

Lower Copay and Oral Administration: Predictors of First-Fill Adherence to New Asthma Prescriptions

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Background: Nonadherence to asthma medications is associated with increased emergency department visits and hospitalizations. If adherence is to be improved, first-fill adherence is the first goal to meet after the physician and patient have decided to begin treatment. Little is known about first-fill adherence with asthma medications and the factors for no-fill.

Objective: The goal of the study was to examine the proportion of patients who fill a new prescription for an asthma medication and analyze characteristics associated with this first-fill.

Methods: This retrospective cohort study linked electronic health records with pharmacy claims. The cohort was comprised of 2023 patients aged 18 years or older who sought care from the Geisinger Clinic, had Geisinger Health Plan pharmacy benefits, and were prescribed an asthma medication for the first time between 2002 and 2006. The primary outcome of interest was first-time prescription filled by the patient within 30 days of the prescription order date. Covariates examined included factors related to the patient (ie, age, sex, and ethnicity), comorbidities and utilization (ie, Charlson comorbidity index, number of office visits, number of additional medications), asthma treatment (ie, delivery route, pharmacologic class), and pharmacy copay amount. A logistic-regression model was used to determine covariates associated with first-fill.

Results: The overall first-fill rate for new asthma medications was 78%. First-fill rate was lower for patients with a copay above the mean of \$12 (odds ratio = 0.76; 95% confidence interval, 0.58-0.99) and higher for patients prescribed oral plus inhaled medications (versus inhaled only, odds ratio = 3.91; 95% confidence interval, 2.15-7.11).

Conclusions: Several factors associated with failing to fill an initial prescription for asthma can be addressed through simple interventions: screening for difficulties a patient may have in filling prescriptions, avoiding nonformulary medications, and recognizing the barrier that high copays present. In addition, for employers and policymakers, decreasing copay may improve adherence and, therefore, asthma control. [*AHDB*. 2009;2(4):174-180.]

Adherence to prescribed medications is necessary to improve outcomes. But “low adherence is ubiquitous and undermines treatment benefits.”¹ Patients with chronic conditions in developed countries take about only half of their medications.^{2,3} The World Health Organization classifies adherence-related factors into 5 dimensions: healthcare-related, socioeconomic, disease-related, therapy-related, and patient-related.⁴ Although the adherence literature is extensive, previous studies have used disparate methods, patient popu-

lations, and definitions, making it difficult to determine which of these factors is most significant.⁵⁻⁷

Adherence in asthma is particularly important. Medication nonadherence among patients with asthma is associated with increased emergency department visits and hospitalizations.³ In addition, adherence among the patient population is low, with adherence to inhaled corticosteroids among the lowest in all patients with chronic conditions.⁸ Understanding and improving patient adherence is one way to improve asthma care.

Much of the adherence literature to date has focused on whether the patient takes the medication as prescribed (assuming that the prescription has been filled) and relies on patient self-reporting, which is unreliable.⁹

First-fill—patient’s filling of a new prescription—is essential to adherence. An accurate estimate of adher-

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ence and treatment effects depends on prescription filling, after which other metrics of adherence (ie, medication taking) can be considered.

In addition, if prescription no-fill is not recognized as a possible cause for treatment failure, a second-line medication could be unnecessarily prescribed, exposing the patient to additional costs and potential side effects. Although the literature on adherence is expansive, understanding first-filling of prescriptions for asthma medication is still in its preliminary stages.¹⁰⁻¹² The present study seeks to add to that understanding.

We hypothesized that the following “dimensions of adherence”⁴ are associated with failure to fill a prescription, patient-related (ie, higher comorbidity index, more office visits, and greater pill burden, as well as age by means of comorbidity and loss of function); condition- and treatment-related (ie, number of asthma medications, inhaled versus oral route of delivery, and controller versus reliever medication); and health-care system–related (ie, higher copay).

To test these hypotheses, we linked prescribing information from Geisinger Clinic electronic health records (EHRs) to pharmacy claims data of one insurer, Geisinger Health Plan (GHP). Through these linked databases we identified prescriptions that were written but ultimately not filled by patients. We used a retrospective cohort design to assess the proportion of patients who filled a first-time prescription for an asthma medication and then examined characteristics associated with first-fill.

