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## Cost-Related Medication Non-Adherence in a Nationally Representative U.S. Population with Self-Reported Glaucoma

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### Abstract

**Purpose:** To determine the rates of cost-related non-adherence to medications among U.S. adults with glaucoma and to determine if participants with glaucoma have more cost-related medication non-adherence than those without glaucoma

**Design:** Cross-sectional study

**Participants:** Participants in the 2016–2017 National Health Interview Survey (NHIS), a cross-sectional survey regarding health topics that is administered annually to a nationally representative sample of non-institutionalized adults in the U.S.

**Methods:** We calculated proportions of NHIS participants with and without self-reported glaucoma who reported cost-related non-adherence over the previous 12 months. We analyzed responses to 7 survey items that dealt with medication cost-related issues to any/all of a participants' medication: Couldn't afford a prescribed medication; Skipped medication doses to save money; Took less medicine to save money; Delayed filling a prescription to save money; Asked doctor for lower cost medication to save money; Bought prescription drugs from another country to save money; Used alternative therapies to save money. We performed univariable and

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In this nationally representative U.S. survey, participants with glaucoma more frequently reported cost-related non-adherence to medications compared to participants without glaucoma.

**Conflict of Interest:** None.

multivariable logistic regression to evaluate the association between self-reported glaucoma diagnosis and responses to these selected questions.

**Main Outcome Measures:** Proportion of participants with and without self-reported glaucoma who reported cost-related non-adherence.

**Results:** Participants with glaucoma reported they could not afford prescribed medication more frequently than participants without glaucoma (8.2% vs 6.4%  $p=0.024$ ). Adjusted predicted proportions from a multivariable model demonstrated that participants with glaucoma responded that they had greater cost-related barriers to medication access.

**Conclusions:** In this nationally representative sample of the U.S. population, after adjustment for confounding variables, participants with glaucoma more frequently reported cost-related non-adherence to medications compared to participants without glaucoma. Providers prescribing medication to patients with glaucoma should be aware of these findings and consider the impact of medication cost on their patients' ability to adhere to therapy.

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## Introduction

The management of glaucoma, like many chronic diseases, involves the use of long-term medications. In glaucoma care, this typically involves the use of topical eye drops; these topical eye drops decrease the risk of glaucomatous progression and irreversible vision loss.<sup>1</sup> Unfortunately, patient adherence to glaucoma eye drops is poor.<sup>2,3</sup>

Worldwide, medical glaucoma treatment is costly to patients with annual topical eyedrops amounting to a significant portion of their median household income.<sup>4</sup> In previous qualitative interview studies, cost has been identified as a barrier to accessing glaucoma medication.<sup>5-9</sup> While prior research suggests that cost plays an important role in medication adherence for patients with glaucoma, it is not known on a national level what proportion of patients with glaucoma have cost-related issues with medication adherence. Further, it is not known how challenges regarding the cost of medication compares between patients with and without glaucoma. Understanding how cost affects glaucoma patient medication adherence is important to policy makers and doctors who take care of patients with glaucoma.

In the present study, we present nationally representative rates of cost-related non-adherence for adults with glaucoma in the U.S. We also tested the hypothesis that people with glaucoma have more cost-related challenges to medication adherence than those without glaucoma.

## Methods

### Data and Analysis Sample

We used data from participants 40 years and older from the National Health Interview Survey (NHIS) taken during the years 2016 and 2017 where questions related to eye health and visual function were included. Secondary analysis of this public dataset (NHIS) was approved by the University of Utah's IRB. We excluded participants under 40 years of age to focus on the age range of participants at greatest risk for glaucoma. NHIS is a cross-sectional survey of the US population administered by the U.S. Bureau of the Census. Data

from 2016 and 2017 were pooled using the methods recommended by NHIS; we treated pooled data as one large sample, as the samples for 2016 and 2017 were from the same geographic areas with the same sample design, did not overlap, and the variables used for variance estimation were the same for both years of NHIS data.<sup>10</sup>

### Variable Definitions

The outcome variables were self-reported responses to yes/no items in NHIS which assessed cost-related barriers to medication adherence over the previous 12 months: Couldn't afford a prescribed medication; Skipped medication doses to save money; Took less medicine to save money; Delayed filling a prescription to save money; Asked doctor for lower cost medication to save money; Bought prescription drugs from another country to save money; Used alternative therapies to save money. For comparison, we aggregated the number of positive responses per participant for the five NHIS statements that directly dealt with difficulties affording medications (couldn't afford prescription medication, skipped medication doses to save money, took less medication to save money, delayed filling med to save money, or used alternative therapies to save money). Participants with glaucoma were identified in NHIS based on self-report of a having been "Told you have glaucoma;" participants with vision impairment were identified by survey responses to "trouble seeing even with glasses or lenses" or "blind or unable to see at all."

