Practical Implications • p 112
Author Information • p 117
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Determinants of Primary Nonadherence in Asthma-Controller and Dyslipidemia Pharmacotherapy

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ABSTRACT

Objective: To describe factors associated with failure to fill initial prescriptions for asthma-controller and dyslipidemia medications.

Study Design: Retrospective cohort analysis.

Methods: A total of 23,176 prescriptions were written by 507 providers between January 1, 2005, and October 31, 2006. Of these, 2243 (1182 asthma controller and 1061 dyslipidemia) were eligible for analysis (ie, not preceded by use of a clinically equivalent drug and written for a patient <65 years of age) and compared with subsequent paid pharmacy claims. If 60 days lapsed from the prescribed date without a paid pharmacy claim for a clinically equivalent drug, the prescription was deemed as unfilled. We compared selected provider, patient, and prescription benefit characteristics associated with filled and unfilled prescriptions by conducting a prescription-level logistic regression analysis.

Results: Initiation failures occurred for 240 asthma-controller (20.3%) and 362 dyslipidemia (34.1%) prescriptions. Approximately 67.9% and 43.2% of the asthma-controller and dyslipidemia prescriptions, respectively, were filled on the same day as prescribed. Of those ultimately filled, 95.0% and 93.2% were filled within 2 weeks. Older age, fewer prior claims, and copayments above $10 were associated with a greater likelihood of initiation failures.

Conclusions: Poor medication adherence among patients prescribed asthma-controller or dyslipidemia medications is a larger problem than can be estimated from administrative pharmacy claims alone. Adherence improvement programs should consider primary nonadherence and use the identified predictive factors to improve interventions and educational efforts. Additional research should explore other characteristics that influence primary nonadherence and the probable healthcare costs associated with initiation failures.

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The full therapeutic benefit of prescription medications is realized only when the patient follows the healthcare provider's recommendations, a concept referred to as medication adherence. Premature treatment discontinuation and other forms of poor medication adherence are common and contribute to adverse drug events, worsening disease, increasing healthcare costs, and decreasing quality of life.[1-3] As a result, there is a wealth of scientific evidence documenting risk factors for poor adherence and effectiveness of interventions to improve adherence.[4-11] Yet these studies often rely on secondary data sources, typically administrative pharmacy claims, to identify patients and measure adherence. Though a powerful source of prescription drug information, administrative data can profile only the medication-taking behavior of patients who have already received therapy, and thus have filled at least 1 prescription.

In contrast, relatively little is known about the extent and causes of primary nonadherence, prescriptions given by a healthcare provider but never filled by the patient. Without an electronic record, connecting physicians' handwritten or oral prescriptions with medication-dispensing records is manual and resource intensive. Thus, studies of primary adherence have relied primarily on patient self-reports or on patient populations receiving prescriptions while hospitalized or receiving emergency care, where computer prescription order entry systems exist. These studies routinely report adherence rates across multiple pharmacotherapies, represent the experience of a single pharmacy, enroll only select patient populations, or report the experience of a non-US patient population. As a result, estimates of primary nonadherence vary widely, with international studies reporting rates from 2% to 30%[12-14] and US studies reporting rates from 2% to 20%.[15,16]

Electronic prescribing (e-prescribing), a solution formerly available only in hospital settings that had an integrated technology platform connecting physicians with pharmacies, is now gaining acceptance in ambulatory care settings.[17] With the increasing use of e-prescribing, identifying

Practical Implications

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and tracking large volumes of unfilled prescriptions have become practical. Horizon Blue Cross Blue Shield of New Jersey (Horizon) in conjunction with its pharmacy benefits manager, CVS Caremark, measured the rate and determinants of initiation failure among individuals receiving initial prescriptions for asthma-controller and dyslipidemia agents.

