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ORIGINAL RESEARCH

The Epidemiology of Prescriptions Abandoned at the Pharmacy

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Background: Picking up prescriptions is an essential but previously unstudied component of adherence for patients who use retail pharmacies. Understanding the epidemiology and correlates of prescription abandonment may have an important effect on health care quality.

Objective: To evaluate the rates and correlates of prescription abandonment.

Design: Cross-sectional cohort study.

Setting: One large retail pharmacy chain and one large pharmacy benefits manager (PBM) in the United States.

Measurements: Prescriptions bottled at the retail pharmacy chain between 1 July 2008 and 30 September 2008 by patients insured by the PBM were identified. Pharmacy data were used to identify medications that were bottled and either dispensed or returned to stock (RTS) or abandoned. Data from the PBM were used to identify previous or subsequent dispensing at any pharmacy. The first (index) prescription in a class for each patient was assigned to 1 of 3 mutually exclusive outcomes: filled, RTS, or RTS with fill (in the 30 days after abandonment, the patient purchased a prescription for a medication in the same medication class at any pharmacy). Outcome rates were assessed by drug class, and generalized estimating equations were used to assess patient,

neighborhood, insurance, and prescription characteristics associated with abandonment.

Results: 10 349 139 index prescriptions were filled by 5 249 380 patients. Overall, 3.27% of index prescriptions were abandoned; 1.77% were RTS and 1.50% were RTS with fill. Patients were least likely to abandon opiate prescriptions. Prescriptions with copayments of \$40 to \$50 and prescriptions costing more than \$50 were 3.40 times and 4.68 times more likely, respectively, to be abandoned than prescriptions with no copayment (P < 0.001 for both comparisons). New users of medications had a 2.74 times greater probability of abandonment than prevalent users (P < 0.001), and prescriptions delivered electronically were 1.64 times more likely to be abandoned than those that were not electronic (P < 0.001).

Limitation: The study included mainly insured patients and analyzed data collected during the summer months only.

Conclusion: Although prescription abandonment represents a small component of medication nonadherence, the correlates to abandonment highlight important opportunities to intervene and thereby improve medication taking.

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onadherence to essential long-term medications represents a central public health problem (1). Numerous studies have demonstrated that patients do not adhere to medications as prescribed (2, 3), leading to excess hospitalizations, morbidity, mortality, and health care costs (4, 5). Improving adherence to essential medications has repeatedly been highlighted as a public health priority (6). However, important gaps remain in our understanding of the causes of nonadherence and the best ways to intervene to support appropriate medication use (7).

Most adherence research is conditional on a patient filling a prescription for a medication, and studies traditionally evaluate refill rates (using claims data), patient reports of subsequent medication use (using self-reported data), or rates of administration once a prescription has been filled (using electronic pill bottles) (8-10). These existing studies of refill rates cannot clearly determine whether a patient does not adhere to therapy because he or she has not followed up with the provider to receive a prescription refill, the provider has not written the prescription, the prescription was written but not delivered to the pharmacy, or the prescription was delivered to the pharmacy but never picked up (that is, abandoned).

Prescriptions abandoned at the pharmacy represent a potential opportunity to intervene and improve adherence. When abandoned, the prescription has been written by the physician and called into, faxed to, or electronically delivered to the pharmacy or hand-delivered by the patient. Some abandoned prescriptions may never be picked up, representing a missed opportunity for therapy, whereas other prescriptions abandoned may be purchased later at the same pharmacy or at another pharmacy, indicating a delay in treatment and pharmacy inefficiency.

Recent studies have used electronic prescribing data to assess rates of "primary nonadherence" (rates at which patients do not fill prescriptions written by physicians) (11, 12); however, we are aware of no previous studies evaluating the rates and predictors of prescription drug abandonment at retail pharmacies for commonly prescribed medications. To better understand the magnitude of the

See also: **Print** Summary for Patients.....I-42 **Web-Only**

Appendix

Appendix Figures

CME quiz

Conversion of graphics into slides

Context

Failure to retrieve prescription medications at the pharmacy is one aspect of nonadherence to therapy.

