

Effects of a Pharmacy-Care Program on Adherence and Outcomes

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ABSTRACT

Objectives: Identify the benefits of a comprehensive pharmacy care program to increase adherence for patients taking highly active antiretroviral therapy (HAART) and assess the effect on the patient's overall health outcome.

Study Design: A retrospective analysis was conducted comparing baseline medication adherence, cluster of differentiation 4 (CD4) cell counts, and viral load in antiretroviral-experienced human immunodeficiency virus-infected patients to the same values after at least 6 months of specialized pharmacy care.

Methods: A total of 64 patients participated in an ongoing pharmacist-managed medication program. All participants received education, assessment, clinical support, therapy review, refill reminders, and custom packaging.

Results: After 6 months of pharmacy care, mean medication adherence increased 28% and mean CD4 cell count increased 38%. The percentage of patients whose viral loads were considered undetectable increased from 28% to 66%. In addition, the number of patients achieving greater than 95% adherence increased 69%.

Conclusions: A comprehensive pharmacy care program demonstrated substantial and sustained improvement in medication adherence, CD4 cell counts, and viral load among HIV patients receiving HAART. Furthermore, based on published data, the increase in CD4 cell counts resulted in a mean overall healthcare cost savings of \$2929.00 per member per year. The role of the pharmacist is critical in promoting medication adherence for the reduction of healthcare costs and the prevention of chronic disease progression.

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Although many chronic-disease management programs exist, few studies have investigated interventions aimed at improving patient adherence to prescribed medication therapy and the effect of such interventions on the patient's overall health outcome.

Adherence to chronic pharmacologic therapies is poor, leading to worsening disease severity and increased costs associated with higher utilization of inpatient and outpatient healthcare services. The total US healthcare economic burden of medication non-adherence is estimated to be as high as \$300 billion annually.¹

We theorized that a retrospective evaluation of a specialty pharmacy-care program would reveal improved adherence to antiretroviral medications and reduced overall healthcare costs.

Barriers to Adherence

Non-adherence can vary from missing 1 dose of 1 medication to missing all doses of all medications for several days. Not following instructions regarding dietary or fluid intake or not taking medications at prescribed time intervals also constitutes non-adherence. The most common contributing factors to non-adherence have been well identified in previous studies. They include various patient factors such as active alcohol or drug use, as well as poor communication between the patient and the healthcare provider. In addition, there are assorted barriers to adherence, such as complex regimen or length of therapy, which make it difficult for a patient to maintain compliance.²

Adherence and HAART

For patients with human immunodeficiency virus (HIV), adherence to highly active antiretroviral therapy (HAART) poses unique challenges. Thirty-one studies from North America indicated a pooled estimate of 55% of the populations achieving adequate levels of adherence to their antiretroviral therapy.³

In the case of chronic diseases, such as hypertension or diabetes, lower levels of adherence, around 70% to 80%, are considered adequate to achieve treatment goals. In the case of HAART, near-perfect adherence is required to obtain a successful treatment outcome.⁴

The goal of HAART is to suppress viral load in the blood to undetectable levels. Adherence to treatment is critical to obtain full benefits of HAART: maximal and durable suppression of viral replication, reduced destruction of cluster of differentiation 4 (CD4) cells, prevention of viral resistance, promotion of immune reconstitution, and slowed disease progression.⁵ Multiple recent studies have found a significant association between poor adherence to HAART and virologic failure. In 2000, Paterson and colleagues demonstrated that patients with 95% or greater adherence had a superior virologic outcome, a greater increase in CD4 counts, and a lower hospitalization rate than did patients with lower levels of adherence.⁶ The findings indicated that patients less than 70% adherent were more than 4 times more likely to experience virologic failure than those patients who were greater than 95% adherent.

Other HAART outcome studies have shown that there is an 11% increased risk of virologic failure for every 10% decrease in adherence. In addition, the findings show that the high levels of adherence required to achieve virological suppression are similar to the levels needed to maintain viral suppression.⁷

Typical Methods to Increase Adherence

The volume of prescriptions at community retail pharmacies has risen substantially over the last several years. Nationwide, pharmacist workload increased from filling fewer than 9 prescriptions per hour in 1992 to 14 prescriptions per hour by 2003.⁸ Aside from the sheer volume of prescriptions, community pharmacists are often interrupted by telephone calls from doctors or patients and questions from pharmacy support personnel or in-store customers. If a retail or mail order pharmacy offers any kind of adherence program, it is often limited in scope.