METHODS

In 2003, Horizon launched an initiative to equip providers with e-prescribing tools, enabling them to have electronic access to patient formulary and prescription drug history information at the point of care. In this retrospective cohort analysis, prescriptions written via iScribe, the CVS Caremark e-prescribing tool accessed and implemented through a handheld personal digital assistant or via the Internet, were compared with administrative pharmacy claims. Prescriptions qualified for comparison if they were prescribed (1) by 1 of 507 providers participating in this initiative; (2) for a target drug (ie, an asthma-controller or dyslipidemia medication) (**Table 1**); (3) between January 1, 2005, and October 31, 2006 (the prescribing period); (4) for a patient younger than age 65 years with full pharmacy benefit coverage from 180 days before (the preperiod) to 60 days after (the follow-up period) the prescribing date; and (5) for a patient with no paid claims in the preperiod for a drug in the applicable treatment category.

All qualifying prescriptions (prescribing events) that met the stated criteria were included. Asthma-controller and dyslipidemia therapies were selected as they represent chronic maintenance medication groups with substantial utilization (providing a sufficient sample size for study) that are routinely included in health improvement, disease management, and adherence improvement efforts. Eligibility was restricted to treatment initiators because primary nonadherence in this population would not be captured by currently available adherence measurement studies. Qualified prescriptions were compared against pharmacy claims inclusive of prescriptions dispensed between January 1, 2005, and December 31, 2006, to accommodate follow-up periods for all prescribing dates.

Data Sources and Uses

Several data sources were used to define qualified prescribing events and to compile the analytical data set. Electronic prescribing records were the source of the healthcare provider name, patient name, prescribed drug name, prescribing date, and prescription plan benefit identification numbers. Provider reference files were the source of prescriber degree (doctor of medicine [MD] or doctor of osteopathy [DO]) and specialty (internal medicine, family/general practice, pediatrics, pulmonary/allergy/immunology). Paid pharmacy claims were the source for identifying filled prescriptions.

For analysis, patient age was grouped into a pediatric group (0-18 years), younger adult group (19-44 years), and 2 older adult groups (45-54 years and 55-64 years). Household income was estimated from US Census projections by zip code and categorized (≤$41,000; $41,001-$51,000; $51,001-$61,000; $61,001-$71,000; and ≥$71,001). Prescription copayments (<$10, $10 to <$15, $15 to <$20, $20 to <$25, and ≥$25, which were based on the natural peaks observed for this client) were assigned to the prescribed medication using the generic, preferred brand, or nonpreferred brand indication as of the prescribing date. For flat-dollar copayment benefit structures, prescription copayment values were taken directly from the benefit; for percentage-based copayments, copayments were determined by applying the percentage to the estimated drug cost. As an example, a 10% coinsurance rate on a $50 drug would result in a $5 copayment. Drug cost was calculated from the monthly values of cost per quantity by drug name, strength, and quantity. As formulary tier assignment was not captured, it was inferred from copayment differentials. Finally, a count of paid pharmacy claims during the preperiod quantified the patient's recent drug utilization experience (none, 1-2 paid claims, 3-8 paid claims, and ≥9 paid claims).

To determine whether a written prescription had been filled with a clinically equivalent drug, paid pharmacy claims data from the follow-up period were compared with the prescribing data file. Time-to-fill was measured as the difference between the initial dispensing date and the prescribing date. As generic substitution and therapeutic interchange are common pharmacy practices, lists of clinically equivalent drugs for each class were derived by clinical consensus.

Analysis

Distributions of key variables by fill status were calculated. Cumulative fill rates were calculated as the sum of all fills divided by the number of applicable prescribing events. Time-to-fill and fill rates by member age were graphed by treatment category. Prescribing event fills were used as the dependent variable in logistic regression models for single and combined class analyses with the groups created for age, sex, prior period claims experience, provider specialty and degrees, household income, copayments, and tier type as the independent variables. The independent variables were included as dummy variables in separate models for each disease and a combined model. Because the members' age distribution differed between the 2 conditions, the individual disease-specific models tested the effects of different age categories. As the disease-specific models produced similar results (for age and other covariates), we combined age groups and only present the overall model results. The disease-specific models are available in the **eAppendix** at **www.ajpblive.com**. Analyses were performed using SAS version 9.1.3 (SAS Institute, Inc., Cary, NC). Differences were assessed for significance within the logistic models or using χ^2 tests, including tests of filled/unfilled for the variable groups.