Methods

Data Source and Settings

Our primary data sources were 2 large, linked data sets: Geisinger Clinic’s EHR and GHP’s claims database. In the case of first-fill of asthma medications, reliable linking of EHR to claims data within a single healthcare system helps address recall bias (prescriptions and fills are accurately recorded), selection bias (all patients with a new asthma prescription are included), and statistical power (the data sets comprise thousands of patients).

The Geisinger Clinic is a multispecialty practice with more than 40 clinic sites and more than 600 providers. An EHR system was installed in all Geisinger Clinic community practice sites and specialty clinics, allowing for the integration of clinical information across diverse settings of care and making all patient information available in digital form. GHP is one part of Geisinger’s diverse payer mix and accounts for 30% of the Geisinger Clinic’s patient volume. Although GHP shares its name with Geisinger Clinic, it is an independent entity and one of the nation’s largest rural health maintenance

KEY POINTS

- ▶ Little is known about first-fill adherence patterns of patients receiving first prescription for asthma medications; adherence is necessary to improve outcomes in this patient population.
- ▶ This is the largest study of its kind to analyze characteristics of first-fill or no-fill for asthma medications. Of the 2023 patients with asthma in this study, 78% filled their first-time prescriptions within 30 days, and 22% did not.
- ▶ Patient copay of <\$12 (the mean) resulted in a higher first-fill adherence rate than a copay of >\$12.
- ▶ Other variables affecting first-fill medication adherence rates included therapeutic class and route of administration, as well as controller and reliever type of medications.

organizations (HMOs). Initially started as a group practice HMO, GHP has expanded into a network model and now has more than 220,000 members.

Sample Selection

The Geisinger Clinic patient population includes residents from central and northeastern Pennsylvania, a predominantly white population. In this study we included patients who were 18 or older at the time of a new asthma prescription; had sought care from the Geisinger Clinic; had GHP pharmacy benefit; and were prescribed a medication to treat asthma between January 2002 and September 2006 that had not been prescribed or filled within the previous 6 months. To ensure that a new asthma prescription could be identified, the patient had to be in the Geisinger Clinic system for at least 1 year before the prescription date.

Eligible medications fell into the following subclasses: sympathomimetics, oral corticosteroids, inhaled corticosteroids, leukotriene modulators, bronchodilators, or a combination of these classes. To eliminate patients who utilized spousal pharmacy benefit, the population included only those who had used their GHP pharmacy benefit at least once prior to the date of the index medication.

Study Variables

Data extracted from the EHR included variables related to the patient and the patient’s socioeconomic status (ie, age, sex, race); comorbidities, based on the Charlson index of comorbid conditions other than HIV;¹³ number of prescriptions for all conditions ordered

within 10 days of the index prescription, and number of office visits 6 months before index prescription; and asthma treatment (number of asthma prescriptions and drug class). The order date was also extracted for purposes of linking to the claims database. Information on asthma severity and chronic obstructive pulmonary disease was not available.

Data from the pharmacy claims database included asthma prescription characteristics (ie, drug class, medication type [controller or reliever], route of delivery, copay amount, fill date) and the outcome (whether the prescription was filled, ie, first-fill). Identifiers from the EHR record were linked to GHP pharmacy claims data.

Statistical Analysis

A patient was designated as a “first-fill” if the first-time prescription resulted in a claim within 30 days of the EHR order date (less than 1% of prescriptions that ultimately generated claims occurred after 30 days; these data are not shown and are classified as “non-fillers”). Bivariate analysis determined characteristics related to first-fill. Categorical variables were analyzed using chi-square tests, Fisher’s exact test, and Cochran-Armitage trend tests. Continuous variables were assessed using *t*-test and Wilcoxon rank-sum test, where appropriate.

A logistic regression model was used to determine those covariates associated with first-fill. Socioeconomic variables (age, sex) and all variables related to asthma prescription characteristics were considered for inclusion in the model. Other variables were considered for inclusion, when bivariate *P* values were $<.10$, using the Bonferroni correction to safeguard against multiple tests of statistical significance on the same data.

Variables were forward-selected for inclusion in the model based on scientific plausibility. Collinear variables were not included. Separate analyses were conducted for a subset of records corresponding to controller (ie, maintenance) medications only, because adherence to these medications is of clinical interest to policymakers. Prescription fill records representing leukotriene modulators only (36/2023, or 1.7% of the total) were excluded from the logistic-regression analysis, because these medications are frequently used for conditions other than asthma. All analyses were conducted with the SPSS statistical software package (version 14.0, Chicago, IL).