Contribution

In this cross-sectional study, the percentage of prescriptions that were abandoned at the pharmacy was low. However, prescriptions for initial therapy, those for expensive drugs, those that required high copayments, and those delivered electronically were significantly more likely to be abandoned than others.

Implication

The increasing use of electronic prescribing may result in an increase in the number of prescriptions that patients fail to retrieve from the pharmacy. Physicians should be alert to factors associated with prescription abandonment.

—The Editors

problem and identify potential strategies to intervene to improve medication adherence, we merged a database from a large retail pharmacy chain with a database from a large pharmacy benefits manager (PBM). This merged data set provides a unique opportunity to assess rates and predictors of abandonment at a discrete point in the medication filling process, as well as subsequent use after abandonment at the same or other pharmacies.

METHODS

This study was approved by the institutional review boards of Partners Healthcare System, Boston, Massachusetts, and Harvard University, Cambridge, Massachusetts.

Data Sources

Retail pharmacy data were provided by CVS (Woonsocket, Rhode Island), a large national pharmacy chain. Pharmacy data contain all prescriptions (regardless of insurer), the mode of transmission (for example, electronic), and whether the script was bottled and then returned to stock (RTS). Insurance claims data were provided by Caremark (Woonsocket, Rhode Island), a large national PBM. The PBM data encompass all claims information either requested by the pharmacy or reimbursed by Caremark and include data from all pharmacies that a patient visited.

Study Period and Cohort Construction

All prescriptions filled and either purchased by a patient or abandoned (referred to here as "RTS") at CVS retail pharmacies were identified during a 3-month period from 1 July 2008 to 30 September 2008 (the identification period). The CVS consumers who receive pharmacy benefits through Caremark were then identified by matching retail transactional data to transactional data from the Caremark database. Among these individuals, all covered and filled prescriptions have a paid pharmacy claim in the Caremark database. Furthermore, all prescriptions that were RTS have transactional

data identifying the copayment charged before the prescription was filled (Appendix Figure 1, available at www.annals .org). CVS pharmacies generally return prescriptions to stock if they are not picked up within 14 days of delivering the prescription.

Electronic pharmacy data from the retail pharmacy and PBM were matched on pharmacy store number, prescription number, fill date, and patient ZIP code. We successfully matched 99.93% of retail transactions with PBM data. Transactional data from the retail pharmacy was used to determine whether a prescription was returned to stock, because these data more accurately reflect internal processes of the pharmacy than data provided by the PBM.

Pharmacy benefits manager claims from the baseline period, 6 months before the identification period (1 January 2008 to 30 June 2008), were used to determine whether prescriptions filled in the identification period were new prescriptions. We defined "new users" as patients who had filled no prescriptions in the same class as the index prescription in the 6 months before the index. Pharmacy benefits manager claims from a 3-month follow-up period, 1 October 2008 to 31 December 2008, were used to assess whether patients who abandoned prescriptions at the pharmacy subsequently filled those prescriptions at the same or another pharmacy. We excluded prescriptions at all CVS pharmacies that had automatic refill programs during the study period because abandonment rates were artificially high in these settings.

Outcomes

For each patient, the first prescription in a class during the identification period was considered the index prescription and the date on which it was written was considered the index date. We assigned each such prescription to 1 of 3 mutually exclusive outcomes: 1) filled prescription, indicating that the patient purchased the prescription; 2) RTS, indicating that the patient abandoned the prescription; or 3) RTS with fill, indicating that the patient abandoned the prescription and it was returned to stock, but the patient purchased a prescription for a medication in the same medication class at the same or another pharmacy. To determine RTS with fill status, we identified all RTS prescriptions and evaluated whether the patient filled a prescription for any medication in the class, determined by the first 4 digits of the Generic Product Index code of the abandoned prescription, from any pharmacy in the 30 days after the RTS fill date. This time frame was selected to conservatively estimate the clinical effect of abandonment. For patients with more than 1 prescription in a given class during the identification period, we considered only the first of these prescriptions so that we did not assign excessive weight to individuals with multiple abandoned prescriptions in the same class. For patients whose index RTS occurred in the first 2 weeks of the identification period, we also considered the prescription an RTS with fill if the patient filled a prescription for a medication in the same class in the previous

14 days, because these patients were probably not without medication at the time of the RTS.