RESULTS

The 2243 qualified prescribing events represented 1182 asthma-controller and 1061 dyslipidemia events and were written for 2116 patients (**Figure 1**). Of the asthma-controller events, a total of 357 (30.2%) were attributed to patients younger than age 19 years and 378 (32.0%) were attributed to patients age 19 to 44 years. For the dyslipidemia prescribing events, only 185 (17.4%) were for patients younger than age 45 years. Among all the prescriptions written, 52.2% were for women (57.3% of asthma-controller prescriptions, 46.5% of dyslipidemia prescriptions). Nearly 30% of dyslipidemia and 18.6% of asthma-controller prescriptions were written for patients with no recent history of prescription medication use. A total of 1733 prescriptions were written by doctors of medicine, 510 were written by doctors of osteopathy, and the remaining 78 were written by nonphysicians. General practitioners, family practitioners, or internal medicine physicians prescribed 77.8% of medications, varying from 61.2% of asthma-controller medications to 86.5% of dyslipidemia medications.

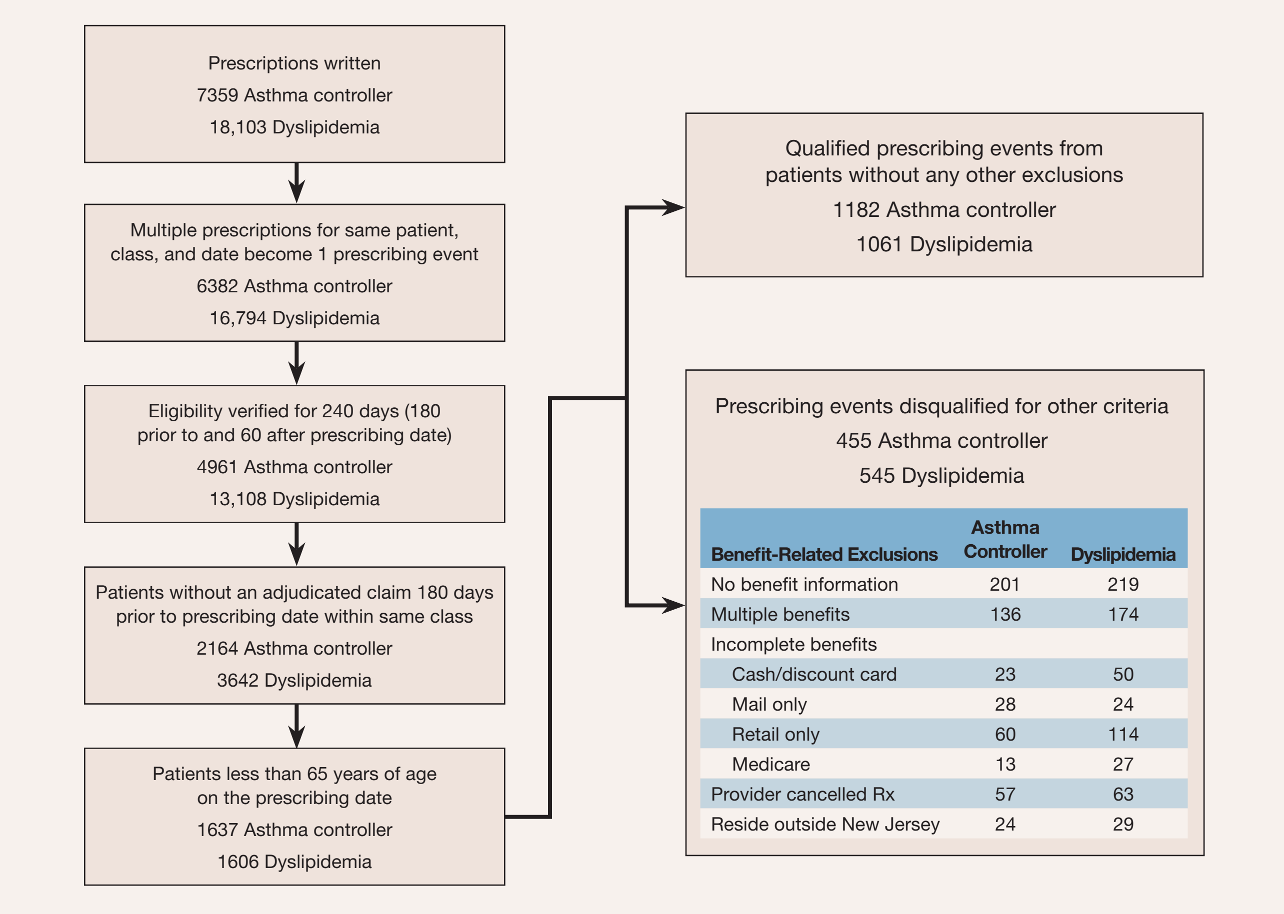
Fill rates varied over time and by several of the characteristics studied. After 60 days, a total of 240 asthma-controller prescriptions (20.3%) and 362 dyslipidemia prescriptions (34.1%) went unfilled (**Table 2**, **Figure 2**).