Helena Foulkes, senior vice president for health services at CVS Caremark, said that 33% of customers with new medications do not return for the first refill.⁹ Retail pharmacies battle this chronic non-adherence by using a variety of tools. Many employ interactive voice response applications targeted at various stages in the course of therapy. All pharmacies offer counseling for patients with new medications, although the majority of patients opt out of this service. Only 17% of customers at chain drug stores actually speak to the pharmacist when offered the opportunity.¹⁰ Additionally, many pharmacies utilize

PRACTICAL IMPLICATIONS

Any discussion of appropriate human immunodeficiency virus therapy must take into consideration the extent of the provided pharmacy services which can best achieve the goals of adherence and improved outcomes.

- Medication management strategies should address underlying causes of non-adherence, educate patients about their drug therapy, provide personal follow-up, and offer convenient reminder packaging.
- Incorporating a pharmacist-managed medication program into clinical practice may allow for the early identification of subjects destined to experience clinical failure resulting from poor adherence.
- Pharmacy benefit managers are urged to remove financial barriers that prevent patients from obtaining highly active antiretroviral therapy and the services of specially trained pharmacists.

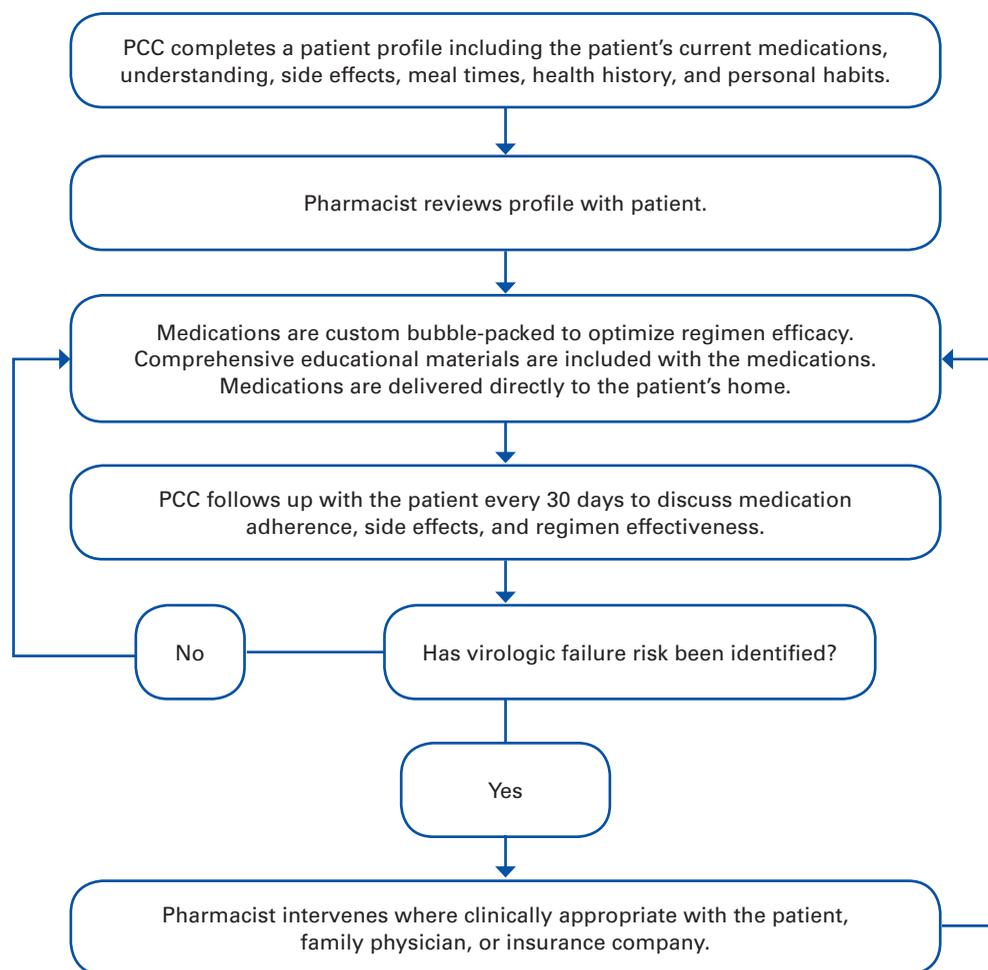
mailings to the patient as a medication refill reminder. A few select pharmacies conduct outreach calls to potentially non-adherent patients, although pharmacists may not be specifically trained in any 1 disease state.

