

Health Affairs

At the Intersection of Health, Health Care and Policy

Cite this article as:

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Adherence Rates In Diabetes Patients

Health Affairs, 31, no.1 (2012):120-129

doi: 10.1377/hlthaff.2011.0931

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DOI: 10.1377/hlthaff.2011.0931
HEALTH AFFAIRS 31,
NO. 1 (2012): 120–129
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An Integrated Pharmacy-Based Program Improved Medication Prescription And Adherence Rates In Diabetes Patients

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ABSTRACT A substantial threat to the overall health of the American public is nonadherence to medications used to treat diabetes, as well as physicians' failure to initiate patients' use of those medications. To address this problem, we evaluated an integrated, pharmacy-based program to improve patients' adherence and physicians' initiation rates. The study included 5,123 patients with diabetes in the intervention group and 24,124 matched patients with diabetes in the control group. The intervention consisted of outreach from both mail-order and retail pharmacists who had specific information from the pharmacy benefit management company on patients' adherence to medications and use of concomitant therapies. The interventions improved patients' medication adherence rates by 2.1 percent and increased physicians' initiation rates by 38 percent, compared to the control group. The benefits were greater in patients who received counseling in the retail setting than in those who received phone calls from pharmacists based in mail-order pharmacies. This suggests that the in-person interaction between the retail pharmacist and patient contributed to improved behavior. The interventions were cost-effective, with a return on investment of approximately \$3 for every \$1 spent. These findings highlight the central role that pharmacists can play in promoting the appropriate initiation of and adherence to therapy for chronic diseases.

The prevalence and cost of treating diabetes in the United States continue to rise.¹ The American Diabetes Association estimated that the total costs in 2007 were \$174 billion for the diagnosed US population alone.² The proper treatment of diabetes requires a combination of self-management, appropriate lifestyle choices, and relevant pharmaceutical therapies.

Despite evidence that medications help control blood glucose levels and reduce morbidity and mortality, however, almost half of patients with diabetes are not adherent to their prescribed medications.^{3,4} Patients with diabetes—

particularly those age forty or older—also benefit from the concomitant use of medications to treat hyperlipidemia (high cholesterol and high triglyceride levels) and to prevent the development of proteinuria (a condition in which the urine contains an abnormal amount of protein, a sign of chronic kidney disease) in accordance with widely accepted practice guidelines.⁵

Ensuring adherence and appropriate treatment has long been the domain of primary care providers. However, as demands on the time of these providers increase, interventions carried out by pharmacists can complement primary care. Indeed, pharmacists are in a unique posi-

tion to monitor patients' adherence and intervene effectively when indicated.⁶

Patients generally receive medications at a retail pharmacy or through the mail from a pharmacy benefit management program. These two methods of obtaining prescriptions usually operate independently. But the pharmacy benefit manager can use the available information from both channels to develop an integrated intervention that improves adherence to existing therapies and encourages the initiation of beneficial therapies.

This study evaluated such a concerted intervention to improve pharmacy care for patients with diabetes. Specifically, the pharmacy benefit management company provided messages to both mail-order and retail pharmacists about patients' adherence to medications. Pharmacists then passed along the information to both patients and their physicians. Patients who were not on statin medications (to treat hyperlipidemia) or angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (to prevent proteinuria) were also counseled about initiating these therapies, and an offer was extended to contact their doctors to discuss the idea.

We assembled a prospective cohort of patients to evaluate this pharmacy intervention program. A secondary objective was to compare the impact of the intervention in the two channels: retail pharmacies and mail-order pharmacies.

Study Data And Methods

SETTING AND PARTICIPANTS A single employer involved in heavy industry in the Midwest participated in the program. CVS Caremark was the pharmacy benefit manager for this employer.

The intervention group consisted of 5,123 patients—employees and covered dependents—with diabetes. *Patients with diabetes* were defined as people at least age forty who were continuously eligible for pharmacy benefit management and who had filled a prescription for a medication to treat diabetes within six months of the program's start. Patients who had filled such medications at a participating CVS retail pharmacy were assigned to the "retail" group. All other patients were assigned to the "pharmacy benefit management" group. The program was active for six months, between October 18, 2009, and April 17, 2010.

PROGRAM INTERVENTIONS The staffs of twelve CVS retail pharmacies in northwest Indiana were trained to deliver interventions, as was the mail-order pharmacy serving this employer. The program interventions are summarized in Exhibit 1. All participants in the study received a welcome

letter and the offer of a free diabetes testing kit. Patients who were late in refilling a medication used to treat diabetes received a follow-up call from a pharmacist, from either the retail setting or the mail-order pharmacy. Patients starting a new medication also had counseling at the time of their first fill of the medication.