Characteristics of Patients and Prescriptions

A prescription was considered new if no other prescriptions in the medication class (determined by Generic Product Index codes) had been filled in the 6 months before the index date. For each index prescription, PBM data were used to identify the copayment charged, whether the prescription was for a generic or brand-name medication, whether the medication was for a chronic or acute condition, and the source of insurance coverage (Medicare, Medicaid, employer sponsored, health plan not through an employer, or cash card or other). We also identified whether the prescription was transmitted electronically (eprescribed) to the pharmacy. Additional information was identified at the patient level: patient age, sex, and the number of unique medications filled in the identification period (a proxy for comorbidity) (13). The ZIP code of the patient's home residence was identified and linked to 2000 census tract data to assign the median income in the ZIP code of residence of each patient (14). We also used census thresholds to determine whether each patient lived in a rural or an urban area, on the basis of the population density of each ZIP code; rural neighborhood was defined as a population density of fewer than 1000 persons per square mile (15).

Statistical Analysis

We used descriptive statistics to summarize the characteristics of patients in our sample who filled prescriptions. We then assessed the proportion of prescriptions that were filled, RTS, and RTS with fill by medication class. Finally, we conducted bivariate and multivariate analyses to assess how patient- and prescription-level covariates were associated with RTS rates, by using generalized estimating equations to account for clustering at the patient level. Our statistical model was a generalized linear model with a log-link function that yielded estimates of relative risk. We estimated variable SEs robustly by using the empirical variance-covariance matrix to address patient-level clustering. Variables were estimated by using a working correlation matrix with an exchangeable structure.

In our bivariate analyses, we assessed the association among medication class, copayment, and brand-name versus generic drug on RTS probability and RTS with fill probability. Sensitivity analyses were conducted by excluding all electronic prescriptions. In the multivariate analysis that included all variables, we sought to understand predictors of true abandonment—that is, patients who did not subsequently refill a prescription—and combined all RTS with fill prescriptions with filled prescriptions. In this manner, our dichotomous outcome was RTS versus either a filled prescription or an RTS prescription with fill. We conducted sensitivity analyses that included total medication copayment burden as a covariate.

Table 1. Patient Characteristics*	
Characteristic	Data
Age, % (n)	
0–17 y	11.8 (617 041)
18–34 y	14.7 (770 208)
35–49 y	23.4 (1 229 463
50-64 y	29.3 (1 538 70
≥65 y	20.8 (1 092 739
Sex, % (n)	
Female	60.1 (3 134 85
Male	39.9 (2 079 78
Urban or rural residence, % (n) Urban (≥1000 persons/mi²) Rural (<1000 persons/mi²)	68.1 (3 061 16 31.9 (1 435 88
Insurance or payment type, % (n)	
Employer-sponsored	59.0 (3 099 45
Cash card/other	4.9 (254 336)
Health plan	24.9 (1 304 74
Medicare Medicaid	6.7 (352 018)
Region, % (n)	4.6 (238 832)
Northeast	35.1 (1 830 01
West	6.9 (360 925)
South	42.2 (2 198 13
Midwest	15.8 (824 603)
Other territories	0.0 (730)
Median family income in ZIP code, \$	61 762.10 (25 349.9)

^{*} Based on a sample of 5 249 380 persons.

Mean unique prescriptions per

patient (SD), n

All analyses were performed by using SAS software, version 9.2 (SAS Institute, Cary, North Carolina).

2.0 (1.6)

Role of the Funding Source

The work was funded by grants from CVS Caremark and a career development award from the National Heart Lung and Blood Institute to Dr. Shrank. The authors retained independent and complete control over the design and implementation of the study as well as the analyses and writing of the manuscript.

RESULTS

Our cohort consisted of 10 349 139 index prescriptions filled by 5 249 380 patients during the identification period. Patients were an average of 47.3 years of age, and 60.1% were female. They filled 2.0 unique prescriptions during the identification period and lived in ZIP codes with an average median income of \$61 762 (Table 1). Most patients had employer-sponsored insurance, yet a substantial number of patients were insured by Medicare, Medicaid, and non-employer-based health plans; approximately 4% used a cash card to receive discounted medications, which probably indicates that they did not have prescription drug coverage.

