Journal of the American Pharmacists Association 57 (2017) 579–584

Contents lists available at ScienceDirect

Journal of the American Pharmacists Association

journal homepage: www.japha.org

RESEARCH

The impact of a retail prescription synchronization program on medication adherence

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ARTICLE INFO

Article history:
Received 15 July 2016
Accepted 26 May 2017

ABSTRACT

Objectives: To understand the impact of prescription synchronization, offered through the ScriptSync® program at CVS pharmacies nationwide, on adherence and reducing visits to the pharmacy.

Design: Cohort study, conducted between March 26, 2015, and December 18, 2015. Program enrollment occurred in August 2015, with a 120-day baseline period preceding enrollment and a 120-day follow-up period.

Setting and participants: CVS retail community pharmacies across the United States. CVS Pharmacy patients voluntarily enrolling in the prescription synchronization program at CVS retail community pharmacies across the United States who filled 3 or more eligible prescriptions before program enrollment. The study included 126,597 patients who enrolled in the program and 81,355 patients who enrolled after the study enrollment period.

Outcome measures: Adherence was defined as the medication possession ratio. The average number of pharmacy visits per month was a second outcome measure.

Results: Exposed patients had a 7.5 percentage point adherence improvement (from 79.6% to 87.1%), compared with a 2.8 percentage point improvement among the unexposed (from 78.1% to 80.9%) for a benefit of 4.7 percentage points ($P < 0.0001$). Among patients with adherence opportunities, the net impact on adherence was 10.6% ($P < 0.0001$). The program resulted in 0.17 fewer visits per month ($P < 0.0001$).

Conclusion: Offering prescription refill synchronization at a large national retail pharmacy chain resulted in improved adherence and fewer visits to the pharmacy in the 4 months following ScriptSync enrollment. Prescription refill synchronization programs should be considered in the care of patients with multiple comorbidities.

Introduction

Nonadherence to essential medications for chronic conditions is a major source of morbidity, mortality, and unnecessary health care costs in the United States.[1-3] Despite a long-standing recognition of the problem, nonadherence remains a prevalent public health problem. A central challenge is that medication taking is a personal activity, and there are numerous reasons that patients fail to adhere to their medications as prescribed, including cost, cultural barriers, lack of understanding, lack of social support, and difficulty getting to the pharmacy.[4-6]

Medication regimen complexity is an additional well-recognized barrier to adherence, as patients with multiple comorbidities often take multiple medications and need to take those medications multiple times per day to manage their conditions. Considering that the average Medicare Part D beneficiary fills 38 prescriptions per year, and those in the top 5% fill 144 prescriptions per year, this complexity can be considerable.[7] Epidemiologic data indicate that complexity is also derived from the number of providers who prescribe medications for a patient, the number of pharmacies used to fill those prescriptions, and, most notably, the extent to which those refills are synchronized on the same day.[7] In one study, patients whose refills were completely unsynchronized had adherence rates that were 8.4 percentage points lower than patients who refilled all their medications on the same day each month.[8]

In response, a number of independent and chain pharmacies have developed prescription refill synchronization

Disclosure: The authors declare no conflicts of interest or financial interests in any product or service mentioned in this article.

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http://dx.doi.org/10.1016/j.japh.2017.05.016
1544-3191/

Key Points

Background:

- Studies on the effectiveness of prescription synchronization programs on adherence improvement have been encouraging, yet have limited generalizability.
- This is a study of the impact of introducing a nationwide medication synchronization program known as ScriptSync at CVS pharmacies on adherence to chronic medications and on the number of pharmacy visits per month.

Findings:

- Patients enrolling in a prescription synchronization program experienced adherence improvements in the first 4 months of program participation. Patients with adherence opportunities experienced even greater improvement.
- Program enrollment also resulted in fewer pharmacy visits per month.

programs. The accumulating body of evidence regarding the effectiveness of synchronization programs on improving adherence has been promising, but studies have been small or selective to particular geographic regions or insurance payers; therefore, it is difficult to generalize data to the broader population of patients using community pharmacies.[9-12] In the summer of 2015, CVS Pharmacy implemented a nationwide medication synchronization program known as ScriptSync®, available at no charge for eligible patients. In this study, we evaluate the impact of ScriptSync on adherence to chronic medications and on the number of pharmacy visits per month. We hypothesized that the ScriptSync program would reduce adherence barriers, thereby improving medication use among patients using multiple medications.

