy.²³ To our knowledge, these models have yet to be used to study adherence in patients with glaucoma. GBTM is used to identify distinctive patterns of behavior in complex longitudinal data sets. GBTM describes the evolution of an outcome, such as persistence, by clustering individuals together who have similar patterns of behavior over time. The majority of studies that have evaluated glaucoma medication adherence using electronic monitoring or medication refill data have not assessed adherence rates beyond 2 years of follow-up.²⁴ Because glaucoma is often a life-long condition and adherence to glaucoma therapy over time is notoriously poor,² it is important to evaluate longer-term patterns of medication adherence. We used GBTM to analyze data from 1,234 patients with glaucoma in a nationwide managed care network over four years of follow-up. The objectives of this study were to 1) identify medication adherence patterns over four years of follow-up, 2) assess whether adherence patterns established during the first year of follow-up persisted during three subsequent years of follow-up, and 3) characterize the sociodemographic characteristics of the most adherent patients.

Methods

Data Source

The Clinformatics DataMart database (OptumInsight, Eden Prairie, MN) contains detailed records of all beneficiaries who had some form of eye care in a large managed care network with members throughout the United States. The dataset contains all individuals with 1 International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) codes²⁵ for eye-related diagnoses (360–379.9), 1 Current Procedural Terminology (CPT) codes²⁶ for any eye-related visits, diagnostic, or therapeutic procedures (65091–68899 or 92002–92499), or any other claim submitted by an ophthalmologist or optometrist from January 1, 2001 through December 31, 2012. For each enrollee, we had access to all medical claims for ocular and non-ocular conditions and sociodemographic information including age, sex, race, education level and income. Additionally, the database has records of all outpatient medication prescriptions filled by enrollees. All enrollees in the medical plan were also fully enrolled in the pharmacy plan. We have used this database in the past to study patients with glaucoma.^{27–29} Since all the data were de-identified to the researchers, the University of Michigan Institutional Review Board approved this as a non-regulated study.

Participants and Sample Selection

We identified all beneficiaries who were 40 years old, were newly diagnosed with open angle glaucoma (OAG), and were continuously enrolled in the plan for 7 years (Figure 1). OAG was identified by ICD-9-CM codes 365.1, 365.10, 365.11, 365.12, 365.15. To improve the certainty that these patients were not miscoded for OAG, we required them to have records of an OAG diagnosis on 3 separate dates. All persons also had to be enrolled

in the plan for 3 years (known as the look-back period) prior to receiving their first diagnosis of OAG to help exclude those with pre-existing disease.³⁰ In addition, all beneficiaries included in the analysis were required to have had 1 eye visit during the 3-year look-back period and 1 eye visit during the 4-year follow-up period to maximize the chance that they had an opportunity to be diagnosed with OAG and prescribed medication during each period. To help ensure that we were only evaluating newly diagnosed patients with OAG, enrollees who had any record of medical, laser or surgical treatment for glaucoma during the 3-year look-back period were also excluded (Figure 1). Non-continuously enrolled beneficiaries were excluded as they could have been prescribed medications during their time outside of the plan that could not be captured. Finally, enrollees were required to have filled 1 prescription for a glaucoma medication during the 4-year follow-up period. Since the outcome of interest was longer-term medication adherence, any beneficiaries were excluded from the analysis who did not have 4 years of follow up after their third OAG diagnosis.

Glaucoma Medications

Glaucoma medications were identified by American Hospital Formulary Service codes. Medications were divided into six classes: topical alpha agonists, beta-blockers, carbonic anhydrase inhibitors, prostaglandin analogues, miotics and oral carbonic anhydrase inhibitors Table 1 (available at <http://aaojournal.org>). Combination agents were treated as prescriptions for the two component medications.

Outcome

Our outcomes of interest were patterns of glaucoma medication adherence over a longer time trajectory (4 years). We measured medication adherence using the MPR, an accepted and frequently used technique to quantify adherence to eye drop medications using prescription refill data.¹⁷ The MPR is defined as the number of days when an individual has the medication available to use at the prescribed frequency divided by the total number of days in the time period of interest. In this analysis, the MPR was defined as the number of days per quarter (91–92 days) where the enrollee had filled his medication prescription. MPR was used in the trajectory models as a continuous variable, as it has been shown that MPR as a continuous variable is a better-performing adherence summary measure than that obtained by dichotomizing adherence.²⁰

Analyses

Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC). Participant characteristics were summarized for the entire sample using means and standard deviations for continuous variables and frequencies and percentages for categorical variables.

Group-based Trajectory Models to Capture Adherence

We used GBTM to classify patterns of glaucoma medication use among our group of patients with OAG²⁰ as it has been used for other chronic therapies such as statins²⁰ and anti-hypertensives.²¹ GBTM estimates the probability that an individual will belong to a

potential adherence “group” based on that individual’s pattern of medication use over a specified time period. The number of trajectory groups is chosen by estimating models using varying numbers of groups and identifying which number of groups best fits the overall adherence pattern data for the entire sample.