Table 1. Classification of Drugs by Generic and Brand Name

Category and Generic Name	Brand Name(s)
Asthma controller	
Beclomethasone	Qvar
Budesonide	Pulmicort Respules and Pulmicort Turbuhaler
Cromolyn	Cromolyn Sodium
Flunisolide	Aerobid and Aerobid-M
Fluticasone	Flovent, Flovent HFA, and Flovent Rotadisk
Fluticasone-salmeterol	Advair Diskus
Formoterol	Foradil Aerolizer
Montelukast	Singulair
Pirbuterol	Maxair Autohaler
Salmeterol	Serevent and Serevent Diskus
Theophylline	Theo-24, Theolair-SR, Theophylline, Theophylline SR, Theo-Time, Uniphyl
Triamcinolone	Azmacort
Zafirlukast	Accolate
Dyslipidemia	
Atorvastatin	Lipitor
Cholestyramine	Cholestyramine
Ezetimibe	Zetia
Ezetimibe-simvastatin	Vytorin
Fenofibrate	Antara, Fenofibrate Micronized, Tricor, Triglide
Fluvastatin	Lescol and Lescol XL
Gemfibrozil	Gemfibrozil
Lovastatin	Lovastatin
Lovastatin-niacin	Advicor
Pravastatin	Pravachol
Rosuvastatin	Crestor
Simvastatin	Zocor

Though 67.9% of asthma-controller and 43.2% of dyslipidemia prescriptions were dispensed on the prescribing date, these prescriptions represented nearly 85.1% and 75.5% of the total dispensed in the follow-up period. Of those ultimately filled, 95.0% of asthma-controller and 93.2% of dyslipidemia medications were filled within 2 weeks of the prescribing date. The unadjusted age-specific fill rates only differed significantly for the older age group receiving dyslipidemia prescriptions, where the fill rate dropped to 59.9% for patients age 55 to 64 years (Table 2). In both cohorts, patients' sex was not associated with filled prescriptions. For dyslipidemia prescriptions, the 60-day

Figure 1. Flow Diagram for Identifying Unique Prescribing Events for Potential Initiators of Asthma-Controller or Dyslipidemia Medications



Benefit-Related Exclusions	Asthma Controller	Dyslipidemia
No benefit information	201	219
Multiple benefits	136	174
Incomplete benefits		
Cash/discount card	23	50
Mail only	28	24
Retail only	60	114
Medicare	13	27
Provider cancelled Rx	57	63
Reside outside New Jersey	24	29

fill rates differed significantly by prescriber degree (DO 72.6% vs MD 64.0%), whereas the degree did not matter for asthma-controller prescriptions, with fill rates around 80%. No significant differences were found for fill rates by specialty.