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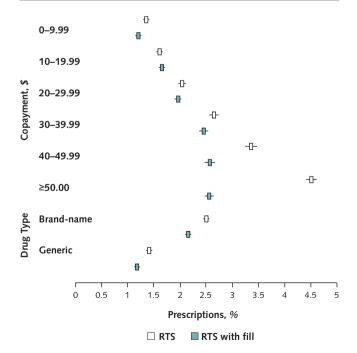
Table 2. Rates of Prescription Fill, RTS, and RTS With Fill, by Drug Class

Drug Class	Prescription Status					
	Filled		RTS		RTS With Fill*	
	Percentage (95% CI)	Number	Percentage (95% CI)	Number	Percentage (95% CI)	Number
Opiate	98.2 (98.1–98.2)	671 488	1.0 (1.0–1.0)	6850	0.9 (0.8-0.9)	5800
Antihypertensive	97.6 (97.5–97.6)	626 631	1.1 (1.1–1.1)	7160	1.3 (1.3-1.4)	8585
Antidepressant	97.0 (96.9–97.0)	443 230	1.4 (1.4-1.5)	6591	1.6 (1.5-1.6)	7176
Statin	97.3 (97.2-97.3)	394 908	1.4 (1.4-1.4)	5654	1.3 (1.3-1.4)	5432
Proton-pump inhibitor	95.6 (95.5–95.7)	250 969	2.6 (2.5-2.7)	6817	1.8 (1.8-1.9)	4817
Diabetes medication						
Oral	97.0 (96.9–97.0)	198 272	1.3 (1.2-1.3)	2614	1.8 (1.7-1.8)	3586
Insulin	94.9 (94.8–95.1)	62 814	2.2 (2.1-2.4)	1482	2.9 (2.7-3.0)	1884
Antibiotic	98.0 (98.0-98.1)	933 701	1.3 (1.3-1.3)	12 131	0.7 (0.7-0.7)	6719
Dermatologic agent	94.6 (94.5–94.7)	477 415	3.0 (2.9-3.0)	15 011	2.4 (2.4-2.5)	12 249
Asthma medication or inhaler	94.4 (94.3-94.5)	339 009	3.5 (3.4-3.6)	12 595	2.1 (2.1-2.2)	7551
Hormone replacement therapy or oral contraceptive	96.9 (96.9–97.0)	326 478	1.3 (1.3-1.3)	4368	1.8 (1.8-1.8)	6032
Antiepileptic	96.4 (96.3-96.4)	200 772	1.7 (1.7-1.8)	3630	1.9 (1.8-2.0)	3956
Cough, cold, or allergy medication	95.1 (95.0-95.3)	132 529	3.6 (3.5-3.7)	4942	1.3 (1.3-1.4)	1824
Osteoporosis medication	96.5 (96.4–96.6)	77 134	1.7 (1.6-1.8)	1346	1.8 (1.7-1.9)	1446
Antipsychotic	95.5 (95.3-95.6)	71 666	2.3 (2.2-2.5)	1754	2.2 (2.1-2.3)	1665
Antiplatelet or anticoagulant	97.8 (97.7-97.9)	59 782	1.0 (0.9-1.1)	611	1.2 (1.1-1.3)	738
Prostate medication	97.5 (97.4–97.7)	51 659	1.3 (1.2–1.4)	679	1.2 (1.1–1.3)	635

RTS = returned to stock.

Approximately 3.27% of all index prescriptions (0.34 million prescriptions) were abandoned; 1.77% of those prescriptions were RTS, and no prescription was filled by the same patient for a medication in the same class in the

Figure. Bivariate relations between prescription cost or brand-name or generic status and rates of abandonment.



We controlled for clustering at the patient level by using generalized estimating equations. Bars indicate 95% CIs. RTS = returned to stock. subsequent 30 days at any pharmacy (RTS), whereas 1.50% were filled at some pharmacy in that time frame (RTS with fill).