We created two GBTMs after the third time beneficiaries received a diagnostic code for OAG. The first classified individuals’ medication use over the first year of follow-up, and the second set of trajectory models classified patterns of adherence over the entire four-year follow-up period. For each trajectory model, one-way analysis of variance and chi-squared tests were used to determine whether covariates that may affect medication adherence differed significantly among the groups who exhibited different patterns of adherence. The covariates included in the analysis were age at OAG diagnosis, sex, race, education level, income, maximum number of glaucoma medication classes filled in any quarter, number of visits with an eye-care provider over the specified follow-up period, clinical risk group (CRG) as a measure of overall health,³¹ type of pharmacy supplying the medication (mail-order vs store pharmacy), co-payment cost of first glaucoma medication prescribed, depression and dementia (ICD-9-CM codes used in the analysis, Table 2 available at <http://aaojournal.org>). We found that five groups had the best data fit by comparing the Bayesian Information Criterion (BIC) of the GBTM models and ensuring that the proportion of the sample in each trajectory group was not <5% as recommended in the literature.^{20, 32} (Table 3). A linear regression model was used to predict the effect of trajectory model group during the first year of follow-up on MPR for the subsequent three years of follow-up. The linear regression model was adjusted for the majority of the covariates listed above that were chosen based on a step-wise selection process to maximize the predictive power of the model. The model generated beta coefficients with 95% confidence intervals (CI). To evaluate trajectory group stability over the entire follow-up period, the percent of beneficiaries who remained in the same trajectory group for all years of follow-up was tabulated along with the percent of beneficiaries who changed to a different trajectory model group after their first year of follow-up. To examine correlates of remaining in a trajectory model group with good adherence over the four-year follow-up period versus transitioning to a worse trajectory pattern after the first year of follow-up, we used logistic regression analyzing the same covariates mentioned above. The model generated odds ratios with 95% CIs. For all analyses, $p < 0.05$ was considered statistically significant.

Results

Overall, 1,234 individuals met the study inclusion criteria. The mean $\pm$ standard deviation (SD) age of beneficiaries included in our analysis was 61.1 ± 10.8 years. Our study population had 689 females (55.8%) and included 891 whites (76.0%), 140 blacks (11.9%), 82 Latinos (7.0%), 52 Asians (4.4%) and 8 (0.7%) persons of other races. The majority of our sample had attended at least some college (890 beneficiaries, 72.9%) and one-third (382 beneficiaries, 32.7%) had an income $\leq$ \$100,000. (Table 4)

The best-fit one-year and four-year GBTMs yielded five distinct patterns of adherence: 1) *Never adherent* (after their index prescription fill), 2) *Persistently very poor adherence*, 3) *Declining Adherence*, 4) *Persistently moderate adherence* and 5) *Persistently good*

adherence. (Figure 2a, 2b) Because GBTM creates groups of persons whose behavior is most similar to each other, subjects may not be in the same group in the two models that have been assessed over different time periods. In the one-year GBTM, 7.5% of enrollees were in the *Never adherent* group, 14.9% were in the *Persistently very poor adherence* group, 9.5% were in the *Declining adherence* group, 48.1% were in the *Persistently moderate adherence* group and 20.0% were in the *Persistently good adherence* group. In the four-year GBTM, 15.6% of enrollees were in the *Never adherent* group, 23.4% were in the *Persistently very poor adherence* group, 9.1% were in the *Declining adherence* group, 37.0% were in the *Persistently moderate adherence* group and 15.0% were in the *Persistently good adherence* group. (Figure 2a and 2b) Those who were in the *Persistently very poor adherence* group had a mean MPR of 16.9% in the first year of follow-up compared to those in the group with *Persistently moderate adherence* who had a mean MPR of 42.2%. The group with *Persistently good adherence* had an MPR >70% over the whole 4-year follow-up period. (Figure 2a, 2b)

Factors Associated with Different Adherence (MPR) Patterns

In the one-year GBTM, those in the group with *Persistently good adherence* were more likely to be older, white and have a higher first medication co-payment cost ($p < 0.05$ for all comparisons, Table 4). Those who were in the *Never adherent* group and those in the *Declining adherence* group were more likely to have lower personal income ($< \$60,000$) and to use store pharmacy pick-up only for their prescriptions instead of using either mail-order or both mail-order and store pharmacy pick-up ($p < 0.02$ for all comparisons). (Table 4) These same socio-demographic characteristics remained significant in the four-year GBTM. (Table 5)

Predictors of Longer Term Adherence (MPR)