Methods

ScriptSync: The intervention program

All patients who obtain their prescriptions at CVS Pharmacy have the opportunity to receive pharmacist-based services (e.g., medication education, counseling, refill assistance) designed to improve medication adherence. In addition to these services, certain patients may be eligible for programs based on their medication use. ScriptSync is one such program; it offers CVS Pharmacy patients with 3 or more maintenance medications the opportunity to pick up all of their eligible 30-day supply prescriptions at the same time in 1 monthly visit to the pharmacy. When a patient enrolls in ScriptSync, the patient's medication regimen is verified by a pharmacist, and the best medication to which to align all enrolled prescriptions to a single "synchronization date" for automatic monthly fulfillment is identified, depending on a discussion with the patient regarding their supply on hand. Additional days' supply, known as "short fills," are provided to the patient for medications that will exhaust before the synchronization date, allowing for all enrolled prescriptions to be filled on the synchronization date. The pharmacist also informs the patient how the ScriptSync process will work going forward. As part of standard care, pharmacists are available for consultation at any time, including the date when a ScriptSync patient comes to pick up aligned prescriptions.

Study design and data source

We conducted a cohort difference in differences study among patients who were eligible to enroll in the ScriptSync program between July 24 and August 20, 2015. For exposed patients, the enrollment date was defined as the actual date of ScriptSync enrollment. Unexposed patients were randomly assigned a start date for the adherence measurement period, which aligned with the enrollment period of exposed patients. Exposure definitions are described later. For both exposed and unexposed patients, the baseline period was the 120 days preceding the program enrollment date. The follow-up period was 120 days, which included the enrollment date. Overall, the total study period ranged from March 26 to December 18, 2015. All data were drawn from the CVS retail pharmacy electronic fill records database.

Patient eligibility

Patients eligible for ScriptSync enrollment filled 1 or more 30-day supply prescriptions for each of 3 or more maintenance medications during the previous 90 days, were at least 18 years old, and had not previously opted out of CVS Pharmacy's automatic prescription refill program. Each week, each CVS Pharmacy store received a list of eligible patients. Pharmacists used this list to call patients to invite them to enroll in ScriptSync. If a patient did not answer the phone, the pharmacist advanced to the next patient on the list. Because of pharmacists' time demands, it was common that some patients on the list did not receive calls at all. Patients who did not answer the phone or who did not receive calls remained on the list over time provided that they continued to be eligible for the ScriptSync program. The same process was followed for both the exposed and unexposed groups.

Exposure

Eligible patients who received a call from a pharmacist and enrolled in ScriptSync during July 24 to August 20, 2015 were considered *exposed*. To identify a group of patients who were as similar as possible to the exposed patients but who had not received a pharmacist call and, therefore, did not have the opportunity to enroll (*unexposed*), we capitalized on a resource constraint present in the daily implementation of the ScriptSync program. These patients composed our pool of unexposed patients, some who would have enrolled if given the opportunity and some who would not have enrolled. Because the exposed patients had all enrolled when given the opportunity, an additional step was needed to remove patients' self-selection bias in enrolling. To do this, we determined which unexposed patients subsequently received a pharmacist call and enrolled in ScriptSync in the 2 months after the study period had ended on December 18, 2015—that is, December 27,

2015, and February 20, 2016. This final group of patients who did not receive an opportunity to enroll during the study enrollment window of July 24 to August 20, 2015, yet were eligible for the program during that time, and further elected to enroll after the study ended composed our final, unexposed group.

To explore whether lower baseline medication adherence was associated with greater improvements in adherence following ScriptSync enrollment, we created a subgroup of exposed and unexposed patients who had medication adherence of 65% or less (defined later) during the baseline period.

Outcomes

For each patient, outcomes were assessed in each of the baseline and follow-up periods, and they included only those medications that each patient had enrolled in ScriptSync. *Medication adherence* was defined as the medication possession ratio (MPR).[13] The numerator was the total days' supply of medications on hand during the 120-day baseline or follow-up period, as determined by the date the patient picked up the prescriptions at the pharmacy (i.e., pick-up date). The denominator was 120 days. When the days' supply on hand exceeded the 120 days in the observation period, the MPR was capped at 1. As a secondary outcome, we assessed the average number of pharmacy visits per month by calculating the number of unique pick-up dates in each of four 30-day intervals and then averaging these 4 measurements.