Non-pharmacy healthcare providers also employ a variety of methods to address a patient's adherence. Physicians often use patient self-report as an initial indication of non-adherence and may offer additional information and education to those patients demonstrating adherence difficulties. Nurses, physician assistants, and case managers frequently use various interviewing techniques to identify those patients most at risk of medication nonadherence and may provide written educational materials and intensive counseling to confront the issue. Strategies that increase collaboration between patient and provider and include patient education have resulted in improved patient outcomes.¹¹ Health insurance payers have demonstrated that decreases in prescription drug copayments can increase medication compliance rates. One health plan's decrease in copayments for medications resulted in a 7% to 14% increase in compliance for 4 of 5 chronic medication classes.¹² Each member of the patient's healthcare team can play a significant role in contributing to a comprehensive adherence support system, although oftentimes they do not.

Design Overview

This was a cohort study analyzing pharmacy claims and patient laboratory data for patients with HIV/acquired immune deficiency syndrome who were served by HealthStat Rx Smyrna, Georgia, a pharmacy specializing in providing medications to homecare patients with chronic diseases. All patients utilizing HealthStat Rx pharmacy services were automatically opted into an enhanced pharmacy-care

Figure 1. Study Flow Diagram



PCC indicates patient care coordinator.

program. All patients for whom antiretroviral medication therapy was prescribed by 1 of 4 infectious disease specialists were included in this study (N = 75). Upon enrollment, patients were informed of the pharmacy-care program details and permission was secured for collection of personal data. The 4 infectious disease specialists were an integral part of correlating the patient's clinical response to the patient's adherence statistics. CD4 cell count and viral load values were collected from the patient's medical chart at time of admission into the pharmacy-care program and then again at the 6-month anniversary of program initiation. The CD4 count serves as the major clinical marker of immune function in patients who have HIV infection. It is the strongest predictor of subsequent disease progression and survival, according to clinical trials and cohort studies.¹⁵ A significant change between 2 tests is approximately a 30% change in the CD4 count. Data analysis was performed on all patients who had been receiving HAART

medications from the specialty pharmacy for at least 6 months. Data collection began with dates of service on June 8, 2004, and concluded with medication refill dates of service on February 22, 2008.

METHODS

Patients prescribed HAART therapy who chose to receive their medications from HealthStat Rx were automatically enrolled in an ongoing comprehensive pharmacist-managed care program. Because of the nature of the enhanced pharmacy-care program, it was not possible to blind either the participants or the clinical pharmacists involved. Patients were required to pay their pharmacy insurance medication copayments; however, there were no additional costs associated with the medication-management program services.

HealthStat Rx provided an enhanced care program consisting of an interview to identify HAART adherence

risk factors, measurement of initial CD4 counts and viral load, education regarding efficacy of HAART therapy, recommendations to optimize effectiveness of the personal regimen, and a minimum of 6 follow-up visits either in person or by telephone during the subsequent 6-month period. The flow of patients through the program is shown in **Figure 1**.

The foundation of the medication-management program is the education the clinical pharmacists have received on HIV treatment principles and current guidelines for use of antiretroviral therapy. Staff pharmacists treating HIV patients in this study were required to complete a combination of at least 20 live and home study hours of HIV pharmacotherapy continuing education per year. The pharmacist in charge overseeing this study was a certified HIV Pharmaceutical Care Specialist. These continuing education programs allow the specialty pharmacist to more comfortably interface with HIV patients as well as providers in their role as a clinician.