A linear regression model was used to identify factors affecting the MPR during the last three years of follow-up. (Table 6) Running the model with the GBTM groups from year 1 as the only predictor variable yielded an R^2 of 0.35. Adding in socio-demographic factors to the model increased the R^2 to 0.45 ($p < 0.0001$ for the F-test comparing the two regression models). Though the trajectory group at year 1 had the greatest impact on predicted MPR over the subsequent 3 years, we also found that older age and higher income were significant in predicting better adherence (a higher MPR) over the subsequent three-years. Black race predicted a lower MPR, similar to findings in electronically monitored patients¹ (Table 6, $p > 0.05$ for all variables). Beneficiaries who used mail order only or both mail order and store pharmacy pick-up had a significantly higher MPR than those who used a store pharmacy only ($\beta = 7.6$, $p = 0.0003$, $\beta = 6.3$, $p < 0.0001$, respectively). (Table 6) For each additional medication class prescribed, a beneficiary's MPR was predicted to decline by 4.0% ($\beta = -4.0$, $p = 0.0008$). (Table 6). For each additional dollar that beneficiaries paid for their co-payment for their index prescription fill, the MPR was predicted to decline by 0.06% over the subsequent three years of follow-up ($\beta = -0.06$, $p = 0.03$). As an example, if a patient was prescribed a medication with a high co-payment cost of \$54 (one standard deviation above the mean for our study population), he would have a 2.9% lower MPR three years later compared to a patient initially prescribed a medication with a low co-payment cost (\$6, one standard deviation below the mean for our study population).

Trajectory Group Stability over Four Years of Follow-Up

Half (49.7%) of all patients who were in a given group in the first year remained in that same group over the four years of follow-up. Nearly all (93.9%) of the patients (n=232) who were in the *Persistently good adherence* group during their first year of follow-up stayed in two highest adherence groups for the entire four-year follow-up period. (Figure 3, Table 7) About two-thirds (63.4%) of the 593 beneficiaries who began in the *Persistently moderate adherence* group remained in this group or improved to the *Persistently good adherence* group over the four years, though roughly one-third (36.6%) went on to have worse patterns of adherence. The overwhelming majority (94.9%) of the 117 beneficiaries who began in the group with *Declining adherence* in year 1 ended up in the *Persistently very poor adherence* or *Never adherent* group in the four years of follow-up. (Figure 3, Table 7) Likewise, of the 277 beneficiaries in the *Never adherent* or *Persistently very poor adherence* groups in year 1, only 10.5% went on to improve their adherence patterns over the four year follow-up period. (Figure 3, Table 7)

Predictors of Maintaining Good Adherence Versus Experiencing a Decline in Adherence Over Time

Since approximately half of all patients were in the *Persistently moderate adherence* group in year one, and nearly two-thirds either maintained this level of adherence or improved over the four years of follow-up, we ran a logistic regression model to identify factors associated with maintaining or improving adherence within this group versus experiencing a decline in longer-term adherence. We defined “maintaining good adherence” as staying in the group with *Persistently moderate adherence* or transitioning to the group with *Persistently good adherence*. We found that non-white race conferred a 40% reduced odds of maintaining good adherence (OR=0.60, CI 0.39-0.93, p=0.02). Beneficiaries with more eye visits over four years were more likely to maintain good adherence (p<0.05 for all comparisons,). (Table 8) Beneficiaries who used both mail order and store pharmacy pick-up as their prescription delivery method as opposed to picking up their prescription at a store pharmacy only were 90% more likely to maintain good adherence over the four years (OR=1.90, CI 1.18-3.05, p=0.008). (Table 7)

Discussion

In this sample of 1,234 patients newly diagnosed and treated for OAG, we found that adherence status during the first year of treatment usually predicts well how people will take their medications over the longer term. Nearly all of those with *Persistently good adherence* in year one continued to have excellent adherence over the four-years. The majority who had poor adherence in year 1-- including those groups who were *Never adherent*, had *Persistently very poor adherence* or had *Declining Adherence*--continued to have poor adherence throughout the four years. Among those with *Persistently moderate adherence* during the first year of follow-up, two-thirds maintained at least this level of adherence or better while roughly one-third went on to have worsening adherence over the four years. This is important because the group with *Persistently moderate adherence* comprised nearly half of all patients (48.1%) during the first year of follow-up. This subgroup of patients may be most amenable to targeted interventions to improve adherence. Persons who exhibited the

best patterns of adherence shared some non-modifiable characteristics such as being white, being older, and having higher income. We also found three important more easily modifiable factors that may contribute towards better longer-term adherence: increased number of visits with an eye-care provider, decreasing medication co-payment cost, and not relying exclusively on store pharmacy pick-up for prescription refills. Some patients with an increased number of eye care visits might have more severe disease or poor intraocular pressure control, and may be more persistent with therapy because they have experienced negative visual symptoms from glaucoma or perhaps are more fearful of losing vision. We cannot know these details from this type of analysis, but we do know that the increased contact with the eye care provider brings with it repeated counseling, education and feedback about the patient's disease status that may help a relatively asymptomatic disease gain salience in the patient's mind.

Our findings suggest that in order to facilitate more targeted delivery of additional services for those who are at risk for poor adherence, it may be very helpful to use prescription refill data to monitor patients' adherence for at least their first year of glaucoma treatment. Our current analysis has shown that if patients are over 70% adherent during their first year of treatment, they are unlikely to have declining adherence over the next few years. Those patients may not require extra contact with the healthcare system to assist with adherence. Unfortunately, however, those patients made up only one-fifth of our sample. For the other 80% of patients, it may be important to bring back patients for more frequent visits to eye care providers for the first 2 years after initiating glaucoma medications to allow more time for discussions between patients and their eye care providers about issues surrounding medication adherence or the consideration of alternative treatments if adherence wanes. Though it may not be necessary for medical decision making purposes to have multiple clinic visits in a year for a patient newly diagnosed with glaucoma who initially has well-controlled intraocular pressure on her new glaucoma medication, it may be important to have this increased contact to facilitate improved longer-term adherence.