For patients in the retail setting who were identified as having diabetes but not on statins, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, the retail pharmacist counseled the patient on his or her next visit to the pharmacy about the need for such medications. The pharmacist also offered to contact the patient's physician to discuss the medication use. With the patient's consent, the prescriber was sent a fax and asked if he or she wished to start the identified medication. The pharmacist made a follow-up call to the patient to inform him or her about the prescriber's decision. An analogous effort was made by the mail-order pharmacist, based on phone outreach to the patient and fax to the doctor.

CONTROL GROUP OF PATIENTS The control group consisted of 24,124 people with diabetes, based on a roughly 5:1 match with program participants. The matching criteria were as follows: similar medication history; sex; number of maintenance medications for twelve months before the program started; age of sixty-five or older (yes or no); Ingenix pharmacy risk group score, which measures disease burden (divided into quartiles);⁷ preferred pharmacy (CVS retail, Caremark mail order, or other pharmacy); recent fill at a CVS retail pharmacy; and medication possession ratio for oral medications to treat diabetes in the twelve months before the program started.

OUTCOMES AND FOLLOW-UP We measured the following two patient-level outcomes: change in adherence to medications used to treat diabetes, defined by total days' supply per month; and initiation rate of concomitant therapies (statins and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers).

Pharmacy claims for the intervention and control groups were obtained for the eighteen-month period between April 18, 2009, and October 17, 2010, and were divided into three six-month periods. We used the six-month period before the program began (April 18, 2009, to October 17, 2009) to identify patients with diabetes, establish what oral medications they were taking to treat diabetes, and identify patients in need of initiating concomitant therapies.

Claims from the six-month program period (October 18, 2009, to April 17, 2010) were examined to identify changes in adherence to oral medications used to treat diabetes and initiation

EXHIBIT 1

Summary Of Diabetes Program Interventions In The CVS Caremark Study

Intervention	Members receiving intervention	Patient group	
		Pharmacy benefit management	Retail
General information	All members	Welcome letter Automated call introducing offer of free diabetes testing kit	Welcome letter Automated call introducing offer of free diabetes testing kit
Initiation of ACE inhibitors/ ARBs and/ or statins	Members missing ADA-recommended medications	Call from pharmacy advisor team to discuss missing therapy; notification that team will contact prescriber Letter sent to member if prescriber does not respond or prefers to discuss with member Call from pharmacy advisor team if prescriber responds with new prescription	In-store consultation with pharmacist about missing therapy when picking up another prescription; notification that store pharmacist will contact prescriber Letter sent to member if prescriber does not respond or prefers to discuss with member Call to member if prescriber declines or agrees to authorize new prescription
Adherence enforcement	Members late in refilling a current prescription	Call from pharmacy advisor team to discuss nonadherence and offer to refill mail prescriptions Offer from pharmacy advisor team of enrollment in ReadyFill Follow-up call from pharmacy advisor team 30 days after initial call to discuss medication	Call from store pharmacist to discuss nonadherence and offer to refill prescription
First-fill counseling (FFC)	Members beginning a new diabetes-related medication	Call from pharmacy advisor team to discuss recently filled new prescription FFC brochure sent to member after FFC intervention delivered Follow-up call from pharmacy advisor team 30 days after first fill to discuss medication	In-store consultation with pharmacist when picking up new prescription FFC brochure given to member with prescription Follow-up call from store pharmacist 2 weeks after first fill to discuss medication

SOURCE Authors' analysis. NOTES ACE is angiotensin-converting enzyme. ARB is angiotensin receptor blocker. ADA is American Diabetes Association.

rates of concomitant medications. Finally, we measured the impact of the program discontinuation on adherence to medications used to treat diabetes in the six-month postprogram period (April 18, 2010, to October 17, 2010).

STATISTICAL ANALYSIS We created segmented linear regression models⁸ to measure the impact of the intervention program on patients' adherence to medications to treat diabetes. We used generalized estimating equations⁹ to account for the repeated observations within patients.