The clinical pharmacist's role in this consultation was to direct patients toward making the right choices to manage and improve their health. Patients began therapy with an educational foundation to set expectations for the treatment. The clinical pharmacist offered services to manage adverse drug reactions and medication side effects, evaluate the patient's ability to adhere to a prescribed medication regimen, and, in consultation with the physician, tailor drug regimens to accommodate specific patient needs. Pharmacists performed chart reviews for each patient to ensure complete and appropriate therapy. The chart reviews included all of the patient's disease states, not just the HAART regimen. The pharmacy focused on filling each patient's full set of prescription drug orders with the purpose of eliminating the possibility of incomplete pharmaceutical care recommendations.

After study enrollment, baseline interviews, and initial medication fill, the patient care coordinator conducted monthly telephone surveys to collect adherence data on the prescribed medication regimen. The patient care coordinator recorded any issues which might have affected the patient's medication adherence, the occurrence of side effects, and any changes in the patient's health, prescribed

Table. Demographic and Baseline Characteristics

Variable	All subjects (N = 64)
Gender, n (%)	
Male	26 (41)
Female	38 (59)
Race/ethnicity, n (%)	
Black	29 (45)
Hispanic	3 (5)
White	32 (50)
Age, y	
Mean (SD)	44.5 (10.7)
Range	25-71
Plasma HIV-1 RNA copies/mL	
Median	7890 (<50-535,720)
CD4 cell count, cells/mm ³	
Median (range)	259 (20-698)

CD4 indicates cluster of differentiation 4; HIV, human immunodeficiency virus; RNA, ribonucleic acid; SD, standard deviation.

therapy, or personal lifestyle. The survey concluded with the confirmation of medication supply on hand and the next scheduled medication delivery date. The clinical pharmacist reviewed each monthly survey prior to refill to identify and resolve any drug therapy problems.

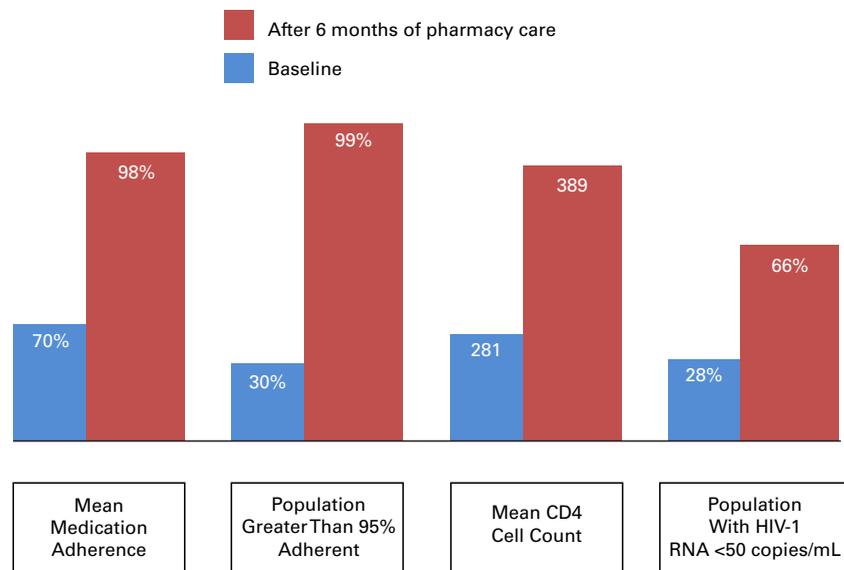
If intervention was necessary, the clinical pharmacist contacted the prescriber, provided clinical recommendations to solve the drug therapy problem identified, documented their activities, and followed up directly with the patient to ensure the problems were resolved. The process repeated every 30 days or more often, if necessary, and continued for as long as the patient remained in the program.

RESULTS

Enrolled in the pharmacy-care program were 75 patients from the selected infectious disease specialists; 11 patients did not meet the 6-month service requirement. Of these 11 patients, 4 could not afford to pay their copayments, 4 changed residences without forwarding contact information, 2 were forced to use a pharmacy benefit manager (PBM) mail-order pharmacy, and 1 patient expired.