Abandonment rates varied by medication class (Table 2). Opiates and antiplatelet medications were least likely to be RTS prescriptions (1.0% and 0.9%, respectively) or RTS with fill (0.8% and 1.1%). Antihypertensives, oral diabetic medications, and statins also had comparatively low abandonment rates. Among daily-use therapies, higher rates of RTS were seen for proton-pump inhibitors (2.6%), asthma medications (3.5%), and insulin (2.2%). Medications used on an as-needed basis, such as dermatologic agents (RTS rate, 2.9%) and cough and cold medications (RTS rate, 3.6%) were also abandoned more commonly.

In bivariate analyses, the copayment charged was strongly associated with rates of abandonment. Prescriptions with copayments of less than \$10 were abandoned 1.4% of the time, and abandonment rates increased consistently to 4.5% for copayments greater than \$50 (Figure). Similarly, abandonment rates were greater for brandname medications than for generic medications (Figure).

These relationships were confirmed in our multivariate models that included all variables being studied. When we compared the associations between prescription- and patient-level variables and true prescription abandonment (RTS with no subsequent fills), medication copayment was most strongly associated with abandonment rates. Compared with prescriptions with no copayment, prescriptions with copayments of \$40.01 to \$50.00 had a 3.40 times greater probability of being abandoned, and prescriptions costing more than \$50.01 had a 4.68 times greater probability of being abandoned (P < 0.001 for all pairwise com-

Prescription was RTS but was subsequently filled at the same or another pharmacy.

parisons with the referent category) (Table 3). Similarly, median income in ZIP code of residence was significantly associated with abandonment rates; patients living in ZIP codes in the highest income quintile were 21% less likely to abandon prescriptions (P < 0.001). Medicaid beneficiaries were 8% more likely to abandon prescriptions than were persons with employer-sponsored health insurance.

Young adults aged 18 to 34 years were most likely to abandon prescriptions. Seniors were 45% less likely to abandon prescriptions than young adults (P < 0.001). Patients with more comorbid conditions were more likely to abandon prescriptions; each additional unique prescription medication filled was associated with a 4% increase in the probability of abandonment (P < 0.001).

New users of medications had more than 2.74 times greater probability of abandonment than prevalent users, and maintenance medications had slightly less probability of being abandoned (P < 0.001 for both comparisons). Of note, prescriptions delivered electronically to the pharmacy had a 64% increase in the probability of being abandoned compared with those that were not electronically delivered (P < 0.001).

DISCUSSION

To our knowledge, ours is the first study to comprehensively evaluate the phenomenon of prescriptions abandoned at the pharmacy. We found that 3.27% of prescriptions bottled at the pharmacy were abandoned and RTS, and on more than half of those occasions, the patient did not fill an alternate prescription for the same medication at any pharmacy. This represents a relatively small proportion of all prescriptions that are filled at pharmacies, comprising a small component of overall medication nonadherence or failure to appropriately use long-term medications. However, the total number of abandoned prescriptions in the population is great, and every essential prescription abandoned could represent an important clinical concern if the patient does not subsequently restart the medication or identify a substitute. Moreover, the likelihood of abandonment for patients who fill multiple medications can be substantial and clinically important.

By evaluating prescription abandonment rates, we assess a discrete event in the continuum of the prescription drug delivery process that may represent an opportunity to intervene and support better medication adherence. Physicians or pharmacists should be aware of the patient and prescription characteristics associated with higher rates of abandonment to assist patients to improve medication use. We have created a simple prediction rule with 4 covariates that providers can use to rapidly assess risk and to best identify who may benefit most from additional counseling or the selection of a less expensive medication (Appendix and Appendix Figure 2, available at www.annals.org).