Understanding adherence patterns can help shape strategies for health-behavior interventions or guide changes in disease management such as recommending laser or incisional surgery. For example, if a patient has *Declining adherence*, it may be key to quickly initiate a discussion to explore potential barriers to adherence such as cost, side effects or inability to instill the eyedrops properly, among others. For a patient who has *Persistently moderate adherence*, discussing how glaucoma medications are most effective if taken consistently to minimize intraocular pressure fluctuation and collaborating with patients to identify ways to better integrate taking eye drops into the daily routine may be critical. For those who are *Never adherent* or have *Persistently poor adherence*, it may be crucial to explore beliefs about glaucoma and its treatment as the patients may not be convinced that these medications will truly help them avoid blindness.^{33,34} Mapping out what types of interventions might be most useful for patients exhibiting different patterns of adherence is an important area for future research.

When comparing our findings with other clinical areas, we see some similarities in patterns of medication use. Among statin users evaluated for 15 months of follow-up, 6 patterns of prescription refill behavior were identified including 1) "adherent" (23%), 2) "irregular

adherence that improved” (11%), 3) “declining adherence” (11%), 4) “poor/occasional adherence” (15%), 5) “rapid decline after initiation” (19%) and 6) “no fills after the index prescription” (23%).²⁰ Our enrollees showed a similar rate of very good adherence, 20.0% over one year and 15.0% over 4 years of follow-up. Persons in the groups with *Persistently very poor adherence* or *Never adherent* comprised 22.4% of our study population in the first year of follow-up and 39.0% of our study population over the four years of follow-up, compared to 57% of those in the statin study. In our study, the prevalence of poor adherence increased over time, highlighting the known concern that adherence with chronic medications is a widespread problem among patients with glaucoma.³¹⁷

Two other researchers have characterized short term patterns of medication use among patients with glaucoma on monotherapy with prostaglandin analogues evaluated with electronic medication monitors.^{35,36} They did not use GBTM as their sample sizes were too small.^{35,36} They identified four main patterns of usage through visual inspection of their data: 1) those who discontinued their medication after a short time period; 2) those who had frequent missed doses with adherence often <60%; 3) those who had frequent drug holidays and adherence <80%; and 4) those who had adherence ~80%. These are similar to our groups of *Never adherent* after the initial prescription fill, *Persistently very poor adherence*, *Declining adherence* and *Persistently good adherence*. We might assume that patients with frequent drug holidays over 2–3 months might go on to have declining adherence patterns over longer-term follow-up. Our analysis identified an additional group, those with *Persistently moderate adherence*. Both Cate³⁰ and Ajit³¹ found that over 60% of their sample was adherent ~80% of the time, which was a much higher rate of good adherence than we found in our study. The high levels of good adherence in these other studies could be due, in part, to the Hawthorne effect, where patients exhibit improved health behavior because they know they are being observed with the electronic dosing monitor, and to the short time period of observation after initiating glaucoma treatment. Some advantages to using prescription drug refill data as opposed to electronic monitoring to assess adherence are that there is no concern about the Hawthorne effect, and longer-term data is more easily obtainable. To our knowledge, this current study has the longest follow-up period for assessing adherence among glaucoma patients.

This study has several limitations. Using medication refill data as a measure of adherence will not identify patients who fill the prescription but do not use it or who use the medication but do not actually instill it properly, and we know that at least 20% of glaucoma patients are not able to instill eye drops properly into their eyes for many reasons,^{37–39} including co-morbid disease such as rheumatoid arthritis or Parkinson’s. Because this study utilizes claims data, we know when a patient has filled a prescription but we do not know when the physician has prescribed the medication. If a patient did not fill a prescribed medication, that medication would not be included in the analysis. We also do not know if a physician prescribed the glaucoma drops for one eye or for both eyes. While this may lead to an overestimation of poor adherence overall if medications are lasting longer than the standard 30 or 90 days because they are only prescribed for one eye, this should not lead to a difference between the distinct groups in the GBTMs as they should all be equally affected by this issue. It is likely that the increase in MPR found for those who use mail order

compared to those who use local pharmacy pick up is due to the difference in a receiving a 90 day supply versus a 30 day supply. However, claims data does not allow us to know whether this finding is due to the convenience of mail order refills or if there is a measurement bias as those who use mail order have fewer opportunities to miss refills. Clinical data were unavailable, and therefore we were not able to evaluate whether family history of glaucoma, severity of disease, visual acuity, intraocular pressure, or other clinical variables impact adherence.

