Community Pharmacy Automatic Refill Program Improves Adherence to Maintenance Therapy and Reduces Wasted Medication

Olga S. Matlin, PhD; Steven M. Kymes, PhD; Alice Averbukh, MBA, MS; Niteesh K. Choudhry, MD, PhD; Troyen A. Brennan, MD, MPH; Andrew Bunton, MBA, CFA; Timothy A. Ducharme, MBA; Peter D. Simmons, RPh; and William H. Shrank, MD, MSHS

ABSTRACT

Objectives: Automatic prescription refill programs are a popular means of improving medication adherence. A concern is the potential for prescription drug wastage and unnecessary healthcare spending. We evaluated the impact of an automatic refill program on patterns of medication use.

Study Design: Retrospective propensity score matched cohort study with multivariable generalized linear modeling.

Methods: The setting of the study was a pharmacy benefit manager administering benefits for patients of retail pharmacies. Participants included patients on medication for chronic conditions; those receiving a 30-day supply (n = 153,964) and a 90-day supply (n = 100,394) were analyzed separately. The intervention was the automatic prescription refill program. Measures included medication possession ratio (MPR) and average days excess at the time of refill. The results are reported across 11 therapeutic classes.

Results: Overall, patients receiving 30-day supplies of medication in the automatic refill program had an MPR that was 3 points higher than those not in the refill program; among those receiving 90-day fills and in the refill program, the MPR was 1.4 points higher (P <.001 for both 30- and 90-day fills). The MPR was higher for members in the refill program across all therapeutic classes. Limiting our analysis to members receiving more than 365 days of medication, we found that patients who received 30-day fills and enrolled in the automatic refill program had 2.5 fewer days' oversupply than those in the control group, whereas automatic refill patients receiving 90-day supplies had 2.18 fewer days' oversupply than the controls (P <.001 for both 30- and 90-day fills).

Conclusions: For this pharmacy provider, automatic refill programs result in improved adherence without adding to medication oversupply.

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Medication nonadherence in patients with chronic disease is a central public health problem. Almost half of American adults are prescribed medication for a chronic disease, and there is strong evidence that patients who are adherent to medication regimens experience better health outcomes and incur lower healthcare costs than those who are not adherent.[1-3] Yet, despite numerous efforts by researchers and clinicians to improve chronic medication use, patients frequently do not adhere to therapy.[4,5]

Medication nonadherence is a multifactorial problem, and numerous interventions have been employed to reduce barriers to appropriate medication use. One response from the pharmacy community has been the development of automatic prescription refill programs. In these programs, patients on prescriptions for maintenance medications with multiple refills are provided a simple mechanism to authorize their next refill before the current supply is exhausted. When the prescription is refilled, the pharmacy advises the patient that the prescription is ready for pick-up at the pharmacy.

Although automatic refill programs were designed to promote patient adherence, a potential concern with these programs is that they may contribute to medication wastage by reducing the patient's involvement in the dispensing process. However, a recent systematic review found no evidence to support or disprove this assertion.[6]

We evaluated the impact of the automatic refill program in the CVS Caremark retail pharmacies, comparing adherence and medication oversupply in a sample of patients who were enrolled in a refill program with a matched sample of patients who refilled their prescriptions using traditional methods.

METHODS

Program Intervention

Retail pharmacy patients were invited to enroll in the CVS automatic refill program if they were prescribed a main-

Take-Away Points

- Community pharmacy-based automatic refill programs are a strategy to increase adherence in patients on medication for chronic disease by increasing convenience of medication refill orders.
- Some have expressed concern that such programs might lead to medication oversupply if not properly managed.
- We found in an evaluation of a national retail chain's automatic refill program that adherence was significantly increased while medication oversupply was reduced compared with a matched sample of people not enrolled in a similar program.
- This was found across 11 therapeutic classes representing the majority of medications prescribed for chronic disease.

tenance medication typically used for the treatment of a chronic disease and had a prescription with at least 1 refill available. If the patient accepted the invitation to enroll, the pharmacy scheduled the next refill for the enrolled prescription to occur prior to the exhaustion of the current supply of medication. When the prescription was available for pick-up, the patient was notified and picked up their refill at the retail location. Future refills for the prescription were scheduled based upon the exhaustion date for the current refill, which was determined by the pick-up date of the current prescription and supply. This process continued until the prescription was discontinued by the patient or prescriber. Refills that were not picked up were returned to stock and not billed to the patient or their payer. In the event a refill is not picked up, 1 more refill is attempted, and if that refill is not picked up, the prescription is removed from the program with no additional refills prepared or notifications issued.