Copayments charged to patients were the strongest predictors of abandonment, suggesting that patients expe-

Table 3. Multivariate-Adjusted Associations Between Patient and Prescription Characteristics and Rates of **Abandonment**

Characteristic	Prescriptions, n*	Unadjusted Frequency of RTS, %	Relative Risk (95% CI)†
Age			
18–34 y	1 222 000	2.4	1.00 (reference
0–17 y	954 000	2.4	0.98 (0.96-1.0
35–49 y	2 270 000	2.0	0.87 (0.86-0.8
50–64 y	3 278 000	1.5	0.65 (0.64-0.6
≥65 y	2 622 000	1.4	0.55 (0.54–0.5
Sex			
Female	6 183 000	1.8	1.00 (reference
Male	4 101 000	1.6	0.88 (0.87–0.8
Urban or rural residence Urban (≥1000	5 919 000	1.7	1.00 (reference
persons/mi ²)	0.017.000		0.05 (0.04.0.0
Rural (<1000 persons/mi ²)	2 917 000	1.7	0.95 (0.94–0.9
Insurance or payment type			
Employer-sponsored	6 000 000	1.8	1.00 (reference
Cash card/other	499 000	2.7	1.01 (0.98–1.0
Health plan	2 424 000	1.6	0.83 (0.81–0.8
Medicare	945 000	1.2	0.96 (0.94–0.9
Medicaid	480 000	2.3	1.08 (1.04–1.1
Income			
\$0-\$41 094	1 876 000	1.9	1.00 (reference
\$41 095–\$51 393	1 851 000	1.8	0.93 (0.92–0.9
\$51 394–\$63 972	1 790 000	1.7	0.90 (0.88–0.9
\$63 973–\$80 330 \$80 331–\$200 001	1 698 000 1 610 000	1.7 1.6	0.86 (0.84–0.8 0.79 (0.77–0.8
Number of unique prescriptions per patient	-	-	1.04 (1.04–1.0
Communit			
Copayment \$0	824 000	1.5	1.00 (reference
\$0.01-\$10.00	5 759 000	1.3	1.21 (1.17–1.2
	1 435 000	1.6	
\$10.01-\$20.00			1.58 (1.53–1.6
\$20.01-\$30.00	1 028 000	2.0	2.05 (1.98–2.1
\$30.01-\$40.00	239 000	2.6	2.60 (2.51–2.6
\$40.01–\$50.00	247 000	3.4	3.40 (3.27–3.5
≥\$50.01	527 000	4.5	4.68 (4.53–4.8
Prescription delivery method			
Not electronic	9 928 000	1.7	1.00 (reference
Electronic	421 000	2.3	1.64 (1.60–1.6
New user			
No	4 190 000	0.9	1.00 (reference
Yes	6 159 000	2.4	2.74 (2.70–2.7
Maintenance drug			
Maintenance drug	3 980 000	1.9	1.00 (reference
Maintenance drug No Yes	3 980 000 6 369 000	1.9 1.7	1.00 (reference 0.97 (0.96–0.9

RTS = returned to stock.

rience "sticker-shock" at the pharmacy and choose not to fill those prescriptions. Improved physician awareness of patient cost-sharing requirements, and communication

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Includes prescriptions that were filled, RTS, and RTS with fill.

[†] Results from a multivariate model that includes all variables listed in the table. The 95% CIs are based on robust SEs that account for clustering at the patient level; the dichotomous outcome is RTS vs. filled prescription or RTS with fill.

about those costs with patients before arrival at the pharmacy, may reduce abandonment rates (16). However, physicians are often unaware of their patients' out-of-pocket costs at the time of prescribing and often believe that pharmacists should play a central role in these discussions (17, 18). The advent of electronic health records may facilitate greater awareness of and communication about medication costs. Moreover, if pharmacies proactively seek to communicate with physicians to identify less costly therapies and thus reduce cost-sharing requirements before the patient attempts to purchase the medication, some benefit may result. Similarly, benefit designs that reduce cost-sharing for the most effective medications, known as "value-based insurance designs," may reduce abandonment rates (19, 20).

New prescriptions are almost 3 times more likely to be abandoned than previously filled prescriptions; particular care could be directed to communicating with patients who are filling new prescriptions to support therapy initiation. Patients with more comorbid conditions abandoned prescriptions at higher rates than those with fewer comorbid conditions, even after patient age was controlled for. In sensitivity analyses controlling for total copayment burden, these relationships were qualitatively unchanged. Our findings highlight the effects of increasing the complexity of a patient's medication regimen and the importance of simplifying therapy when possible (21).