In conclusion, monitoring adherence for at least one year for patients newly prescribed glaucoma medications could help better tailor educational and counseling interventions and disease management strategies. These changes could potentially improve adherence and outcomes for patients with glaucoma over the longer term.. With the aging population, there is a projected mismatch between patient demand for ophthalmic care and the ophthalmologist workforce, and so paraprofessional staff may need to play an increasing role in providing this extra contact between patients and the eye-care system through novel health care delivery pathways.^{40–42}

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Selection of beneficiaries for analysis.
Abbreviations: OAG, Open-Angle Glaucoma

Figure 2.
a. Group Based Trajectory Models^a Demonstrating Patterns of Glaucoma Medication Adherence Over One Year of Follow-up
b. Group Based Trajectory Models^a Demonstrating Patterns of Glaucoma Medication Adherence Over Four Years of Follow-up
The Medication Possession Ratio is the number of days the patient had the correct amount of medication in-hand divided by the total number of days of follow-up.

Figure 3.

Trajectory Group Stability Over Four Years of Follow-Up

This graph describes the movement of participants between trajectory groups from one year of follow-up to four years of follow-up. The numbers noted on the y axis (and specified above each bar) denote the total number of persons in each trajectory group during the first year. The shaded portions of each bar identify the percent of participants who changed to any of the five different trajectory groups when analyzed over four years of follow-up.

Table 3

Trajectory Model Best-Fit Criteria for One and Four Years of Follow-up

<u>One-year trajectory model selection</u>							
Model	Groups, n	BIC	Patients in each group (%)				
			1	2	3	4	5 6 7
1	2	-2366	30.7	69.3	-	-	- - -
2	3	-2141	16.4	53.0	30.6	-	- - -
3	4	-2108	11.4	21.2	46.2	21.2	- - -
4	5	-2078	10.9	16.8	6.8	44.8	20.7 - -
5	6	-2081	7.1	2.5	42.5	7.9	19.9 20.0 -
6	7	-2087	7.5	12.5	5.7	6.2	40.5 21.0 6.6

<u>Four-year trajectory model selection</u>							
Model	Groups, n	BIC	Patients in each group (%)				
			1	2	3	4	5 6 7
1	2	-10375	34.8	65.2	-	-	- - -
2	3	-9151	22.7	38.8	38.6	-	- - -
3	4	-8785	21.1	26.2	37.4	15.3	- - -
4	5	-8367	15.3	23.7	9.3	36.6	15.1 - -
5	6	-8132	14.9	4.5	24.6	34.0	8.4 13.6 -
6	7	-7993	12.6	4.2	8.8	23.7	33.8 3.1 13.8

BIC, Bayesian Information Criterion.

Highlighted rows show the number of groups that best fit the overall adherence pattern data for the entire sample by identifying the number of groups that simultaneously gives the lowest BIC while ensuring that the proportion of the sample in each trajectory group was not <5%.

Table 4

Demographic Characteristics, One Year Trajectory Model

Covariate N (%) or Mean (Standard Deviation)	Value	Never Adherent	Very Poorly Adherent	Declining Adherence	Persistent Moderate Adherence	Persistent Good Adherence	Overall	p-value
Total		93 (7.5)	184 (14.9)	117 (9.5)	593 (48.1)	247 (20.0)	1,234	
Age at OAG diagnosis		64.9 (12.4)	59.9 (10.5)	59.5 (10.6)	60.6 (10.5)	62.5 (10.8)	61.1 (10.8)	0.0002 ^a
Sex	Male	35 (37.6)	86 (46.7)	49 (41.9)	274 (46.2)	101 (40.9)	545 (44.2)	0.35 ^b
	Female	58 (62.4)	98 (53.3)	68 (58.1)	319 (53.8)	146 (59.1)	689 (55.8)	
Race (N_{miss}=61)	White	61 (68.5)	134 (75.7)	71 (64.0)	424 (75.7)	201 (85.2)	891 (76.0)	0.0003 ^b
	Black	17 (19.1)	23 (13.0)	24 (21.6)	64 (11.4)	12 (5.1)	140 (11.9)	
	Latino	9 (10.1)	15 (8.5)	12 (10.8)	35 (6.3)	11 (4.7)	82 (7.0)	
	Asian	2 (2.2)	5 (2.8)	4 (3.6)	30 (5.4)	11 (4.7)	52 (4.4)	
	Other	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.3)	1 (0.4)	8 (0.7)	
Education (N_{miss}=14)	Less than high school	1 (1.1)	3 (1.7)	2 (1.7)	4 (0.7)	0 (0.0)	10 (0.8)	0.8 ^b
	High school diploma	26 (28.9)	51 (28.2)	35 (30.2)	150 (25.6)	58 (23.6)	320 (26.2)	
	Some college	44 (48.9)	82 (45.3)	50 (43.1)	272 (46.3)	115 (46.7)	563 (46.1)	
	College Diploma	19 (21.1)	44 (24.3)	28 (24.1)	158 (26.9)	72 (29.3)	321 (26.3)	
	Advanced degree	0 (0.0)	1 (0.6)	1 (0.9)	3 (0.5)	1 (0.4)	6 (0.5)	
Income (N_{miss}=68)	< \$30K	12 (14.1)	14 (8.1)	11 (10.3)	42 (7.5)	17 (7.1)	96 (8.2)	0.02 ^b
	\$30K – \$60K	37 (43.5)	64 (37.0)	46 (43.0)	210 (37.3)	63 (26.5)	420 (36.0)	
	\$60K – \$100K	17 (20.0)	32 (18.5)	20 (18.7)	128 (22.7)	71 (29.8)	268 (23.0)	
	\$100K – \$125K	8 (9.4)	19 (11.0)	8 (7.5)	64 (11.4)	24 (10.1)	123 (10.5)	
	> \$125K	11 (12.9)	44 (25.4)	22 (20.6)	119 (21.1)	63 (26.5)	259 (22.2)	
Clinical Risk Group	1 (Healthiest)	7 (7.5)	24 (13.0)	13 (11.1)	76 (12.8)	21 (8.5)	141 (11.4)	0.13 ^b
	2	85 (91.4)	151 (82.1)	97 (82.9)	481 (81.1)	218 (88.3)	1,032 (83.6)	
	3 (Least healthy)	1 (1.1)	9 (4.9)	7 (6.0)	36 (6.1)	8 (3.2)	61 (4.9)	
Depression		8 (8.6)	15 (8.2)	14 (12.0)	54 (9.1)	22 (8.9)	113 (9.2)	0.9 ^b