After adjustment for numerous provider, patient, and plan design characteristics, only patient age, recent history of pharmacy claims, and out-of-pocket cost for the prescription (copayment) remained significant predictors of filling a prescription in the combined class analysis, with similar but unreported results in the single class results. Compared with the youngest age group (age ≤18 years), the probability of filling a prescription decreased with each successive age group, reaching statistical significance among patients age 45 to 54 years (odds ratio [OR] = 0.55) and age 55 to 64 years (OR = 0.45). Recent pharmacy claim history also showed a consistent relationship, with ORs increasing from 0.09 (for individuals with no recent claims) to 0.65 (for individuals with 3-8 recent claims) compared with individuals who had 9 or more claims. Compared with prescriptions with estimated copayments of $25 or more, only the lowest cost prescriptions (ie, those with copayments of <$10) had significantly higher odds of being filled (see eAppendix at www.ajpblive.com).

DISCUSSION

Our results indicate that about 20% of asthma-controller and 34% of dyslipidemia prescriptions written to initiate therapy went unfilled and that patient out-of-pocket costs, age, and recent use of prescription medications were significant predictors of primary adherence. To our knowledge, no studies have directly assessed failure to initiate prescribed chronic disease therapy by matching electronic prescription records with pharmacy claims in an ambulatory care population. Yet there is a wealth of indirect evidence against which to compare these results. Most of that evidence is derived from studies with significantly different designs, patient populations, follow-up time, or drug mixes.

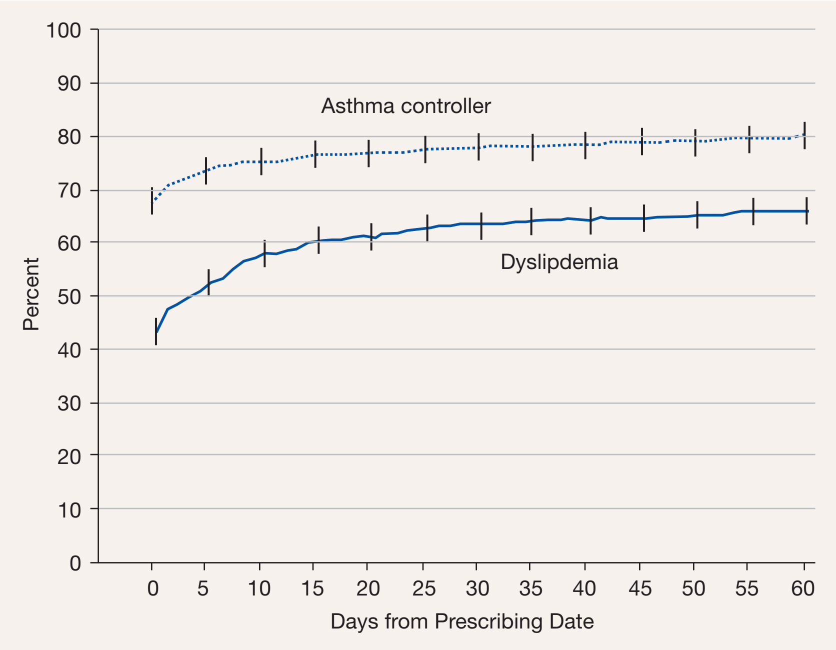
Rates of first fill adherence with various medications prescribed during visits to or on discharge from an

Table 2. **Distribution of Provider and Patient Characteristics Associated With Filled and Unfilled Eligible Prescribing Events by Treatment Category**