Covariates

We assessed differences between exposed and unexposed patients for the following covariates: patient-level age, sex, and primary insurance payer (commercial, Medicare, Medicaid, or self-pay); census ZIP code–level median income, education level, and region of residence.[14] Using all filled medication claims in the baseline period, we also compared each of the following covariates: 1 or more prescriptions for a medication used to treat diabetes, high cholesterol, or hypertension (list of medications in Appendix), number of unique drug classes, percentage of total medication days filled as 90-day supply, duration of therapy (in days), and monthly average out-of-pocket cost per prescription fill. ScriptSync programmatic and operational covariates were also compared at the patient level: number of medications used by a patient enrolled in the ScriptSync program, number of CVS pharmacies where a patient filled 1 or more prescriptions, and whether the patient was enrolled in the automatic refill program.

Statistical analysis

Descriptive characteristics were compared between exposed and unexposed patients using a chi-square (for dichotomous outcomes) or *t* test (for continuous outcomes). To model the impact of program enrollment, we conducted difference in differences analyses, comparing the outcome in each of the baseline and follow-up periods for each of the exposed and unexposed groups. The linear regression model included an indicator variable for exposure (1 = exposed; 0 = unexposed), an indicator variable for period (1 = follow-up; 0 = baseline), and an interaction variable for Exposure × Time. The subgroup analysis among patients with adherence of 65% or less at baseline followed the same approach. Finally, we conducted a sensitivity analysis to explore whether results were consistent when the initial 30-day synchronization fill, which may appear to inflate adherence artificially because of the synchronization process, was included (all 120 days) or excluded from the follow-up period (90 days).

The primary purpose for conducting this study was quality improvement—namely, to understand whether the ScriptSync program was associated with improved adherence and reduced visits to the pharmacy. This study was conducted as part of CVS retail pharmacy's health care operations, and as such was deemed exempt from human subjects' oversight by the Chesapeake Institutional Review Board. The use of data and all database records were fully compliant with patient confidentiality requirements under the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Results

The final study groups included 126,597 exposed and 81,355 unexposed patients (Table 1). Although differences between exposed and unexposed patients are statistically significant for most characteristics because of large sample size, characteristics are relatively similar between the 2 study groups. Exposed patients were less likely to be female (55.7% in exposed vs. 59.7% in unexposed), reside in the western region of the United States (14.0% vs. 20.8%), have commercial insurance (55.4% vs. 52.7%), and be enrolled in CVS Pharmacy's automatic refill program (83.1% vs. 80.7%). On average, exposed patients used fewer medication classes (7.5 vs. 8.4) than unexposed patients did. Medication adherence increased between baseline and follow-up for patients in both the exposed and unexposed groups (Figure 1). Exposed patients' adherence improved by 7.5 percentage points, from 79.6% to 87.1%, compared with a 2.8–percentage point improvement among the unexposed (from 78.1% to 80.9%). Comparing these changes between the exposed and unexposed groups, ScriptSync enrollment was associated with an additional 4.7% point ($P < 0.0001$) increase in adherence. Among the subgroup of patients with baseline adherence of 65% or less, ScriptSync enrollment was associated with a 36.5% point adherence increase (42.6%-79.1%) in exposed patients. Unexposed patient adherence increased by 25.9% points (41.7%-67.6%). The net increase was 10.6% points ($P < 0.0001$). Results from our sensitivity analysis, which excluded the first 30 days of the follow-up period, were consistent with the main analysis: adherence increased 7.8 percentage points among exposed patients (from 79.6% to 87.4%) and 4.3 percentage points in the unexposed group (from 78.1% to 82.4%), for an impact of 3.5 percentage points ($P < 0.0001$; data not shown).

In the exposed group, ScriptSync enrollment was associated with an average 0.14 reduction in the number of visits to the pharmacy per month (from 1.52 to 1.37; Table 2). In the unexposed group, the average number of visits to the pharmacy per month increased by 0.03 (from 1.33 to 1.36), for an impact of 0.17 ($P < 0.0001$).