Covariate N (%) or Mean (Standard Deviation)	Value	Never Adherent	Very Poorly Adherent	Declining Adherence	Persistent Moderate Adherence	Persistent Good Adherence	Overall	p-value
Dementia		6 (6.5)	4 (2.2)	2 (1.7)	19 (3.2)	7 (2.8)	38 (3.1)	0.30 ^b
Max Number of Medication Classes ^c		0.0 (0.0)	1.2 (0.4)	1.1 (0.4)	1.3 (0.6)	1.2 (0.5)	1.2 (0.6)	<0.0001 ^a
Number of Eye Visits ^d	0-2	51 (54.8)	75 (40.8)	56 (47.9)	294 (49.6)	108 (43.7)	584 (47.3)	0.05 ^b
	3	16 (17.2)	57 (31.0)	27 (23.1)	127 (21.4)	74 (30.0)	301 (24.4)	
	4	9 (9.7)	19 (10.3)	10 (8.5)	79 (13.3)	32 (13.0)	149 (12.1)	
	5 +	17 (18.3)	33 (17.9)	24 (20.5)	93 (15.7)	33 (13.4)	200 (16.2)	
Prescription Delivery Method	Mail Order Only	6 (6.5)	7 (3.8)	12 (10.3)	42 (7.1)	55 (22.3)	122 (9.9)	< 0.0001 ^b
	Pharmacy Only	82 (88.2)	139 (75.5)	93 (79.5)	391 (65.9)	107 (43.3)	812 (65.8)	
	Both	5 (5.4)	38 (20.7)	12 (10.3)	160 (27.0)	85 (34.4)	300 (24.3)	
First Co-payment (\$) ^e		24.5 (22.6)	27.1 (22.5)	27.1 (19.1)	30.8 (22.0)	36.5 (30.9)	30.6 (24.1)	< 0.0001 ^a

^a One-way analysis of variance^b Chi-square test^c Max Number of Medication Classes, refers to the highest number of glaucoma medication classes dispensed in any single quarter during the first year of follow-up.^d Number of Eye Visits, refers to the number of eye care provider visits during the first year of follow-up.^e First co-payment (\$), refers to the average cost of the co-payment(s) for a beneficiary's index prescription fill (more than one medication may be included in that index fill).