At the conclusion of the six-month program, we measured cumulative therapy initiation rates for angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and statins for patients not using them at baseline. We then compared these rates and determined the relative difference between the intervention and control groups, and within intervention channels, using Kruskal-Wallis chi-square tests.¹⁰

We constructed a logistic regression model of patient-level therapy initiation to account for the impact of patient and therapy characteristics. In addition to the group membership indicator, the

model included missing therapy type and intervention channel, as well as sex, age, and median household income of the patient's ZIP code as a measure of socioeconomic status. It also included pharmacy risk group scores as a measure of disease burden.

LIMITATIONS There are several limitations associated with our study. The program was implemented for a single employer, and the results might not be typical of a more broadly implemented program. The employer was an industrial concern in an urban setting and employed mainly blue-collar workers, who had a relatively high prevalence of diabetes.

Additionally, the program lasted only six months. It is possible that the impact of these interventions may lessen over a more extended period as patients become less sensitive to the outreach activities.

Finally, we chose to look at patients' monthly supply of medications to treat diabetes as our adherence measure, to provide a reliable statistic on a month-to-month basis that would be sensitive to the interventions. We realize that the lit-

erature predominantly uses medication possession ratio or proportion of days covered as the preferred predictors of medication adherence.¹¹

Study Results

The intervention and control groups had similar sex distributions, use of CVS retail and mail pharmacies, and prevalence of patients without concomitant use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and statins (Exhibit 2). Patients in the intervention group who were not taking these medications were targeted for the initiation intervention described in Exhibit 1. Compared to the control group, the intervention group had a slightly lower baseline disease burden, was older, and had a lower socioeconomic status (Exhibit 2).

ADHERENCE RESULTS Exhibit 3 presents the monthly use of medications to treat diabetes over the eighteen months of the study period, ex-

pressed in total days' supply per month. The intervention group increased its use during the program period.

Exhibit 4 shows the segmented regression results for the adherence intervention. Compared to patients in the control group, patients in the intervention group had an additional 0.75 (2.1 percent) days' supply per month during the program period and a nonsignificant 0.35 (1.0 percent) more days' supply per month in the postprogram period.

The intervention was more effective with patients who used retail pharmacies, resulting in an additional 1.4 (3.9 percent) days' supply per month during the program and a nonsignificant 0.41 (1.2 percent) more days' supply per month in the postprogram period. In comparison, the mail-order pharmacy intervention group had 0.58 (1.7 percent) additional days' supply per month during the program and a nonsignificant 0.34 (1.0 percent) more days' supply per month

EXHIBIT 2

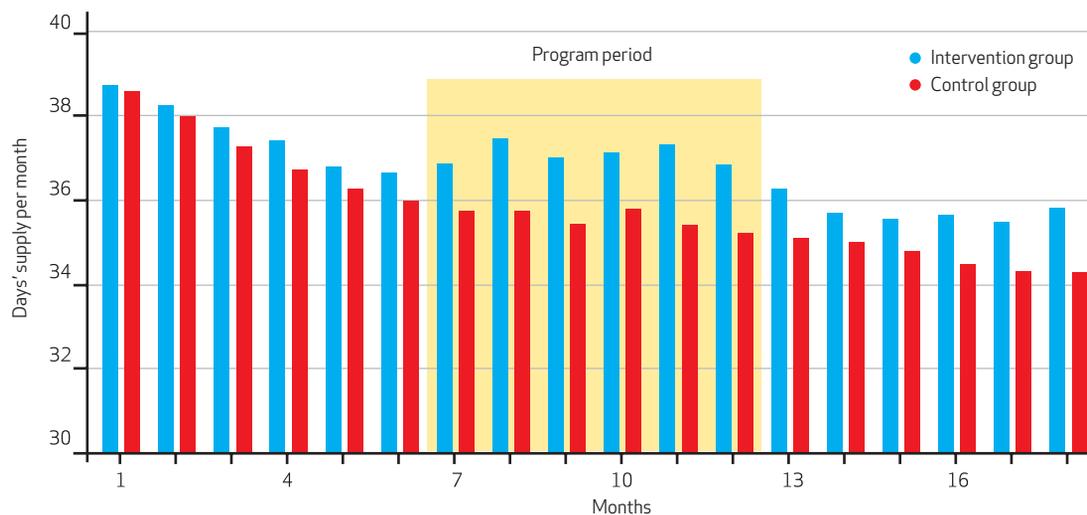
Baseline Characteristics Of Study Cohorts In The CVS Caremark Study, By Site Of Pharmacy Intervention