	No. (%)			
	Asthma Controller		Dyslipidemia	
Characteristics	Filled (n = 942)	Unfilled (n = 240)	Filled (n = 699)	Unfilled (n = 362)
Provider characteristics				
Degree				
Doctor of medicine	726 (79.9)	183 (20.1)	527[a] (64.0)	297 (36.0)
Doctor of osteopathy	216 (79.1)	57 (20.9)	172 (72.6)	65 (27.4)
Specialty				
Internal medicine	223 (80.5)	54 (19.5)	366 (63.4)	211 (36.6)
Family/general practice	354 (79.4)	92 (20.6)	310 (69.5)	136 (30.5)
Pediatrics	205 (84.0)	39 (16.0)	9 (60.0)	6 (40.0)
Pulmonary/allergy/immunology	160 (74.4)	55 (25.6)	14 (60.9)	9 (39.1)
Patient characteristics				
Sex				
Female	547 (80.8)	130 (19.2)	332 (67.3)	161 (32.7)
Male	395 (78.2)	110 (21.8)	367 (64.6)	201 (35.4)
Age, y				
0-18	293 (82.1)	64 (17.9)	1 (33.3)	2 (66.7)
19-44	305 (80.7)	73 (19.3)	131 (72.0)	51 (28.0)
45-54	190 (76.9)	57 (23.1)	274 (70.8)	113 (29.2)
55-64	154 (77.0)	46 (23.0)	293[b] (59.9)	196 (40.1)
Claims, past 6 months				
None	117[b] (53.2)	103 (46.8)	93[b] (29.6)	221 (70.4)
1-2 (low)	150 (82.0)	33 (18.0)	115 (73.2)	42 (26.8)
3-8 (medium)	348 (85.7)	58 (14.3)	233 (80.3)	57 (19.7)
≥9 (high)	327 (87.7)	46 (12.3)	258 (86.0)	42 (14.0)
Household income, $				
≤41,000	150 (76.5)	46 (23.5)	125 (71.0)	51 (29.0)
41,001-51,000	186 (77.2)	55 (22.8)	143 (67.5)	69 (32.5)
51,001-61,000	221 (79.8)	56 (20.2)	150 (64.1)	84 (35.9)
61,001-71,000	166 (85.1)	29 (14.9)	128 (69.6)	56 (30.4)
≥71,001	119 (80.2)	54 (19.8)	153 (60.0)	102 (40.0)
Estimated copayment, $				
<10	127[c] (87.6)	18 (12.4)	81[b] (73.6)	29 (26.4)
10 to <15	354 (79.0)	94 (21.0)	267 (71.6)	106 (28.4)
15 to <20	144 (73.1)	53 (26.9)	134 (64.4)	74 (35.6)
20 to <25	181 (85.0)	312 (15.0)	88 (63.3)	51 (36.7)
≥25	136 (76.0)	43 (24.0)	129 (55.8)	102 (44.2)
Drug benefit tier structure				
One tier	83 (80.6)	20 (19.4)	53 (60.9)	9.4 (39.1)
Two tiers	583 (80.7)	139 (19.3)	417 (70.2)	177 (29.8)
Three tiers	276 (77.3)	81 (22.78)	229[c] (60.3)	151 (39.7)

[a]*P* <.05.
[b]*P* <.001.
[c]*P* <.01.

Figure 2. **Fill Rates and 95% Confidence Intervals by Day from Prescribing Date for Treatment-Naive Patients Under 65 Years of Age Receiving Asthma-Controller or Dyslipidemia Therapy**



were dispensed and retrieved. In a medical records review of 32 pediatric Medicaid patients, Bronstein et al[35] reported that 30.3% and 30.9% of preventive and acute respiratory prescriptions, respectively, went unfilled after a full year. In a recent study, Williams et al[15] studied inhaled corticosteroid fill rates among 1064 asthma patients, comparing electronic prescription records with pharmacy claims. In this population, 92% of patients filled their inhaled corticosteroid prescription within 90 days (83% within the first 7 days).

emergency department vary from 65% to 99%.[18-25] Among studies of community-based pharmacies that focused on a broad range of prescription drugs, 1 reported prescription fill rates of 87%,[26] whereas several others reported rates in excess of 96%.[27-30] From a population-based survey of 3926 residents in the southeastern United States who had seen a healthcare provider in the past year, Wroth and Pathman[16] reported that 894 individuals (21.6%) responded affirmatively to the question, "In the past 12 months, did you delay filling a prescription or not get it at all?" In a comparative study of 9 national surveys, Kirking et al[31] reported on medication underuse, which includes primary nonadherence, with estimates that varied from 2.4% to 27%. Finally, Kennedy et al[32] reported that 4.4% of Medicare beneficiaries failed to fill or refill 1 or more prescriptions in 2004. Esposito et al[33] reported that 8.0% of individuals who used military pharmacies reported failing to claim at least 1 prescription in the previous year.