A total of 64 patients participated in the study for at least 6 months and were included in the data analysis. The mean age of the study participant was 44.5 years and 59% of the participants were female (**Table**); 50% of the program participants were white, 45% were black, and 5% were Hispanic. The patients took a mean of 5.9 different daily chronic medications. The mean duration of HAART therapy prior to enrollment was 9.4 years. Of 64 patients, 4 were HAART treatment-naïve at time of enrollment. In

Figure 2. All Subjects (N = 64)



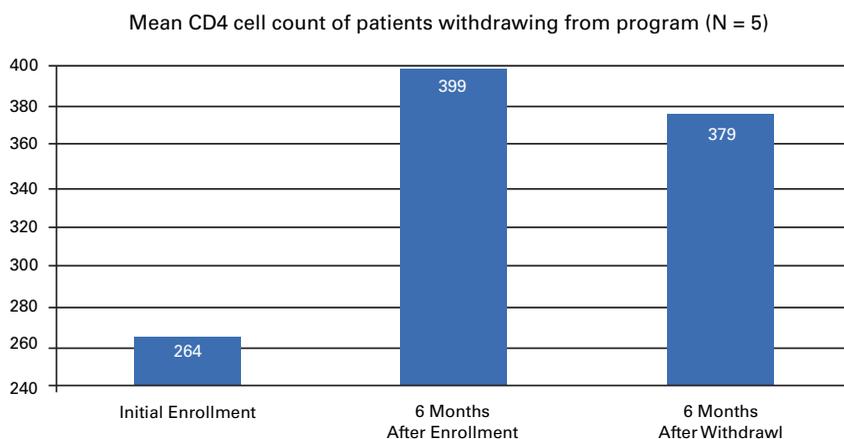
CD4 indicates cluster of differentiation 4; HIV, human immunodeficiency virus; RNA, ribonucleic acid.

total, 6048 doses of antiretroviral medications were dispensed over 44 months. The pharmacists and patient care coordinators logged 4480 exchanges. The most common of these were educating patients about their medications, resolving medication problems, reinforcing physician instructions to patients about their medications, reminding patients of the importance of adherence, and communicating with physicians.

Adherence and Outcomes

Mean medication adherence was calculated from the

Figure 3. Outcomes Improvement Did Not Persist in Those Patients Returning to Usual Pharmacy Care After Completion of 6 Months Enhanced Pharmacy Care



CD4 indicates cluster of differentiation 4.

medication possession ratio (MPR) (supplies of medication received relative to amount prescribed) by using prescription dispensing records from the specialty pharmacy. MPR has been widely used and validated as a proxy for drug adherence.¹⁴

Data analysis showed that medication adherence was increased by 28% over baseline. By a second measure, there was a 69% increase in patients who were at least 95% adherent to all medications; 95% represents the commonly applied definition of an acceptable level of adherence to HAART.^{6,7} In addition, mean CD4 cell count increased from 281 (cells/ μ L) to 389 (38% over baseline). Furthermore, the percentage of patients whose viral loads were considered undetectable (HIV-1 RNA

<50 copies/mL) increased from 28% to 66%. The complete results are summarized in **Figure 2**.

DISCUSSION

This study sought to investigate the effect of a comprehensive pharmacy-care program composed of clinical pharmacist education, intensive personal support, and blister-packed medications on medication adherence to HAART, and to associate this intervention with improved CD4 cell counts and viral loads. Our findings showed marked improvements in rates of medication adherence to levels consistently above 95%, increased CD4 counts, and decreased viral loads. In addition, our findings are consistent with other studies' conclusions that continued pharmacy involvement is a requirement for persistence of these changes.^{15,16} The positive effects on adherence quickly dissipated when the pharmacy-care program ended. From the original study group of 64 patients, 5 returned to retail/mail-order pharmacy after completion of at least 6 months of enhanced pharmacy care; 4 of these 5 patients (80%) had decreasing CD4 cell counts within 6 months of program withdrawal. See **Figure 3**.