Characteristic	Cohort		p value
	Intervention	Control	
FULL SAMPLE			
Number of patients	5,123	24,124	— ^a
Male (%)	56.9	56.7	0.80
Primarily use mail-order pharmacy (%)	34.8	35.6	0.27
Primarily use CVS retail pharmacy (%)	30.6	30.6	0.97
No recent use of ACE inhibitors/ARBs (%)	31.4	31.4	0.96
No recent use of statins (%)	32.8	32.0	0.31
Pharmacy risk group score (mean)	5.62	5.77	< 0.01
Age (mean number of years)	64.1	62.9	< 0.01
Median household income in ZIP code	\$42,369	\$46,323	< 0.01
RETAIL GROUP			
Number of patients	1,101	5,115	— ^a
Male (%)	54.1	53.7	0.80
Primarily use mail-order pharmacy (%)	19.5	19.9	0.76
Primarily use CVS retail pharmacy (%)	79.0	78.6	0.76
No recent use of ACE inhibitors/ARBs (%)	32.1	31.6	0.75
No recent use of statins (%)	32.6	32.4	0.89
Pharmacy risk group score (mean)	5.83	5.96	0.32
Age (mean number of years)	63.7	62.5	0.01
Median household income in ZIP code	\$43,284	\$47,819	< 0.01
PHARMACY BENEFIT MANAGEMENT GROUP			
Number of patients	4,022	19,009	— ^a
Male (%)	57.7	57.5	0.86
Primarily use mail-order pharmacy (%)	39.0	39.8	0.31
Primarily use CVS retail pharmacy (%)	17.4	17.7	0.65
No recent use of ACE inhibitors/ARBs (%)	31.2	31.3	0.91
No recent use of statins (%)	32.8	31.9	0.28
Pharmacy risk group score (mean)	5.56	5.72	0.01
Age (mean number of years)	64.2	63.0	< 0.01
Median household income in ZIP code	\$42,119	\$45,920	< 0.01

SOURCE Authors' analysis. **NOTES** p values were determined from Kruskal-Wallis chi-square test (Note 10 in text). ACE is angiotensin-converting enzyme. ARB is angiotensin receptor blocker. ^aNot applicable.

EXHIBIT 3

Patients' Monthly Supply Of Oral Medications To Treat Diabetes, Intervention And Control Groups, In The CVS Caremark Study, Before-, During-, And After-Program Phases



SOURCE Authors' analysis.

in the postprogram period.

INITIATION OF APPROPRIATE CONCOMITANT THERAPIES Exhibit 5 shows a comparison of the initiation rates of concomitant medications between the intervention and control groups for each medication type. Some intervention- and control-group patients initiated these therapies without program interventions, largely because their doctors independently decided to follow widely recognized treatment guidelines. However, compared to the control group, the intervention group had a 39 percent higher initiation rate for angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and a 22 percent higher initiation rate for statins. Again, the intervention proved more effective with the retail group.

The regression model revealed that patients in the intervention group had an overall 38 percent

greater likelihood of initiating a concomitant therapy during the six months of the program, compared to the control group (95% confidence interval: 25, 52; $p < 0.01$; data not shown).

The success of the retail intervention was probably based on the fact that the retail pharmacist succeeded more often than the mail-order pharmacist in delivering the intervention message to the patient and consequently to the prescriber. Pharmacists overall reached 54.4 percent of the patients identified for initiation opportunities. Retail pharmacists made contact 72.1 percent of the time, compared to 49.6 percent of the time for mail-order pharmacists. Pharmacists' rates of contacting patients were similar across medication types.

EXHIBIT 4

Estimated Program And Postprogram Impact On Monthly Supply Of Oral Medications To Treat Diabetes, CVS Caremark Study

Study group	During program			After program		
	Percent change	95% CI	p value	Percent change	95% CI	p value
Full sample	2.1	1.0, 3.3	< 0.01	1.0	-0.5, 2.5	0.17
Retail group	3.9	1.6, 6.2	< 0.01	1.2	-1.8, 4.2	0.43
Pharmacy benefit management group	1.7	0.3, 3.0	0.02	1.0	-0.7, 2.7	0.26

SOURCE Authors' analysis. NOTES "After program" is the six-month period after the end of the six-month program. p values represent significance of parameter estimate difference from regression model. Percent change was calculated by dividing that parameter estimate by the mean days' supply per month from the relevant control-group channel. CI is confidence interval.