Setting and Participants

We conducted a retrospective cohort analysis comparing 2 outcomes—medication adherence and number of excess days of therapy on hand at the time of prescription pick-up—between a sample of patients enrolled in an automatic refill program at CVS pharmacies (refill cohort) and a propensity matched control group of patients not enrolled in the program (control cohort). The sample consisted of CVS retail patients continuously enrolled in a Caremark commercial pharmacy benefits plan from January 1, 2010, to December 31, 2011. The integrated data set included CVS Caremark pharmacy benefit claims and data from the CVS retail pharmacy identifying the patients participating in the automatic refill program. The therapeutic classes considered in these analyses were all essential chronic medications: angiotensin-converting enzyme inhibitors, antihypertensive combinations, angiotensin II receptor blockers, beta-blockers, biguanides, calcium-channel blockers, contraceptives, serotonin-norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, statins, and thyroid hormone replacement medications. All cohort patients were required to have filled at least 1 of the study medications during the 6-month baseline period to be eligible for inclusion.

For the refill cohort, we limited our sample to patients who filled 1 of the study medications and were not enrolled in the automatic refill program between January 1 and June 30, 2010, but enrolled the study medication in the program between July 1 and December 31, 2010. Patients in the control cohort had identical criteria, with the exception of the requirement of enrolling a prescription in the automatic refill program. Enrolling in the CVS automatic refill program requires 2 prescription fills: the first to identify program eligibility and the second to provide the first automatic fill. Therefore, patients in the control cohort were limited to those with 2 medication fills within 90 days of each other for each studied therapy. The baseline period between January 1 and June 30, 2010, was used to derive demographic and baseline utilization variables. The impact of the automatic refill program was measured during the 12 months subsequent to the index fill, defined as the patient-specific program enrollment (refill cohort) or matched first fill date in the period (control cohort). In our analyses, the date of the first fill after July 1, 2010, was considered the index date for patients in the refill cohort. The index date for the control cohort was the first fill after July 1, 2010, for the therapeutic class.

Control cohort patients were matched to refill cohort patients using a greedy nearest-neighbor method to match on propensity scores.[7] In addition to the standard demographic and clinical baseline variables used in our propensity score estimate, we constructed 2 parameters to control for potential confounding unique to the study question. First, to adjust for baseline differences in adherence behavior, we calculated the time between exhaustion of the final fill in the baseline period and the index fill to provide a proxy for baseline adherence behavior. Second, we adjusted for duration of therapy by identifying the date of the first fill in the therapeutic class in the baseline period. The variables included in the propensity score calculation are described in Tables 1A and 1B. The quality of the match was evaluated by estimating the standardized difference in means, with a value of 0.1 indicating a sufficiently small difference. We also used logistic regression to estimate the probability of assignment to the refill cohort as a function of the variables included in the propensity score, with a C statistic of 0.5 indicating nondifferential distribution of characteristics.

Table 1A. Source Population and Matched Sample for Analysis (30-day fillers only)

	Source Population		Matched Sample			
	Control	Refill	Control	Refill	*P*	Standardized Δ
N	408,630	81,794	76,211	77,736		
Age, years	55.12	55.78	56.14	56.08	.47	0.0009
Gender, female	60.07%	60.18%	59.64%	59.88%	<.01	0.0041
PRG[a] score	2.89	2.99	3.03	3.02	.30	0.0056
Days' gap since last fill in baseline	8.36	6.86	7.64	7.91	.02	0.0169
Payer, %						
Employer	67.53	67.04	67.98	68.02	.53	0.046
Commercial health plan	20.24	22.82	22.27	22.24		
Medicare Part D	8.19	7.89	8.20	8.10		
Medicaid	1.22	1.66	1.55	1.64		
Index month, %						
July	80.57	27.27	28.43	27.93	.28	0.0076
August	14.99	26.7	26.76	26.88		
September	3.12	23.23	22.86	22.99		
October	1.28	21.52	20.71	20.94		
November	0.04	1.28	1.24	1.26		
Switched therapies	20.13%	19.37%	20.28%	19.22%	<.01	0.0215
Neighborhood characteristics						
Poverty	12.32%	12.39%	12.42%	12.37%	.26	0.0029
Household median income	$62,462	$62,580	$62,290	$62,446	.22	0.0024
Therapeutic class distribution within cohort,[b] %						
ACE inhibitor	12.78	13.58	14.2		N/A	N/A
Antihypertensive combinations	8.59	8.33	8.8			
ARB	4.27	4.21	4.4			
Beta-blocker	11.14	11.33	11.9			
Biguanides	4.77	5.1	5.3			
Calcium-channel blocker	6.64	6.81	7.1			
Contraceptives	8.64	8.05	8.2			
SNRI	2.91	3.18	3.2			
SSRI	11.5	10.73	10.8			
Statin	17.21	16.98	17.9			
Thyroid hormones	7.23	7.88	8.2			