Relevant covariates included in our analysis were age, gender, race, Hispanic ethnicity, educational attainment, uninsured status, Medicare/Medicaid status, poverty ratio (a ratio of the household income to the federal poverty threshold), and self-reported prior diagnosis of a chronic medical condition (hypertension, high cholesterol, heart disease, stroke, emphysema, chronic obstructive pulmonary disease, asthma, cancer, or diabetes).

### Analyses

Based on NHIS design, we calculated the weighted proportions of participants for each sociodemographic group stratified by glaucoma response. Unadjusted *P* values from Pearson  $\chi^2$  tests are reported. We used separate univariable logistic regression models to determine if glaucoma diagnosis (predictor) was associated with any of the seven questions concerning cost-related barriers to medication adherence (outcome). Unadjusted negative binomial regression was used to evaluate the association of glaucoma diagnosis with the number of cost-related medication non-adherence issues.

Multivariable logistic regression was performed and adjusted for age, gender, race, ethnicity, education, medical co-morbidities, uninsured status, Medicare/Medicaid status, and poverty ratio using multiple imputation. All analyses accounted for the complex design of NHIS, including sampling weights, units, and strata, and were conducted using Stata version 16.

### Results

Table 1 presents participant characteristics. 40,380 participants were included in the study; 1,930 (weighted %: 4.0) reported having glaucoma and 38,450 (weighted %: 96.0) reported not having glaucoma. Participants with glaucoma were more likely to be female, older, black race, have another medical comorbidity, lower educational attainment, lower household

income, and to have vision impairment ( $p<0.001$  for all comparisons). Participants with glaucoma were less likely to be uninsured ( $p<0.001$ ) and more likely to be insured by Medicaid ( $p=0.01$ ) or Medicare ( $p<0.001$ ) than participants without glaucoma.

### Frequency of cost-related issues with medication adherence

Compared to NHIS respondents without glaucoma, those with glaucoma more frequently could not afford prescribed medication (8.2% vs 6.4%  $p=0.024$ ; Table 2). Of participants with glaucoma, 22.6% had asked their doctor for lower cost medication to save money.

The adjusted predicted proportion of participants with glaucoma who had been prescribed medications was greater than among those without glaucoma (77.4% [73.8–80.9] vs. 65.5% [64.9–66.2],  $p<0.001$ ). In the multivariable model, participants with glaucoma had greater cost-related barriers to medication access and more frequently endorsed all the NHIS medication cost-related statements except for “bought prescription drugs from another country to save money” (Table 2;  $p<0.05$  for all other comparisons). Both groups only had a small number of participants that bought medications from another country (1.8% [1.6–2.0] in participants without glaucoma and 1.8% [0.8–2.7] in participants with glaucoma,  $p=0.967$ ).

The responses to the five questions directly related to cost-related non-adherence were summed; participants with glaucoma self-reported more cost-related medication non-adherence issues than patients without glaucoma (0.32 [95%CI: 0.26–0.39] compared to 0.24 [95% CI: 0.23–0.25],  $p=0.003$ ).

## Discussion

In this study of a large, nationally representative sample, we found that individuals with glaucoma were more likely to face cost-related challenges that could affect medication adherence. Participants with glaucoma were more likely to report that they could not afford medications compared to those without glaucoma. Participants with glaucoma also more frequently self-reported other health co-morbidities, which likely increases medication burden. Participants with glaucoma also had lower income and lower educational attainment, which are known to affect glaucoma medication adherence.<sup>11</sup> After adjusting for co-morbidities and other potential confounders in our multivariable analyses, we found that participants with glaucoma were also significantly more likely to skip/delay/take less medication, look for alternative therapies due to the cost, and ask their doctors for lower cost medications than participants without glaucoma. When these cost-related medication non-adherence responses were aggregated, we also saw that participants with glaucoma had greater difficulties affording medications than those without glaucoma.