Table 5

Demographic Characteristics Four-Year Trajectory Model

Covariate N (%) or Mean (Standard Deviation)	Value	Never Adherent	Very Poorly Adherent	Declining Adherence	Persistent Moderate Adherence	Persistent Good Adherence	Overall	p-value
Total		192 (15.6)	289 (23.4)	112 (9.1)	456 (37.0)	185 (15.0)	1,234	
Age at OAG diagnosis		60.8 (11.4)	61.0 (10.7)	58.1 (11.5)	60.9 (10.2)	63.7 (10.9)	61.1 (10.8)	0.0005 ^a
Sex	Male	82 (42.7)	119 (41.2)	55 (49.1)	217 (47.6)	72 (38.9)	545 (44.2)	0.16 ^b
	Female	110 (57.3)	170 (58.8)	57 (50.9)	239 (52.4)	113 (61.1)	689 (55.8)	
Race (N_{miss}=61)	White	116 (64.4)	195 (71.7)	79 (73.8)	352 (80.5)	149 (84.2)	891 (76.0)	0.0003 ^b
	Black	33 (18.3)	39 (14.3)	18 (16.8)	41 (9.4)	9 (5.1)	140 (11.9)	
	Latino	21 (11.7)	25 (9.2)	4 (3.7)	24 (5.5)	8 (4.5)	82 (7.0)	
	Asian	10 (5.6)	10 (3.7)	6 (5.6)	16 (3.7)	10 (5.6)	52 (4.4)	
	Other	0 (0.0)	3 (1.1)	0 (0.0)	4 (0.9)	1 (0.6)	8 (0.7)	
Education (N_{miss}=14)	Less than high school	4 (2.1)	2 (0.7)	1 (0.9)	3 (0.7)	0 (0.0)	10 (0.8)	0.06 ^b
	High school diploma	56 (29.6)	84 (29.5)	37 (33.6)	103 (22.8)	40 (21.6)	320 (26.2)	
	Some college	84 (44.4)	121 (42.5)	49 (44.5)	227 (50.3)	82 (44.3)	563 (46.1)	
	College Diploma	44 (23.3)	77 (27.0)	23 (20.9)	114 (25.3)	63 (34.1)	321 (26.3)	
	Advanced degree	1 (0.5)	1 (0.4)	0 (0.0)	4 (0.9)	0 (0.0)	6 (0.5)	
Income (N_{miss}=68)	< \$30K	22 (12.6)	20 (7.4)	10 (9.4)	30 (6.9)	14 (7.7)	96 (8.2)	0.001 ^b
	\$30K – \$60K	75 (42.9)	106 (39.3)	47 (44.3)	152 (35.0)	40 (22.1)	420 (36.0)	
	\$60K – \$100K	33 (18.9)	53 (19.6)	19 (17.9)	106 (24.4)	57 (31.5)	268 (23.0)	
	\$100K – \$125K	12 (6.9)	26 (9.6)	8 (7.5)	55 (12.7)	22 (12.2)	123 (10.5)	
	> \$125K	33 (18.9)	65 (24.1)	22 (20.8)	91 (21.0)	48 (26.5)	259 (22.2)	
Clinical Risk Group	1 (Healthiest)	16 (8.3)	30 (10.4)	18 (16.1)	64 (14.0)	13 (7.0)	141 (11.4)	0.04 ^b
	2	167 (87.0)	249 (86.2)	85 (75.9)	367 (80.5)	164 (88.6)	1,032 (83.6)	
	3 (Least healthy)	9 (4.7)	10 (3.5)	9 (8.0)	25 (5.5)	8 (4.3)	61 (4.9)	
Depression		25 (13.0)	26 (9.0)	9 (8.0)	42 (9.2)	11 (5.9)	113 (9.2)	0.21 ^b

Covariate N (%) or Mean (Standard Deviation)	Value	Never Adherent	Very Poorly Adherent	Declining Adherence	Persistent Moderate Adherence	Persistent Good Adherence	Overall	p-value
Dementia		9 (4.7)	7 (2.4)	3 (2.7)	13 (2.9)	6 (3.2)	38 (3.1)	0.7 ^b
Max Number of Medication Classes^c		1.3 (0.6)	1.6 (0.9)	1.4 (0.7)	1.8 (0.9)	1.6 (0.9)	1.6 (0.9)	< 0.0001 ^a
Number of Eye Visits^d	1 – 7	96 (50.0)	81 (28.0)	50 (44.6)	83 (18.2)	40 (21.6)	350 (28.4)	< 0.0001 ^b
	8 – 10	40 (20.8)	69 (23.9)	19 (17.0)	119 (26.1)	45 (24.3)	292 (23.7)	
	11 – 14	24 (12.5)	63 (21.8)	20 (17.9)	144 (31.6)	49 (26.5)	300 (24.3)	
	15 +	32 (16.7)	76 (26.3)	23 (20.5)	110 (24.1)	51 (27.6)	292 (23.7)	
Prescription Delivery Method								
	Mail Order Only	13 (6.8)	22 (7.6)	11 (9.8)	38 (8.3)	38 (20.5)	122 (9.9)	< 0.0001 ^b
	Pharmacy Only	170 (88.5)	205 (70.9)	86 (76.8)	273 (59.9)	78 (42.2)	812 (65.8)	
	Both	9 (4.7)	62 (21.5)	15 (13.4)	145 (31.8)	69 (37.3)	300 (24.3)	
First Copayment (\$)^e		28.6 (23.3)	27.7 (20.8)	29.2 (19.6)	31.1 (23.0)	36.6 (32.6)	30.6 (24.1)	0.002 ^a

^a One-way analysis of variance^b Chi-square test^c Maximum number of medication classes, refers to the highest number of glaucoma medication classes dispensed in one quarter during the four years of follow-up.^d Number of Eye Visits, refers to the number of eye care provider visits during the four years of follow-up.^e First co-payment (\$), refers to the average cost of the co-payment(s) for a beneficiary's index prescription fill (more than one medication may be included in that index fill).