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; delta (Δ), difference; N/A, not applicable; PRG, pharmacy risk group; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
[a]PRG is a measure of comorbidity. A higher score indicates worse comorbidity.
[b]The match between the refill and control cohorts was stratified within therapeutic class; thus, there is perfect concordance.
Source: CVS Caremark pharmacy claims data from January 1, 2010, to December 31, 2011.

Outcome Measures

We evaluated 2 outcomes in this study: adherence and medication oversupply. Adherence was measured using the medication possession ratio (MPR), defined as the number of days of medication dispensed during the year divided by the number of days that the person should have been on therapy.[8] We reported 2 measures of medication oversupply: a) the proportion of patients receiving more than 365 days of medication during the exposure period and b) the average days oversupply on hand at the time of prescription pick-up during the exposure period. To ensure that the second metric was not biased by patients who are nonadherent, we only reported the days' supply on hand at the time of refill for patients who received more than 365 days of medication.

Table 1B. Source Population and Matched Sample for Analysis (90-day fillers only)

	Source Population		Matched Sample			
	Control	Refill	Control	Refill	*P*	Standardized Δ
N	735,796	52,364	49,820	50,574		
Age, years	59.59	59.30	56.48	56.31	.58	0.0015
Gender, female	55.59%	56.72%	56.52%	56.70%	.57	0.0036
PRG[a] score	2.86	3.23	3.24	3.25	.64	0.0014
Days gap since last fill in baseline	8.84	6.58	6.32	5.85	<.01	0.0292
Payer, %						
Employer	71.17	85.88	86.18	86.24	.44	0.0003
Commercial health plan	5.08	8.86	8.98	8.80		
Medicare Part D	4.58	4.93	4.85	4.96		
Medicaid	0.0	0.0	0.0	0.0		
Index month, %						
July	55.93	40.80	42.14	41.77	.62	0.0076
August	38.92	38.50	38.64	38.66		
September	4.55	11.82	11.20	11.33		
October	0.57	8.44	7.62	7.82		
November	0.02	0.44	0.40	0.42		
Switched therapies	19.07%	21.31%	22.71%	21.08%	<.01	0.0391
Neighborhood characteristics						
Poverty	11.15%	11.25%	11.01%	11.28%	<.01	0.0212
Household median income	$64,170	$64,485	$65,400	$64,386	<.01	0.0148
Therapeutic class distribution within cohort,[b] %						
ACE inhibitor	14.06	14.45	14.8		N/A	N/A
Antihypertensive combinations	2.63	2.62	8.4			
ARB	8.59	8.13	4.5			
Beta-blocker	4.69	4.37	13.4			
Biguanides	12.99	13.04	5.2			
Calcium-channel blocker	4.52	5.04	7.4			
Contraceptives	7.02	7.25	6.4			
SNRI	6.7	6.31	2.2			
SSRI	2.11	2.23	7.2			
Statin	7.26	7.2	20.6			
Thyroid hormones	19.86	19.72	9.9			

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; delta (Δ), difference; N/A, not applicable; PRG, pharmacy risk group; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
[a]PRG is a measure of comorbidity. A higher score indicates worse comorbidity.
[b]The match between the refill and control cohorts was stratified within therapeutic class; thus, there is perfect concordance.
Source: CVS Caremark pharmacy claims data from January 1, 2010, to December 31, 2011.

Statistical Approach

The significance of differences between the refill and control cohorts in each subgroup was evaluated using multivariable generalized linear modeling with clustering of observations by client type and therapeutic class to adjust standard errors. We conducted separate analyses for patients who received only 30-day supplies and those who received at least one 90-day fill during the evaluation period, as days supplied per fill is known to impact adherence to medication.[9]

All statistical analyses were conducted using SAS version 9.1 (SAS Institute, Cary, North Carolina). All analyses were conducted on a Health Insurance Portability and Accountability Act–qualified limited data set; thus, they did not require review by an institutional review board.