Table 1
Baseline characteristics of 207,952 patients

Characteristic	Exposed N = 126,597	Unexposed N = 81,355	*P* value[a]
Demographics			
Mean age	60.5	60.1	< 0.0001
Female	55.7%	59.7%	< 0.0001
Northeast	23.7%	21.6%	< 0.0001
Midwest	17.8%	15.3%	< 0.0001
South	44.2%	41.9%	< 0.0001
West	14%	20.8%	< 0.0001
College educated	31.4%	29.2%	< 0.0001
Median income	$60,709	$58,544	< 0.0001
Payer			
Commercial	55.4%	52.7%	< 0.0001
Medicare Part D	7.9%	10.5%	0.0849
Medicaid	35.4%	35.8%	< 0.0001
Self pay (cash)	1.2%	1%	< 0.0001
Conditions			
Diabetes	26.3%	28.9%	< 0.0001
Hypertension	78.1%	79.1%	< 0.0001
High cholesterol	55.6%	56.2%	0.0046
Condition class count	7.5	8.4	< 0.0001
Utilization			
Average number of stores visited	1.1	1.1	< 0.0001
Percent of days as 90-day supply	10.6%	11.6%	< 0.0001
Participation in automatic refill program	83.1%	80.7%	< 0.0001
Average therapy duration (days)	116.4	118.4	< 0.0001
Monthly average patient out-of-pocket cost per fill	$11.38	$11.70	0.0004
Average number of ScriptSync-enrolled medications	2.3	2	< 0.0001

[a] *P* value for chi-square or *t* test comparing the differences between exposed and unexposed patients.

Discussion

In this study, patient enrollment in a prescription refill synchronization program at a large national retail pharmacy chain was associated with a 4.7–percentage point overall improvement in medication adherence. Among patients who were less adherent at baseline, we observed an even greater improvement in adherence of 10.6 percentage points. Consistent with the objectives of the ScriptSync program, the average number of visits to the pharmacy per month decreased by 0.17 visits.

The ScriptSync program's impact on adherence is similar to or greater than previous studies of pharmacist counseling (2.1%), elimination of copayments (4%-6%), and minimal effectiveness of educational campaigns.[15–18] The greater improvement we observed was likely due, in part, to the program's eligibility criteria, which identified patients taking at least 3 medications. Patients taking a greater number of

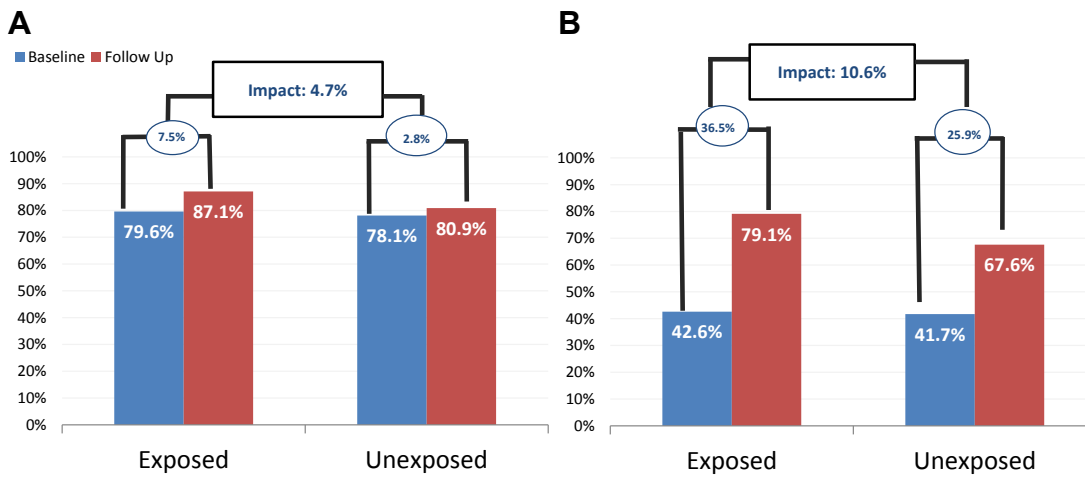

Figure 1. Adherence impact of ScriptSync at retail. (A) Average adherence (days of therapy) in baseline and follow-up between exposed and unexposed patients—overall. (B) Average adherence (days of therapy) in baseline and follow-up between exposed and unexposed patients—among patients with adherence opportunities. Blue indicates baseline, and red indicates follow-up.