This analysis also highlights issues that were common among participants with and without glaucoma. Buying medications outside the US was not common among NHIS participants. The most commonly endorsed measure to address the cost burden of medications among those with glaucoma was that they “Asked doctor for lower cost medication to save money.” However, only 20% of NHIS participants asked their doctor for a lower cost medication, which is in line with previous work that demonstrated that the majority of glaucoma office

visits did not involve discussions of medication cost or problems affording medications initiated by either the physician or the patient.<sup>12</sup>

While some NHIS participants asked their provider for a less expensive medication, this statement does not directly imply that an individual was non-adherent to their therapy. We cannot conclude from this statement that a participant is having difficulty affording their glaucoma medication(s) or obtaining their medications. A more direct statement related to cost-related medication nonadherence was “Couldn’t afford a prescribed medication,” which affected 8.2% of participants with glaucoma and 6.4% of participants without glaucoma, a statistically significant difference, even after adjustment for potential confounding factors.

Questions that directly called into questions an individual’s medication adherence – skipped medication doses to save money; took less medicine to save money; and delayed filling a prescription to save money – were affirmed in 9.1–12.7% of participants with glaucoma in the adjusted models. Participants with glaucoma also used alternative therapies to save (7.0% - adjusted proportion) calling into question their adherence to prescribed medication(s). In aggregate, when we summed the responses to the five questions directly related to cost-related non-adherence, participants with glaucoma self-reported greater cost-related medication non-adherence than patients without glaucoma (0.32 vs 0.24 summed responses).

Many of the strategies to decrease medication cost that were detected in the present study were also found in a previous study of a group of interviewed patients in the United Kingdom’s National Health Service.<sup>13</sup> However, our study is the first to look at these cost-related medication adherence issues in a U.S. nationally-represented survey. Also, unlike previous studies, that had qualitatively looked at the topic of adherence, our study allows for quantification of results and comparison between those with and without self-reported glaucoma.

There are limitations to our study. For one, glaucoma diagnosis was self-reported because of the nature of this survey. Self-reported eye disease has been shown to have high specificity and low sensitivity; meaning glaucoma diagnoses may have been underestimates in this sample.<sup>14</sup> Prevalence of glaucoma in our study was 4%, which was higher than previous historical estimates of glaucoma, however, the clinical ability to diagnose glaucoma has changed over time with advent of newer imaging modalities.<sup>15</sup> Further, our study demonstrated that participants with self-reported glaucoma were more likely to be older, have lower income, and of black race, which is consistent with results from previous epidemiological and survey studies.<sup>15,16</sup> Survey responses may also have been affected by recall and social-desirability biases. However, we would not expect these biases to affect those with and without glaucoma differently; in fact they would likely lead to underreporting of cost related medication adherence issues in NHIS, which would bias results toward the null hypothesis. Additionally, participants did not report cost-related barriers specifically related to glaucoma medications, but rather barriers to any (or all) of the medication(s) that they take. Finally, these data did not contain detail on disease severity and participant perceptions of their disease; both of which may influence the value individuals place on their glaucoma medications, which may in turn affect cost-related medication adherence issues.

Some of these limitations may be able to be overcome in smaller surveys that contain greater detail on participants' glaucoma and glaucoma treatment; though a strength of the current study is the number of participants in the NHIS survey and the generalizability of a nationally representative survey.

In data from the 2016–2017 NHIS, a nationally representative U.S. Population survey, participants with glaucoma more frequently experienced cost-related medication issues compared to those without glaucoma. Primary care providers and eye care professionals should be prepared to discuss cost-related barriers to medication adherence with their patients who have glaucoma, and to consider alternative medications and interventions.

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**Table 1.**

Characteristics of Study Population, in NHIS participants surveyed in the years 2016–2017.

Characteristic	No Glaucoma <sup>a</sup>	Glaucoma <sup>a</sup>	P value <sup>b</sup>
<b>Total n, (weighted %)</b>	N= 38450 (96.0%)	N = 1930 (4%)	
<b>Age, years</b>			
40–64	23651 (69.4%)	566 (33%)	<0.001
65–74	8704 (18.6%)	606 (30.8%)	
75–84	4339 (8.9%)	487 (24.5%)	
85+	1756 (3.1%)	273 (11.7%)	
<b>Sex</b>			
Male	17382 (47.7%)	752 (41.4%)	<0.001
Female	21068 (52.3%)	1178 (58.6%)	
<b>Race/Ethnicity</b>			
White	31765 (80.7%)	1457 (75.32%)	<0.001
Black	3967 (11.1%)	346 (16.9%)	
Asian	1717 (5.8%)	69 (4.8%)	
American Indian or Alaska Native	376 (0.9%)	22 (0.9%)	
Multiple Race	626 (1.4%)	36 (2.1%)	
<b>Ethnic</b>			
Not Hispanic	34839 (87.4%)	1758 (87.9%)	0.66
Hispanic	3611 (12.6%)	172 (12.1%)	
<b>Education</b>			
Less than high school	4868 (12.8%)	342 (17.7%)	<0.001
High School Diploma	16493 (41.6%)	863 (44.1%)	
Associate Degree	4632 (11.8%)	206 (10.8%)	
College Graduate	12311 (33.9%)	512 (27.5%)	
<b>Other co-morbidity<sup>c</sup></b>			
Yes	27828 (69.9%)	1722 (88.0%)	<0.001
No	10622 (30.1%)	208 (12.0%)	
<b>Vision impairment<sup>d</sup></b>			
Yes	5120 (12.3%)	617 (31.4%)	<0.001
No	33317 (87.7%)	1313 (68.6%)	
<b>Uninsured</b>			
Yes	2469 (7.1%)	50 (2.6%)	<0.001
No	35871 (92.9%)	1977 (97.4%)	
<b>Medicaid</b>			
Yes	4035 (10.0%)	253 (12.5%)	0.01