Variations in abandonment rates by drug class were also informative. High rates of abandonment of insulin may suggest inefficiencies in the delivery system for these medications, which are not as easily packaged into monthly supplies as other medications and may be a source of substantial morbidity if patients who require insulin therapy experience any gaps in therapy. Higher rates of abandonment of proton-pump inhibitors, an often overutilized medication (22), or as-needed medications for symptomatic conditions may not signify as much clinical risk and may result from the availability of alternate, over-the-counter options that may be more cost-effective for patients. The extremely low rate of opiate abandonment probably indicates less cost-sensitivity and a greater demand for the medication than for other classes. Many states do not allow electronic prescribing of opiates; sensitivity analyses that excluded electronic prescriptions continued to demonstrate lower rates of opiate abandonment than of other classes. Patient addiction or plans to divert opiates may also contribute to reduced rates of abandonment.

Prescriptions delivered electronically to the pharmacy were almost 65% more likely to be abandoned than those delivered by other means. This finding is not surprising, because some patients who receive electronic prescriptions do not have to hand-deliver the prescription to the pharmacy or otherwise initiate the fill request themselves. Because they lack a patient-initiated step, electronic prescriptions may be more likely to be delivered to the pharmacy for patients who never intended to fill the prescription. However, this finding highlights unintended consequences of electronic prescribing. One feature of electronic prescribing that has been widely promoted is the improved ability to document medication lists. If these lists represent what was ordered and not what was filled, they may serve to obfuscate rather than clarify therapeutic regimens. Moreover, if electronic prescriptions are contributing to pharmacy inefficiency rather than simplification, additional costs may result from electronic prescribing. In urban areas, electronic prescribing may be even more complex as prescribers must identify the correct pharmacy from many competitors. Inaccurate electronic prescriptions, delivered to the wrong pharmacy, may also lead to greater rates of abandonment and may explain greater abandonment rates in urban than rural regions. Pharmacies can choose to be more selective about filling electronic prescriptions before the patient's arrival in order to improve efficiency. Physicians may choose to print a reminder for patients when prescriptions are electronically delivered to the pharmacy to help them remember that a prescription is waiting.

This study also highlights an important source of unnecessary cost and inefficiency in the delivery of prescription drugs. Every prescription that is bottled and then returned to stock has an associated cost to the pharmacy, estimated at more than \$10 per prescription (23). In total, more than 3.6 billion prescriptions were filled at pharmacies in the United States in 2008 (24). Assuming a national abandonment rate similar to these findings, more than 110 million prescriptions are abandoned at U.S. pharmacies annually. Conservatively estimating the cost to the pharmacy of each abandoned prescription to be \$5, abandoned prescriptions probably cost pharmacies more than half a billion dollars annually in the United States. These costs could increase substantially as more prescriptions are delivered electronically.

By requiring patients to have data in the PBM system, our study probably underrepresents patients who were uninsured, which would lead to conservative estimates of rates of abandonment. We included a large sample of Medicaid beneficiaries, who have low incomes, as well as patients who purchased medications with a cash card, who most likely did not have comprehensive coverage. However, those who signed up for a cash card may differ somehow from other uninsured patients, limiting generalizability to that population. Patients who use CVS pharmacies are probably representative of patients who use other large pharmacy chains, but they may differ from patients who purchase prescriptions at grocery stores or independent pharmacies (25). In addition, we cannot comment on abandonment at mail-order pharmacies, where rates may be substantially lower.

We dichotomized prescription delivery into "electronic prescriptions" and "all others." Among nonelectronically transmitted prescriptions, we did not have systematic information about whether prescriptions were phoned or faxed in by the physician. These prescriptions

may have abandonment rates that more closely resemble those of electronic prescriptions, leading to conservative comparisons of the rate of abandonment of electronic prescriptions with hand-delivery. We did not have patientlevel data on income level. Linkage to census-level data is common in health services research (14, 26), but it offers a less precise measure of the relation between these variables and abandonment. We also could not determine whether patients identified someone else to purchase their medication for them and how that may have affected abandonment rates.