Table 6

Factors Predicting Adherence for the Last Three Years of Follow-Up

Covariate	Value	Beta Coefficient ^a	P-Value
Intercept		42.2	
Trajectory Model Group	Never Adherent	−42.4	< 0.0001
	Very Poorly Adherent	−33.4	< 0.0001
	Declining Adherence	−44.3	< 0.0001
	Persistent Moderate Adherence	−18.5	< 0.0001
	Persistent Good Adherence	REF	
Age at Third OAG Diagnosis		0.2	0.0002
Sex	Male	REF	
	Female	1.5	0.2
Race	White	REF	
	Black	−3.7	0.04
	Latino	−3.0	0.2
	Asian	−4.8	0.09
	Other	0.8	0.9
Income	< \$30,000	REF	
	\$30,000 – <\$60,000	3.8	0.04
	\$60,000 – <\$100,000	7.6	0.0002
	\$100,000 – <\$125,000	9.2	0.0001
	\$125,000	4.2	0.04
Max Number of Medication Classes ^b		−4.0	0.0008
Number of Eye Visits ^c	0 – 2	REF	
	3	1.8	0.2
	4	2.0	0.3
	5 +	−1.2	0.5
Prescription Delivery Method	Mail Order Only	7.6	0.0003
	Pharmacy Only	REF	
	Both	6.3	< 0.0001
First Copayment		−0.06	0.03

OAG, open angle-glaucoma

^a Beta coefficients that are negative indicate worse adherence compared to the reference group and beta coefficients that are positive indicate better adherence compared to the reference group.

^b Maximum number of medication classes, refers to the highest number of glaucoma medication classes dispensed in any single quarter during the first year of follow-up.

^c Number of eye visits, refers to the total number of visits to an eyecare provider over the first year of follow-up.

Table 7

Trajectory Group Stability over Four Years of Follow-Up

Group movement between one-year and four-year groups, (n, row percent)					
	Group, All Four Years				
Group, First Year	Group 1 (Never Adherent)	Group 2 (Very Poorly Adherent)	Group 3 (Declining Adherence)	Group 4 (Persistent Moderate Adherence)	Group 5 (Persistent Good Adherence)
Group 1 (Never Adherent)	47 (50.5)	43 (46.2)	1 (1.1)	2 (2.2)	0 (0.0)
Group 2 (Very Poorly Adherent)	40 (21.7)	92 (50.0)	25 (13.6)	27 (14.7)	0 (0.0)
Group 3 (Declining Adherence)	79 (67.5)	32 (27.4)	2 (1.7)	3 (2.6)	1 (0.9)
Group 4 (Persistently Moderate Adherence)	26 (4.4)	121 (20.4)	70 (11.8)	332 (56.0)	44 (7.4)
Group 5 (Persistently Good Adherence)	0 (0.0)	1 (0.4)	14 (5.7)	92 (37.2)	140 (56.7)

Highlighted cells show how many beneficiaries started off in a given trajectory group during their first year of follow-up and stayed in that particular trajectory group for their entire four years of follow-up.

Table 8

Odds of Maintaining Moderate Adherence or Improving Adherence Over 4 Years Among those with *Persistent Moderate Adherence* in Year 1^a

Covariate	Value	OR (95% CI)	P-Value
Age at OAG Diagnosis		1.03 (1.01, 1.06)	0.003
Sex	Male	REF	
	Female	0.92 (0.63, 1.36)	0.7
Race	White	REF	
	Non-White	0.60 (0.39, 0.93)	0.02
Education	High School or Less	REF	
	Some College	1.05 (0.63, 1.74)	0.9
	College Degree or Higher	0.79 (0.41, 1.50)	0.5
Income	< \$30,000	REF	
	\$30,000 – < \$60,000	1.04 (0.48, 2.24)	0.9
	\$60,000 – < \$100,000	1.68 (0.71, 3.99)	0.2
	\$100,000 – < \$125,000	1.85 (0.69, 4.97)	0.2
	\$125,000	1.28 (0.51, 3.21)	0.6
Clinical Risk Group	1 (Healthiest)	REF	
	2	0.72 (0.40, 1.30)	0.3
	3 (Least Healthy)	0.92 (0.34, 2.49)	0.9
Depression		0.78 (0.41, 1.49)	0.4
Dementia		0.38 (0.13, 1.15)	0.1
Maximum Number of Medication Classes ^b		1.13 (0.88, 1.46)	0.3
Number of Eye Visits ^c	1 – 7	REF	
	8 – 10	1.71 (1.01, 2.89)	0.05
	11 – 14	2.34 (1.38, 3.95)	0.002
	15 +	1.89 (1.05, 3.43)	0.03
Prescription Delivery Method	Mail Order Only	1.32 (0.63, 2.78)	0.5
	Store Pharmacy Only	REF	
	Both	1.90 (1.18, 3.05)	0.008

OAG, Open-angle glaucoma; OR, Odds Ratio

^a Logistic regression predicting the odds of maintaining good adherence (staying in the *Persistent moderate adherence* group or improving to the *Persistent good adherence* group) versus exhibiting worse adherence (switching to the *Declining Adherence*, *Very poorly adherent*, or *Never adherent* groups) over four years of follow-up among beneficiaries who were part of the *Persistent moderate adherence* group during their first year of follow-up.

^b Maximum number of medication classes, refers to the highest number of glaucoma medication classes dispensed in one quarter during the four years of follow-up.

^c Number of eye visits, refers to the total number of visits to an eyecare provider over the four years of follow-up.