Table 2. Comparison of Medication Possession Ratio Between Refill and Control Cohorts

	30-Day Fillers			90-Day Fillers		
	MPR Refill	MPR Control	Adjusted Δ[a]	MPR Refill	MPR Control	Adjusted Δ[b]
Total across classes	83.5%	80.7%	3.0%	89.8%	88.8%	1.4%
ACE inhibitors	84.8%	82.4%	2.2%	90.8%	89.6%	1.1%
Antihypertensive combinations	83.4%	80.5%	2.9%	89.2%	88.1%	1.0%
ARBs	82.6%	79.7%	3.0%	89.5%	88.4%	0.9%
Beta-blockers	88.1%	86.2%	2.4%	91.1%	90.3%	0.6%
Biguanides	80.6%	77.6%	2.7%	87.3%	86.0%	1.2%
Calcium-channel blockers	85.0%	82.7%	2.1%	90.9%	90.0%	0.8%
Contraceptives	81.9%	75.9%	6.0%	89.3%	86.8%	2.4%
SNRIs	81.5%	78.1%	3.4%	88.6%	88.0%	0.6% (NS)
SSRIs	78.3%	75.5%	2.7%	87.0%	85.0%	1.9%
Statins	84.0%	81.2%	2.7%	90.0%	88.5%	1.3%
Thyroid hormones	89.5%	87.7%	1.4%	93.2%	92.4%	0.6%

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; delta (Δ), difference; MPR, medication possession ratio; NS, not significant; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
[a]Adjusted for demographic and clinical confounding factors. Difference in percentage points between the refill and control cohorts; a positive difference indicates that the refill cohort has better adherence than control. All classes significant at $P < .001$.
[b]All significant at $P < .05$, except as noted.
Source: CVS Caremark pharmacy claims data from January 1, 2010, to December 31, 2011.

RESULTS

We identified 77,736 patients who received a 30-day supply of medication and 50,574 who received a 90-day supply and were also enrolled in the automatic refill program. These were matched to 76,228 and 49,820 control members for the 30- and 90-day supply analyses, respectively, selected from a sample of control members who met qualification for the automatic refill program (Table 1). Overall, the majority of patients were women, more likely to be enrolled in an employer-sponsored plan, and more likely to be on a statin or antihypertension therapy. After matching, the analysis population was similar to the source population for the key variables. In comparing the refill and control cohorts after matching, we found that the standardized differences for all variables were less than 0.10. In addition, the C statistic for classification between the refill and control cohorts was 0.52 for the 30-day fillers and 0.51 for 90-day fillers, indicating an excellent overall match.

In Table 2 we detail the impact of the automatic refill program on patient adherence. In both the 30- and 90-day analyses, patients in the refill cohort had significantly greater adherence than those in the control cohort. After adjustment, refill cohort patients with a 30-day fill had an overall MPR that was 3.0 points higher than that of controls, and the 90-day refill cohort had an MPR that was 1.4 points higher than that of controls ($P < .001$ in both cases). Although the magnitude of the difference varied across therapeutic classes, there was no class in which the control cohort had better adherence than the refill cohort. The difference was statistically significant for all therapeutic classes except the 90-day serotonin-norepinephrine reuptake inhibitor (SNRI) medication users.

In addition, members of the refill cohort were less likely to receive an oversupply of medication (ie, MPR >100%). In the 30-day analyses, 17.9% of the refill cohort patients received more than a 365-day supply compared with 18.6% of the control cohort patients ($P < .001$). In the 90-day analyses, we found a similar relationship, with 26.6% of the refill cohort receiving more than 365 days of supply compared with 27.8% of the control cohort ($P < .001$). In the 30-day user analysis, oversupplied patients in the refill cohort refilled 3.32 days early, while the control group patients filled 5.82 days early ($P < .001$). In the 90-day analysis, the oversupplied automatic refill cohort patients filled 7.19 days early, while the control group patients filled 9.38 days early ($P < .001$) (Table 3). Across all therapeutic classes, the refill cohort filled later than the control cohort, resulting in less oversupply. All differences were directionally similar and statistically significant, except for 90-day fill patients on calcium-channel blockers or SNRIs.