Results

Records for 2023 predominantly Caucasian patients met all inclusion criteria. Of these, 65% were female,

and 96% were Caucasian. The median age was 49 years, and 3% were 65 years or older.

More than two thirds of patients (68%) were prescribed either reliever medications or both reliever plus controller medications; about one third (32%) were prescribed controller medications only. Two thirds (67%) of the current asthma prescriptions were administered via inhaler only; one third of prescriptions (33%) were either oral or oral medications plus inhalers. Most prescriptions (80%) were for 1 asthma medication; 17% were for 2 medications.

All patients in the data set had medications ordered for comorbid conditions within 10 days of the new asthma prescription. For the majority of patients (52%), the number of medications ordered for other conditions was 2 or 3; for 34%, 4 or more were ordered.

The mean copay was \$12 (standard deviation 13, median 9, mode 10).

Overall, 78% (1586) of patients filled their first-time prescriptions within a 30-day period (**Table 1**). Copays less than \$12 resulted in a first-fill rate of 74%; copays more than \$12 resulted in a 69% first-fill rate ($P = .17$). In a logistic-regression model, prescriptions with copays of more than \$12 were only three quarters (odds ratio = 0.76; 95% confidence interval, 0.58-0.99) as likely to be filled as prescriptions with copays less than \$12 (**Table 2**).

First-fill rates differed by therapeutic class and route of administration (Table 1). First-fill was decreased for those prescribed inhaled steroids only (first-fill, 65%; $P <.001$) and leukotriene modulators only (first-fill, 56%; $P <.001$), whereas the subclasses (1) oral steroids, inhaled steroids, and sympathomimetics, and (2) oral steroids and sympathomimetics were positively associated with first-fill (first-fill, 92% and 95%, respectively; $P <.001$).

First-fill rate was associated with prescriptions for controller and for reliever medications (first-fill, 87%; $P <.001$), as well as prescriptions for inhaler and oral medications (first-fill, 91%; $P <.001$), as were the number of asthma medications (first-fill for more than 3, 88%; $P <.001$) and the number of total medications (first-fill for more than 1, 81%; $P <.001$).

Factors that had no relationship to first-fill rate include age, sex, race, Charlson comorbidity index, or total number of office visits.

Predictors of First-Fill from a Logistic-Regression Model

Individual predictors were considered in a logistic-regression model to determine the best predictors of first-fill (**Tables 2, 3**). For all asthma-specific medications,

first-fill was associated with prescriptions for oral medications (as compared with the reference category of inhaled medication only) and prescriptions for both oral and inhaled medications (compared with inhaled medication only).

First-time prescriptions for asthma medications were less likely to be filled by patients whose copay was greater than the mean.

Within the subset of controller asthma medications, the effects of oral route (versus inhaled) and of higher copay were larger than for the entire set of records. In this subset, total pill burden and the number of office visits within the previous 6 months were also associated with first-fill, although the 95% confidence intervals included 1.0.

Discussion

Using linked EHR and pharmacy claim data, we compiled a large sample of patients with asthma who had new prescriptions and estimated first-fill and its associations with medication type and prescription characteristics. This is the largest study of this kind to date.

First-fill in this study for all types of asthma medication was 78%. New asthma prescriptions were more likely to be filled if they were for oral medications (as compared with inhaled medications). New asthma prescriptions were less likely to be filled among patients whose copay was greater than the mean.

Lack of first-fill in this study is comparable with previous estimates in asthma of 8% to 30%,^{10-12,14} and studies of other conditions using similar populations.^{15,16} Unlike previous studies, in our study there was no significant difference in first-fill between age-groups, sex, or comorbid conditions as measured by the Charlson comorbidity index. This contradicts a previous study of first-fill of primary care medications.¹⁷

Active prescriptions for oral asthma medication, or both oral and inhaled medications, were associated with first-fill compared with inhaled medication alone. The association between inhaled controller medication and no-fill in our study is notably different from the findings of Williams and colleagues, who found a first-fill rate of 92% for inhaled corticosteroids.¹² Based on our clinical experience, it appears that patients associate inhalers with short-term, symptomatic relief, making our result counterintuitive. The most likely explanation is confounding of medication route by disease severity. Patients who feel sick and are told that steroids will make them feel better will fill their prescriptions; those with mild disease or without an active exacerbation will be less likely to fill a prescription.