EXHIBIT 5
Initiation Rates Of Concomitant Therapy During The CVS Caremark Program

Therapy	Study cohort initiation rate (%)		Estimated improvement		p value
	Intervention	Control	Percent	95% CI	
FULL SAMPLE					
ACE inhibitors/ARBs	19.6	14.1	39	26, 53	< 0.01
Statins	20.4	16.8	22	9, 34	< 0.01
RETAIL GROUP					
ACE inhibitors/ARBs	23.2	13.8	68	39, 99	< 0.01
Statins	27.6	16.5	67	40, 94	< 0.01
PHARMACY BENEFIT MANAGEMENT GROUP					
ACE inhibitors/ARBs	18.6	14.1	31	16, 47	< 0.01
Statins	18.5	16.9	9	-4, 23	0.18

SOURCE Authors' analysis. **NOTES** Confidence intervals were calculated from least-square means. *p* values were determined from Kruskal-Wallis chi-square test (Note 10 in text). ACE is angiotensin-converting enzyme. ARB is angiotensin receptor blocker. CI is confidence interval.

Discussion

Despite evidence of the benefits of optimal medication adherence,¹²⁻¹⁴ lack of adherence in patients with diabetes is a common problem.¹⁵⁻¹⁷ Better adherence has been shown to improve health outcomes and lower the overall cost of health care.^{12,14,18} Simple programs may improve adherence and help doctors and patients with diabetes initiate appropriate concomitant therapies, such as statins and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. These programs can strike an optimal balance between costs and benefits, so that appropriate increases in pharmacy spending will result in overall reductions in total health care cost, while simultaneously improving quality.

Our study found that pharmacist counseling can improve rates of adherence to medications for patients with diabetes and can improve rates of initiation of appropriate concomitant therapies. Patients identified to receive the integrated intervention were 2.1 percent more adherent to existing medications for treatment of their diabetes. In addition, patients without a recent history of appropriate therapy for cholesterol management or blood pressure control were 38 percent more likely to initiate that therapy because of pharmacist outreach to both patient and physician.

The benefits were greater in patients who received counseling in the retail setting than in those who received phone calls from mail-order pharmacy-based pharmacists. This suggests that the in-person interaction between the retail pharmacist and patient was a contributing factor to improved behavior.

The latter outcome is not a surprise, because it has been suggested by previous research that we and others have completed.⁶ The more personal

nature of the face-to-face interaction and patients' familiarity with the retail setting no doubt contribute to the stronger effect. The limits of phone-based interventions in diabetes care have recently been emphasized by the poor results of telephonic interventions used by disease management firms.¹⁹

In addition to the importance of glycemic (blood sugar) control, patients with diabetes benefit from the management of other cardiovascular and kidney disease risk factors, with the use of either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to control blood pressure²⁰⁻²² and statins to control lipid levels.²³⁻²⁵ However, various studies have shown that patients with diabetes often go without these medications, largely as a result of physician oversight.²⁶ The pharmacist's ability to notify physicians of possible improvements in care through initiation of these therapies is a potentially important quality intervention. This intervention can also reduce downstream health care costs by preventing complications.

We recognized that statins, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers might be contraindicated for some patients with diabetes. As a result, pharmacists' communications with physicians made it clear that this could be the case. Making suggestions of this sort is clearly within the expected professional responsibility of the pharmacist, and most physicians welcome such suggestions. For study purposes, we assumed that the rates of such contraindications were similar in the intervention and control groups, based on control-group matching.

OTHER STUDIES Our results can be placed in the context of similar research on the improved use of medications. A wide variety of studies have

examined the subject of improving medication management for patients with diabetes, and for common chronic medications more broadly,²⁷ but the results have been varied.

An intensive diabetes education program described by Carole Cranor and Dale Christensen found dramatic improvements in hemoglobin A1c levels among patients with diabetes from Asheville, North Carolina,²⁸ and an increased percentage of patients using angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, from 27 percent to 65 percent.²⁹ But a meta-analysis of studies focusing on interventions to improve chronic medication adherence delivered by community pharmacists found that only eight of eighteen studies had significant results at any point in time.³⁰

Moreover, a recent literature review of adherence interventions suggested that “current methods of improving medication adherence for chronic health problems are mostly complex, labor-intensive (and thus expensive), and not predictably effective.”^{31(p2877)} The programs reviewed included combinations of more convenient care, information, counseling, reminders, self-monitoring, reinforcement, family therapy, and other forms of additional supervision or attention. Even the most effective interventions had only modest effects.³¹

ADVANTAGES OF PHARMACIST INTERVENTIONS

We believe that the results of our study demonstrate the efficacy of our pharmacist-based interventions in improving adherence and getting patients to start taking medications they need. The program was also cost-effective in its design. We used comprehensive data on medication use from our designated pharmacy benefit management database to develop our interventions. Then we took advantage of the fact that we could integrate our clinical messages into the work flow of both the retail pharmacies and the mail-order facilities. Short counseling sessions could be accommodated within the current staffing levels of both pharmacies.