Table 3. Comparison of Oversupply[a] Between Refill and Control Cohorts

	30-Day Fillers			90-Day Fillers		
	Excess Days Refill	Excess Days Control	Observed Δ[b]	Excess Days Refill	Excess Days Control	Observed Δ[b]
Total across classes	3.32	5.82	–2.50	7.19	9.38	–2.18
ACE inhibitors	2.42	5.04	–2.62	5.31	8.02	–2.71
Antihypertensive combinations	4.10	6.17	–2.07	8.12	9.33	–1.21
ARBs	2.33	5.12	–2.79	3.73	6.60	–2.87
Beta-blockers	2.18	5.27	–3.09	5.73	8.55	–2.82
Biguanides	2.46	5.53	–3.07	5.35	8.43	–3.08
Calcium-channel blocker	2.51	4.87	–2.36	6.95	7.14	–0.20 (NS)
Contraceptives	1.91	4.43	–2.52	4.22	8.51	–4.30
SNRIs	5.19	6.54	–1.35	11.56	13.02	–1.46 (NS)
SSRIs	3.53	6.45	–2.92	7.14	9.76	–2.62
Statins	2.23	6.00	–3.77	4.18	7.26	–3.08
Thyroid hormones	4.13	6.21	–2.08	10.23	12.43	–2.20

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; delta (Δ), difference; NS, not significant; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
[a]Excess days at time of fill.
[b]Negative difference indicates that the refill cohort received medication later than control. Adjusted *P* value for the difference is <.001, unless specified otherwise.
Source: CVS Caremark pharmacy claims data July 1, 2011, to December 31, 2011; sample limited to members receiving over 365 days of medication during year.

DISCUSSION

Automatic medication refill programs provide a simple solution to address a component of the medication nonadherence problem by making medication refills more convenient for patients. In our evaluation of the CVS automated refill program for retail patients, we found that the members enrolled in the refill program had significantly improved medication adherence compared with a matched cohort of members not enrolled in the program across 11 therapeutic classes prescribed for the management of chronic disease.

Improved medication adherence was obtained without an increase in medication oversupply. In the United States, there is particular concern with oversupply contributing to increased regimen complexity, opiate abuse, antibiotic resistance, and environmental toxicity.[10] Some policy makers have expressed concern regarding the impact of medication wastage on limited healthcare budgets.[11] We found that members enrolled in this automatic refill program were less likely to receive more than a year's supply of medication and had less oversupply than did members of the matched control group. Interestingly, this was an outcome expected by commentators in Europe who conducted reviews and studies of similar refill programs. These authors suggested that putting the pharmacist in control of the refill process would reduce the tendency of the patient to stockpile medication, thus reducing oversupply.[6,12] Our findings support this hypothesis.

We found high rates of oversupply in both cohorts—18% in the 30-day supply refill cohort and 19% in the control cohort—while among those receiving a 90-day supply, the proportions were 26.6% for the refill cohort and 27.8% for the control cohort. However, our findings support a hypothesis that automatic refill programs help to reduce, not exacerbate, the problem of prescription drug oversupply. Although further consideration regarding approaches to reduce oversupply is needed, it is not likely that placing barriers on the involvement of pharmacists in the prescription refill process will reduce the problem of medication oversupply.

Limitations

As with all research, our study has several limitations. First, this investigation considered the experience of 1 national retail pharmacy chain, so we cannot know the extent to which this experience is generalizable to other retail or mail-order pharmacies. However, CVS has a national footprint and our experience is likely representative of other national and regional chain pharmacies. Second, our adherence results are based upon pharmacy claims data; we cannot know if medication dispensed was actu-

ally taken, or by whom. Nonetheless, this is a common and well-accepted method to measure adherence. Third, patients in the refill cohort chose to participate in the program, whereas the controls were selected from a broader sample of CVS patients. Although we used propensity score matching to reduce confounding, and confirmed using well-accepted methods that our match was excellent, we cannot know the impact of unknown confounding factors, including self-selection bias, on our results. Therefore, we are careful not to overstate our confidence in our findings. If there is bias present, it favors improved adherence behavior, but the influence on oversupply behavior is less clear. Finally, we limited our examination to patients who were established medication users; however, among people with chronic disease, this reflects the vast majority of medication users.

CONCLUSIONS

Medication adherence remains a major public health problem, and improving adherence has been demonstrated to have an attractive return on investment. Easing the refill process is one method to remove barriers to adherence. We have demonstrated that automatic refill programs can improve adherence across a range of therapeutic classes and payer types, and we have also provided evidence that this improvement is gained without an increase in the frequency or magnitude of medication oversupply.

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Author Affiliations: Division of Enterprise Research and Analytic Development, CVS Health (OSM, SMK, AA, TAB, AB, TAD, PDS, WHS), Northbrook, IL; Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School (NKC), Boston, MA.

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Address correspondence to: Steven M. Kymes, PhD, CVS/caremark, 2211 Sanders Rd, NBT 326, Northbrook, IL 60062. E-mail: Steven.Kymes@CVSHealth.com.

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