Table 2
Average number of monthly pharmacy visits per patient in baseline and follow-up study periods, by study group

Group	Previsits		Postvisits		Visit delta		Impact	*P* value
	Mean	SD	Mean	SD	Mean	SD		
Exposed	1.52	0.59	1.37	0.47	−0.14	0.52	−0.17	< .0001
Unexposed	1.33	0.48	1.36	0.50	0.03	0.41		

medications have greater adherence difficulties because of the need to manage multiple refill times, trouble getting to the pharmacy, and other factors.[19] The ScriptSync program simplifies medication refills to a single date, with the added benefit of reducing needed pharmacy visits to 1 pick-up date per month.

Indeed, the adherence impact we found is consistent with the 3-5 percentage point improvement in adherence among Medicare Part D beneficiaries using a synchronized mail service,[12] and it is more conservative than that observed with appointment-based medication synchronization (ABMS) models, in which adherence improved 20 percentage points among enrollees compared with controls.[10,11] The large differences observed in these ABMS studies may have been due to differences in study design and patient selection. In addition, these studies focused on narrower population subsets, including patients filling at rural midwestern pharmacies,[10] community pharmacies in a single U.S. state,[11] and Medicare Part D beneficiaries using mail pharmacy services.[12] Our study recruited a large cohort of retail pharmacy users in a nationwide program, included multiple payer types, and leveraged a rigorous design to address concerns of enrollment bias, with broader generalizability to adult patients using community-based pharmacies.

Although we expected the number of visits to the pharmacy per month to approach a single visit (if the program worked "perfectly"), the average number of pharmacy visits per patient declined by only 0.17 visits. Although it is not possible to disentangle the reasons for the small decline because of data limitations, we hypothesize that changing medical needs, insurance changes, or other reasons, such as picking up retail store items or acute medications, may have contributed to the smaller decline.

There are several limitations to the study. The study was not randomized, and many demographic and drug use characteristics were statistically different between exposed and unexposed patients at baseline. In addition, most patients had relatively high baseline adherence, suggesting that self-selection bias is also present, in which patients more motivated to take care of their health were more likely to enroll. To reduce this bias, our design compared exposed patients who chose to participate in the program and unexposed patients who chose to participate 4 months later. We believe these design and analytic approaches make it unlikely that the results we observed were due to confounding or self-selection bias.

As described earlier, the study was launched as a quality improvement evaluation. To respond to CVS Pharmacy's need for the most timely, actionable insights to improve the program, we studied each patient for only 4 months after enrollment. Although we cannot definitively comment on the long-term sustainability of the program on adherence, mounting literature on the effectiveness of synchronization programs has shown sustained adherence improvements over 12-month periods.[10–12] It is likely that patients experienced other events that would affect both program participation and adherence, such as insurance plan and medication changes during the baseline and follow-up periods. Exposed and unexposed patients also experienced CVS Pharmacy's standard care services, which were designed to improve medication adherence. A particular advantage of our study design with a control group is that these natural changes and the receipt of CVS's standard medication adherence improvement services are present in both the unexposed and exposed groups, and so are cancelled out in the difference in differences analysis. With this approach, the results describe the isolated impact of the ScriptSync program alone. Our outcomes focused on patient behavior and medication adherence, not clinical outcomes. Medication adherence is a widely used outcome for the measurement of clinical quality[13,20] and is consistently associated with better clinical outcomes.[2,21-23]

Conclusion

CVS Pharmacy's nationwide ScriptSync program to simplify pick-up of complex medication regimens was associated with a significant, positive improvement in adherence to therapy. Refill synchronization will not eradicate the problem of nonadherence, but it should be considered an important approach in the arsenal of interventions to improve care for patients with multiple comorbidities taking multiple medications. The long-term effects on patient drug use behaviors, health outcomes, total health care costs, and programmatic cost effectiveness of synchronization programs require further study.

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Appendix

Generic product indicators to treat diabetes, high cholesterol, and hypertension

Condition	Generic product indicator
High cholesterol	3910; 3920; 3930003000; 3940; 3945; 3948; 399940; 409925
Diabetes	2715; 2717; 2720; 2725; 2728; 2750; 2755; 2760; 2770; 279925; 279930; 279930027003; 279940; 279950; 279960; 279965; 279970; 279978; 279980
Hypertension	3310; 33200010; 33200020; 33200021; 33200022; 33200030; 33200040; 3330; 3399; 4000003; 34000010; 4000013; 34000015; 4000018;34000020;34000024; 34000030; 3610; 615;3617; 362010; 36202030; 62030; 369915; 69918; 369920; 369930; 369940; 369945; 369960; 369967; 369968; 37500010; 37500030; 3760; 3799000230