Characteristic	No Glaucoma <sup>a</sup>	Glaucoma <sup>a</sup>	P value <sup>b</sup>
No	34341 (89.3%)	1674 (87.5%)	
<b>Medicare</b>			
Yes	15827 (33.2%)	1427 (69.83%)	<b>&lt;0.001</b>
No	22587 (66.78%)	503 (30.2%)	
<b>Income (% of poverty level)<sup>e</sup></b>			
0–99.9%	4209 (9.3%)	294 (13.6%)	<b>&lt;0.001</b>
100–199.9%	6814 (16.2%)	446 (19.3%)	
200–399.9%	11023 (27.8%)	597 (31.8%)	
400+%	16404 (46.7%)	1930 (35.4%)	

<sup>a</sup> Participants self-report whether they have been told they have glaucoma or not in the preceding 12 months. Participants 40 years and older were included in this analysis.

<sup>b</sup> p-values are calculated using design-adjusted Pearson chi-squared test.

<sup>c</sup> Other medical diagnosis = self-reported diagnosis of hypertension, high cholesterol, heart disease, stroke, emphysema, COPD, asthma, cancer, or diabetes

<sup>d</sup> Vision impairment = self-reported “trouble seeing even with glasses or lenses” or “blind or unable to see at all”

<sup>e</sup> Multiple imputation was used for missing income (poverty level) data.

**Table 2.**

Unadjusted and adjusted proportions of patients with and without glaucoma that had medication cost-related issues

Unadjusted Proportions			
NHIS Question	No Glaucoma % [ 95% CI]	Glaucoma % [ 95% CI]	P Value <sup>b</sup>
Prescribed med	72.8% [72.1–73.5]	91.2% [89.5–93.0]	<0.001
Could not afford meds	6.4% [6.0–6.8]	8.2% [6.5–10.0]	0.024
Skipped med to save	5.7% [5.3–6.1]	6.2% [4.5–7.8]	0.598
Took less to save	6.0% [5.6–6.3]	6.5% [4.8–8.2]	0.539
Delay filling	7.2% [6.8–7.6]	8.8% [6.9–19.6]	0.088
Asked for cheaper med	20.3% [19.4–21.1]	22.6% [20.2–25.0]	0.053
Bought another country	1.7% [1.5–2.0]	1.6% [0.8–2.5]	0.828
Alternative to save	4.0% [3.7–4.2]	4.8% [3.5–6.0]	0.212
Adjusted Predicted Proportions <sup>a</sup>			
	No Glaucoma	Glaucoma	P Value <sup>b</sup>
Prescribed med	65.5% [64.9–66.2]	77.4% [73.8–80.9]	<0.001
Could not afford meds	6.5% [6.1–6.9]	8.9% [7.0–10.8]	0.005
Skipped med to save	6.5% [6.0–7.0]	9.1% [6.6–11.5]	0.016
Took less to save	6.7% [6.2–7.2]	9.4% [6.9–11.8]	0.016
Delay filling	8.1% [7.5–8.6]	12.7% [10.0–15.3]	<0.001
Asked for cheaper med	20.3% [19.4–21.2]	25.1% [22.6–27.7]	<0.001
Bought another country	1.8% [1.6–2.0]	1.8% [0.8–2.7]	0.967
Alternative to save	4.3% [4.0–4.6]	7.0% [5.1–8.9]	0.001

<sup>a</sup> Adjusted for: age, gender race, ethnicity, education, medical morbidities, uninsured status, Medicare/Medicaid status, and poverty ratio using multiple imputation.

<sup>b</sup> P values are calculated using design-adjusted Pearson chi-squared test.