Table 1 Differences in First-Fill of Asthma Medications

Variable	Adherent patients, N (%) ^a	P
Overall medications ordered	1586/2023 (78)	
Medications ordered, by subclass		<.001 ^b
Sympathomimetics only	833/1091 (76)	
Oral steroids only	324/396 (82)	
Inhaled steroids and sympathomimetics	122/154 (79)	
Oral steroids and sympathomimetics	124/130 (95)	
Inhaled steroids only	60/93 (65)	
Leukotriene modulators and sympathomimetics	36/43 (84)	
Leukotriene modulators only	20/36 (56)	
Oral steroids, inhaled steroids, and sympathomimetics	23/25 (92)	
Bronchodilators only	8/9 (89)	
Other combinations	36/46 (78)	
Type of medication		<.001 ^b
Controller only	481/646 (74)	
Reliever only	707/1024 (78)	
Controller and reliever	308/353 (87)	
Route of administration		<.001 ^c
Inhaler	1031/1353 (76)	
Oral	351/445 (79)	
Inhaler and oral	204/225 (91)	
Asthma drugs ordered, N		<.001 ^c
1	1245/1625 (77)	
2	298/349 (85)	
3+	43/49 (88)	
Total drugs ordered (±10 days), N		<.001 ^c
1	171/262 (65)	
2-3	856/1062 (81)	
4-7	505/632 (80)	
8+	54/67 (81)	.17 ^b
Copay amount		
\$0-\$12.00	1197/1512 (74)	
\$12.01+	389/510 (69)	
Office visits in previous 6 mo, N		.903 ^c
0	5/7 (71)	
1-4	1313/1670 (79)	
5-9	235/306 (77)	
10+	33/40 (83)	

Note: Compliance was defined as prescription fill for an asthma medication within 30 days of initial order.
^aBecause a patient can have multiple prescriptions, the totals will not add up to 100%.
^bChi-square test.
^cCochran-Armitage trend test.

Table 2 Multiple-Regression Model for Predicting 30-Day First-Fill (N = 2023)

Variable	Odds ratio (95% confidence interval)
Patient-associated	
Office visits	0.99 (0.94-1.04)
Pill burden	1.05 (0.98-1.12)
Route of asthma medication: treatment-associated	
Inhaled only	(reference)
Oral only	1.28 (0.96-1.71)
Oral and inhaled	3.91 (2.15-7.11)
Copay: healthcare system-associated	
Greater than mean	0.76 (0.58-0.99)

Our most notable result is a positive relationship between copay above the \$12 mean and prescription no-fill. It is unlikely that this result is confounded by socioeconomic status, because this HMO-enrolled population is somewhat homogeneous; however, this remains a possibility, given our lack of income or education data. Our result agrees with previous studies, which have shown that copay increases as small as \$2 can significantly reduce adherence.¹⁸

The copay effect was greater in the group that was prescribed only controller medications. Further research is needed to test the hypothesis that patients with longer-term use of asthma medications tend not to fill those requiring higher copay, explaining the stronger effect among the controller medication subgroup. This has important policy implications; public health is improved when patients are compliant with asthma controller medications. As employers turn to value-based benefit design,¹⁹ improving first-fill for these medications would be of public and economic benefit.

Successful initiatives to improve patient medication adherence in chronic medical conditions have been multifactorial.⁶ The present study links 2 factors to adherence—lower copay and oral medications. There are practical measures providers can take to improve first prescription fill, including screening for difficulties the patient may have in filling the prescription (eg, asking “Do you have any difficulty getting this medicine at the pharmacy?”) and optimizing regimens to avoid no-fill (eg, avoiding nonformulary medications and medications with higher copay). Reducing copay can improve compliance and thus improve asthma control,¹⁹ an important factor for employers and policymakers.