One study assessed primary adherence with dyslipidemia medications specifically. In a study of 71 veterans identified in a primary care setting, Mann et al[34] reported that 10% hadn't filled a statin prescription as reported in a 6-month follow-up survey. A few studies assessed fill rates for asthma and respiratory medications. In a rural Australian patient population, Watts et al[14] reported that only 251 of 359 (70%) respiratory medication prescriptions

Previous studies reported that primary adherence rates vary by numerous patient, prescriber, and treatment characteristics, including patient age and sex,[13,15,16] education and income status,[16,24] therapeutic class of prescribed medication,[26] comorbidities/health status,[15,16] patient–physician relationship and patient satisfaction with care,[15,20] and insurance coverage. In our study, noncompliance was more common for dyslipidemia therapy than asthma-controller therapy. That result was consistent with previous findings in which illness burden,[9] patient perception of the consequences of treatment avoidance,[36] and lower patient motivation to treat asymptomatic conditions all were implicated as causes of nonadherence.[37]

Our study participants had pharmacy insurance; however, primary adherence rates were significantly higher if the member's out-of-pocket cost for the prescription was less than $10, a result that is consistent with self-reported reasons for primary nonadherence,[30] the effect of insurance status,[23,24] and with studies of secondary adherence that consistently report lower adherence with higher out-of-pocket costs.[38-43] With the exception of the study by Ekedahl and Månsson,[13] who reported marginally higher nonadherence rates among the elderly, each study referenced above indicates a higher primary adherence rate among older adults. Yet our results indicate an inverse relationship between age and primary adherence, with progressively lower rates among patients age 45 to 54 years and 55 to 64 years compared with patients age 18 to 44 years. It is particularly interesting to note that this inverse relationship persists after adjustment for numerous potential confounders, especially recent pharmacy claims.

As there is a positive correlation between prescription medication use and age, it is possible that the generally poorer health status of older adults and greater use of the healthcare system are the actual drivers of adherence behavior in older aged populations. We speculate that this relationship exists because a history of filling prescriptions indicates a general willingness to fill prescriptions as well as a higher level of illness burden, which can translate to an increased motivation to initiate and remain on treatment.[44] In the study by Williams et al[15] of respiratory medication fill rates, patients with a recent history of short-acting beta-agonist use were more likely to fill their prescription, a result consistent with our findings, though our results were not limited to medications indicated for the treatment of similar health conditions.

There are limitations to the current study. First, administrative pharmacy data are surrogate measures for medication adherence and do not guarantee that the patient consumed the medication. Second, a 6-month washout period is insufficient to state with certainty that all eligible prescriptions were intended to initiate therapy. However, exploratory analysis on this topic suggests a low misclassification rate (<5%), and extended washout periods reduce sample sizes by excluding members with less continuous benefit eligibility. These results also were limited to the experiences of a select prescriber population who were identified and targeted for iScribe adoption based on prescribing activity. The study also was limited to only 2 chronic medication classes, which had substantial variation in primary adherence. We would not recommend generalizing these results to other therapeutic classes. Further, the study population excluded participants age ≥65 years; a conscious limitation to prevent the introduction of Medicare Part D from affecting our adherence results. Finally, there are several potential predictors of nonadherence that we could not account for with e-prescribing and paid pharmacy data, such as burden of illness, patient–physician communications, and patient knowledge, attitudes, and beliefs. Future research should include both older adults and other chronic medication classes. Results of such studies would have significant policy implications as the Centers for Medicare & Medicaid Services evaluates e-prescribing requirements and standards.

CONCLUSIONS

As healthcare costs continue to increase, greater focus is being placed on the costs associated with chronic conditions. One known way to mitigate costs and associated clinical effects is through medication management. The first step in appropriate medication management is initiation of the correct treatment. It is essential to ensure that patients initiate treatment, especially for the management of chronic health conditions, and our results confirm that a substantial proportion of chronic medication prescriptions go unfilled.

Our results provide at least 3 insights that may translate to improved interventions and educational opportunities. First, a prescription was likely to be filled quickly or not at all, a fact that ought to improve the timing of interventions. Second, patient age and pharmacy history are easily acquired and could support physician education and point-of-care information to assist prescribers with the removal of treatment barriers faced by patients. Finally, the evidence that only prescriptions with an out-of-pocket cost of less than $10 per prescription were most likely to be filled should inform prescription benefit designs intended to maximize adherence to therapy.