With regard to the costs of the program, each identified patient received a welcome letter and a series of interactive voice-response calls (Exhibit 1), for an average cost of \$1.00 per person. For the retail cohort, the retail counseling interventions took two to five minutes of a pharmacist’s time. The first-fill counseling sessions were supported by a brochure that cost approximately fifty cents per copy.

For the pharmacy benefit management group, a pharmacy technician would phone a patient, explain the purpose of the call, comply with the privacy regulations of the Health Insurance Portability and Accountability Act of 1996, and transfer the call to a pharmacist, who would deliver

Programs to improve adherence should be continuous.

the counseling session. On average, the technician portion of the call took 4.4 minutes, and the pharmacist portion, 11.5 minutes. In total, the labor and support costs of delivering the pilot program were approximately \$200,000 for the study population of 63,000 beneficiaries.

These costs can be put in perspective by estimating the health care cost reduction effectuated by proper adherence and initiation of therapy. Multiple analyses have provided evidence that medication adherence reduces direct health care spending for people with diabetes.^{12,13,18} We have also examined additional savings opportunities from initiation of therapy and using alternative, lower-cost therapies.^{20,24,32-34}

Using this information, we estimated the total financial value of our integrated pharmacy interventions to be more than \$600,000 in health care cost avoidance for the study population of 63,000 beneficiaries. This saving is made up of \$630,000 resulting from a 2.1 percent increase in adherence and nearly \$200,000 resulting from the initiation of therapies, with a counterbalancing additional \$200,000 in pharmacy costs because of higher use. In summary, the return on investment was approximately 3:1.

We realize that extending this type of program to other diseases and interventions might involve some additional costs at both mail-order and retail pharmacies, but we believe that the cost-benefit ratio will continue to be positive. Furthermore, the program is clearly scalable. As of April 2011 the program was available to more than twelve million enrollees in the pharmacy benefit management company.

Finally, the pilot setting allowed us to evaluate patterns of use of oral medications to treat diabetes after the intervention was stopped. As might be expected, the adherence in the intervention and control groups rapidly became similar. This finding suggests that programs to improve adherence should be continuous because the patient’s tendency to lapse is ever present.

We acknowledge that this type of integrated program can be delivered much more cost-effectively when the pharmacy benefit management company and the retail pharmacies are part of the same organization, especially with regard to the development of efficient work flows. But

we believe that the use of comprehensive pharmacy benefit management to improve adherence and initiate medications in the retail setting is generalizable. Other pharmacy benefit managers without a retail channel are pursuing similar interventions.

In summary, the program we have described here delivered sustained gains in adherence and initiation of therapy, which waned once the program ended. Results were achieved by using a comprehensive database from the pharmacy

benefit manager and both mail-order and retail pharmacies. These interventions provided comprehensive reach in an efficient fashion and hence appear quite sustainable and scalable over time. In a health care system eagerly seeking programs that can reduce costs and improve care, such simple, pharmacist-based counseling programs to improve adherence to existing medication regimens and initiate missing therapies should be of great value. ■

All work on this article was funded by CVS Caremark.

NOTES

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In this month's *Health Affairs*, Troyen Brennan from CVS Caremark, along with coauthors from that company and Harvard Medical School, report on their study of a program to boost patients' use of and adherence to diabetes medicines.

Under the program, pharmacists reached out to patients by mail, by phone, or in person in retail pharmacies. All methods improved patients' adherence somewhat, although the in-person interactions were the most effective. All also had a marked effect on prompting physicians to ensure that their patients started on medication. The interventions were cost-effective, the authors say, producing a return on investment of approximately \$3 for every \$1 spent.

The authors also gained insight into the problem of time-limited interventions. "Patients adhere

while the intervention is in place, but once it ends, adherence drops off very rapidly," says Brennan. "If you're going to make these interventions work, you need to keep them going."

Brennan is executive vice president and chief medical officer of CVS Caremark, an integrated pharmacy services provider with headquarters in Woonsocket, Rhode Island. Before joining CVS Caremark, he was chief medical officer of Aetna.

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