Table 3 Multiple-Regression Model for Predicting 30-Day First-Fill in Users of Controller Asthma Medications (N = 646)

Variable	Odds ratio (95% confidence interval)
Patient-associated	
Office visits	1.04 (0.95-1.13)
Pill burden	1.08 (0.97-1.19)
Route of asthma medication: treatment-associated	
Inhaled only	(reference)
Oral only	1.88 (1.16-2.60)
Oral and inhaled	4.31 (0.90-20.6)
Copay: healthcare system-associated	
Greater than mean	0.41 (0.25-0.57)

Limitations

The failure of this study to find associations between lack of first-fill and age or ethnicity was most likely because of insufficient power. Only 3% of the population (n = 60) was 65 years or older, and only 4% was non-Caucasian. In contrast, if this finding is true and is not due to a type I error, it could support the conclusions of other studies on patient adherence in general, which have shown no associations with age or ethnicity in, for example, adherence with antihypertensives.²⁰ Finally, it could be that in this population of HMO patients, ethnicity- or age-based inequities of care were not significant.

Linking EHR data with claims data allowed us to incorporate patient and prescription characteristics not available in adherence studies limited to claims data. However, because the study was limited to electronic data, no direct contact was made with patients to determine their perception of the severity of their disease or the effectiveness of their prescribed treatment. In addition, without patient follow-up, we might have underestimated prescription fills. A subset of patients might have been incorrectly categorized as noncompliant if they filled their prescription using a pharmacy benefit plan other than GHP, or paid out of pocket. We attempted to diminish the possibility of this error by excluding patients from analysis who did not fill at least 1 other prescription through GHP prior to the index prescription.

Conclusion

Higher copays and inhaled asthma medications (as

compared with oral medications) are associated with failure to fill first-time prescriptions for asthma medication. Our findings should be generalized with caution to other healthcare systems, minority populations, or older patients. Future research should focus on identifying the different stages of the prescription cycle, from first-fill to medication adherence to refill to requesting a new prescription from the physician, and quantifying success at each step using data from multiple linked sources. ■

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STAKEHOLDER PERSPECTIVE

Medication Adherence: Is Lower Copay the Best Strategy to Improve Care and Reduce Costs?

This study of first prescription fill rates in patients with asthma contributes unique information about the complex puzzle of medication adherence. Like many recent articles on this topic, it highlights the impact of lower patient pay on improving adherence. But does this represent the best use of funds to improve care and lower costs?

Many studies highlight the significant impact of poor adherence on overall healthcare costs, and other studies show that adherence can be improved.

In 2001, the cost burden for the United States related to poor patient adherence was estimated at \$100 billion annually.¹ In 2003, the World Health Organization estimated that approximately 50% of patients with asthma did not take their medications as prescribed.²

Following diagnosis, the primary treatment issues concerning the vast majority of ambulatory patients consists of getting them on the right medication and maintaining their adherence. But we must not assume

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that lowering patient cost is the only strategy that can improve medication compliance. Prescribing medications with fewer side effects and less frequent dosing can also improve compliance. Should incentives include guiding patients to the highest value drugs, or apply equally to all drugs, regardless of value?

The present article highlights that only 78% of patients in this study actually filled their first prescription for asthma. This problem remains largely undetected. Future e-prescribing systems may inform physicians when their patients fail to pick up that first prescription. Other programs may include physician-dispensing or analytic systems that detect patients who have been diagnosed with a medical condition but have no follow-up therapy.

Programs to help patients maintain adherence can focus on incentives (such as lower patient pay), refill reminders, or interventions supported by analytics that detect adherence issues. Lowering copayments or coinsurance provides an easy-to-implement solution with proved short-term benefits; however, little is known about the long-term, lasting impact of this approach. Other potential incentives may tie lower patient pay, contribution to health savings accounts, or lower deductibles to completion of health risk assessments, participation in disease management programs, or maintaining adherence for defined durations (eg, every 6 months).

This begs the question whether lowering patient pay offers better value than other services, such as those that detect and notify providers of poor adherence. Lowering patient pay by \$5 for every chronic medication would cost upwards of 10 times more than intervention services that focus on adherence plus other medication therapy problems, missing preventive services, and gaps in evidence-based care.

How does the value of low pay compare with wellness or with care management programs? We need a lot more evidence on identifying the best services that will provide the best value to improve care and lower costs. Although improved medication adherence should be a primary area of focus, we do not yet have the evidence on what combination of approaches will deliver us the best value. Until then, I look forward to more studies that will shed light on this complex issue.

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