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Authorship Information: Concept and design (JNL, DSH, RGP, MHP, SAJ, JEB); acquisition of data (DSH, SAJ); analysis and interpretation of data (JNL, DSH); drafting of the manuscript (JNL, DSH, MHP, JEB); critical revision of the manuscript for important intellectual content (JNL, DSH, RGP, SAJ, JEB); statistical analysis (JNL, DSH); administrative, technical, or logistic support (DSH, MHP); and supervision (DSH, RGP, JEB).

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eAppendix. **Odds Ratio Estimates from Logistic Models Predicting Filling Within 60 Days**

	Combined Model		Asthma		Dyslipidemia	
Characteristic/Condition	OR	95% CI	OR	95% CI	OR	95% CI
Condition						
Asthma	1.00		NA		NA	
Dyslipidemia	1.26	0.97, 1.64	NA		NA	
Age, y						
≤18	1.00		1.00		NA	
≤44	NA		NA		1.00	
19-44	0.76	0.47, 1.23	NA		NA	
19-49	NA		0.66	0.40, 1.11	NA	
45-54	0.55[a]	0.33, 0.91	NA		0.83	0.53, 1.31
50-64	NA		0.58	0.33, 1.03	NA	
55-64	0.45[a]	0.27, 0.74	NA		0.63[a]	0.41, 0.98
Claims at 6 months						
None	0.09[a]	0.06, 0.12	0.12[a]	0.08, 0.19	0.06[a]	0.04, 0.10
1-2 (low)	0.45[a]	0.31, 0.64	0.47[a]	0.28, 0.79	0.39[a]	0.23, 0.64
3-8 (medium)	0.65[a]	0.48, 0.89	0.68	0.44, 1.06	0.64	0.41, 1.00
≥9 (high)	1.00		1.00		1.00	
Sex						
Female	1.00		1.00		1.00	
Male	1.06	0.85, 1.32	0.82	0.60, 1.13	1.40[a]	1.03, 1.93
Provider						
Doctor of medicine	1.00		1.00		1.00	
Doctor of osteopathy	1.07	0.81, 1.40	0.99	0.68, 1.45	1.19	0.80, 1.78
Specialty						
Internal medicine	1.00		1.00		1.00	
Pulmonary/allergy/immunology	0.88	0.59, 1.31	0.80	0.49, 1.31	NA	
Family practitioner	1.15	0.89, 1.48	1.04	0.68, 1.57	1.14	0.81, 1.60
Pediatrician	1.37	0.80, 2.38	1.29	0.67, 2.48	NA	
Other	NA		NA		0.65	0.37, 1.13
Household income, $						
≤41,000	0.91	0.64, 1.28	0.71	0.44, 1.15	1.14	0.70, 1.88
41,001-51,000	0.91	0.66, 1.26	0.81	0.51, 1.29	1.04	0.65, 1.65
51,001-61,000	0.83	0.60, 1.13	0.84	0.53, 1.34	0.81	0.52, 1.26
61,001-71,000	1.26	0.89, 1.79	1.34	0.79, 2.30	1.25	0.77, 2.02
>71,000	1.00		1.00		1.00	
Copayment level, $						
<10	1.76[a]	1.09, 2.83	2.03	0.99, 4.20	1.51	0.78, 2.93
10 to <15	1.14	0.77, 1.68	0.97	0.54, 1.74	1.27	0.74, 2.18
15 to <20	1.04	0.74, 1.47	0.76	0.45, 1.28	1.19	0.75, 1.90
20 to <25	1.10	0.75, 1.60	1.50	0.86, 2.62	0.70	0.41, 1.20
≥25	1.00					
Formulary tier						
1	1.08	0.71, 1.62	1.51	0.82, 2.78	0.83	0.46, 1.50
2	1.03	0.75, 1.43	1.12	0.69, 1.82	0.95	0.61, 1.49
3	1.00					

CI indicates confidence interval; NA, not applicable; OR, odds ratio.
[a]Statistically significant; defined as a CI that excludes 1.0.