We did not require continuous enrollment in Caremark for inclusion in the study because we wanted to assess the broadest and most representative population available. As a result, we may not have complete claims either before or after the index prescription, because patients may have changed insurance plans. Since this analysis took place in 1 calendar year, we do not think this led to significant misclassification, and it should not affect the primary outcome, which was classified by using retail pharmacy claims alone. We identified index prescriptions during the summer months, a time when more patients may go on vacation, which may have led to an anticonservative bias. We also cannot assign causality to any associations between the covariates and outcome and recognize that these covariates may be markers of other patient or prescription characteristics.

Finally, although abandonment is inefficient for pharmacy practice, from a clinical perspective not all abandonment is necessarily bad. For example, a physician may send an electronic prescription to a pharmacy for a symptomatic condition and recommend that the patient fill the prescription only if symptoms do not resolve. Although this may be a reasonable approach clinically, it may introduce additional resource consumption and inefficiency at the pharmacy. In addition, simply purchasing the medication is necessary but not sufficient for appropriate adherence. Patients may still not adhere to treatment with medications that have been purchased.

In conclusion, to our knowledge this study is the first to document the rates of prescription abandonment at retail pharmacies, a discrete and potentially actionable locus on the path to appropriately adhering to medication therapy. As we seek to find strategies to better support medication adherence, cost may be an important determinant, consistent with previous findings (27, 28). Interventions that help steer patients to more affordable medications and benefit designs that enhance affordability of highly effective medications may reduce abandonment of the most essential medications (17, 18). In addition, interventions targeting patients filling new prescriptions may stimulate more appropriate medication adherence. Further study is needed to understand how electronic prescribing may contribute to pharmacy inefficiency and how electronic prescribing systems can communicate to pharmacies to identify and document abandoned prescriptions to enhance documentation and the quality of care.

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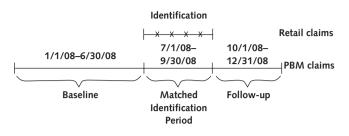
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Appendix Figure 1. Cohort identification.



The Xs on the "Identification" bar indicate filled claims. PBM = pharmacy benefits manager.

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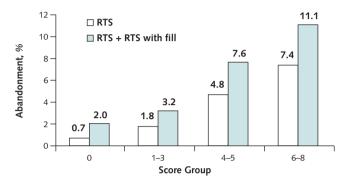
APPENDIX: SCORING SYSTEM USED TO PREDICT PRESCRIPTION ABANDONMENT AT THE PHARMACY

We created and tested a prediction rule for physicians or pharmacists to identify patients at high risk for prescription abandonment. Using results from our fully adjusted generalized estimating equation model, we identified covariates with the strongest relation to prescription abandonment. We then randomly selected half of our cohort and created a more parsimonious model that included the 5 covariates most strongly correlated with the outcome. We used the magnitude of the coefficients of that model to create weighted scores for each of the variables, rounding scores to the nearest integral to improve usability. We then applied those scoring rules to the other half of our sample cohort to assess the extent to which these variables can be used to predict abandonment rates. For the purposes of the prediction rule, we evaluated 2 outcomes: RTS excluding patients with subsequent fill and all RTS. Although RTS without subsequent fill is the outcome with the greatest clinical relevance and would be most useful for clinicians, pharmacists may also benefit from a prediction rule that helps them identify patients at high risk for abandonment prescriptions from that pharmacy, because abandonment is a source of pharmacy inefficiency. We graphically presented the relationships and found natural thresholds in the data that seemed most appropriate for prediction.

Using results from the fully adjusted model, we identified the 4 covariates most strongly correlated with the outcome (medication copayment had 2 levels) (Appendix Figure 2). The scoring rules developed on half of the sample are shown, as are the relationship between patient-level scores and rates of abandonment in the other half of the sample.

Appendix Figure 2. Scoring system used to predict prescription abandonment at the pharmacy.

Variable	Points
New user	2
Electronic prescription	2
Age 18–34 y	1
Copayment \$30-\$50	2
Copayment >\$50	3



By using 4 covariates (patient age, electronic prescription, new prescription, and copayment [2 levels]), physicians or pharmacists can identify patients who are at greater risk for abandoning prescriptions. RTS = returned to stock.

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