Studies have demonstrated a direct association between annual per-patient expenditures and CD4 cell counts. Findings show that patients in the lowest CD4 cell count category (<50 cells/ μ L) expend up to 2.6 times more healthcare dollars per year than patients in the highest CD4 cell count category.¹⁷ Applying the overall healthcare costs formula from previous studies¹⁸ to the 64 patients in this study, the increase in CD4 cell count resulted in an overall healthcare savings of \$2929.00 per member per year. An illustration of the calculations is shown in **Figure 4**.

HIV, like many other diseases, progresses through clearly defined stages. Each stage of the disease, as determined by CD4 cell count and viral load status, is more expensive to treat than the previous stage. Current HIV clinical methodology is somewhat reactive in that clinicians will consider changing a patient's HAART regimen after the patient experiences virologic failure. It is an established fact that drug resistance and non-adherence are the 2 main causes of virologic failure. What's needed is a prevention plan that identifies virologic failure *risk* before it occurs. The comprehensive pharmacy-care program described in this study fulfills that prevention need. This program has been successful because of the pharmacist's comprehensive knowledge of medications and his/her ability to make an assessment of all the patient's medication.

Recommendations

Based on our experience and consistent with the recommendations of others,¹⁵ we suggest that medication-management programs should follow the strategy of addressing underlying causes of poor adherence, educating patients, providing personal follow-up, and promoting convenience through reminder packaging. In our experience, pharmacists are essential healthcare professionals in this process of evaluation and follow-up and vital members of the healthcare team approach to the problem of medication non-adherence.

As has been confirmed in other settings, patient self-reported adherence, the most commonly used adherence

Figure 4. Mean Costs of HIV Care in 2003 Stratified by CD4 Cell Count¹⁴

CD4 Stratum (cells/ μ L)	Applied to All Subjects (N = 64) Baseline	Applied to All Subjects After 6 Months of Pharmacy Care
<50 = \$57,565 per patient per year	5 Patients = \$287,825	2 Patients = \$115,130
50-200 = \$35,483	20 Patients = \$709,660	13 Patients = \$461,279
200-500 = \$26,848	29 Patients = \$778,592	32 Patients = \$859,136
>500 = \$21,869	10 Patients = \$218,690	17 Patients = \$371,773
Total cost of HIV care for 64 subjects	\$1,994,767	\$1,807,318
Mean cost per patient per year	\$31,168	\$28,239

CD4 indicates cluster of differentiation 4 cells; HIV, human immunodeficiency virus.

measure, seriously overestimates adherence to antiretroviral medications.¹⁹ If clinicians are relying on viral load and self-report to detect non-adherence, they are actually detecting non-adherence after it has occurred for some time. A measurement strategy that detects poor levels of adherence, which put patients at risk of virologic failure, should be used in routine clinical practice. By having a measure of adherence that is frequently updated, it is possible that clinicians could use this tool as an early warning system alerting them to their patients' non-adherence *before* virologic failure occurs.

An increasing number of HIV patients are not eligible for the clinical services described in this study because of tightening restrictions placed on them by their PBM. These patients are being forced to obtain their HIV medications from the PBM-contracted mail-order pharmacy. Obtaining medications from multiple pharmacies can result in incomplete medication therapy management. PBMs forcing patients to use mail order solely for the short-term cost-savings on the drugs may actually result in increased overall healthcare costs for the insurance carrier. Consequently, PBMs should consider: (1) removing any financial barriers that may prevent patients from obtaining their HAART medications (ie, eliminate patient co-pays), and (2) offering HIV-positive members several comprehensive pharmacy-care programs from which to choose.

The results of our patient-focused team approach to promote better patient adherence offers a number of lessons for the practice of pharmacy as well. The clinical pharmacist must interact directly with the patient to evaluate effectiveness of their HAART, offer guidance, and execute a thorough care plan. The personal relationship developed with the patient gives a clinical pharmacist the opportunity to ensure optimal outcomes and demonstrate their value to the healthcare system; therefore, we recommend that pharmacist-managed medication programs standardize their patient-care protocol, communicate with prescribers, and document their interventions to ensure consistency and quality.

CONCLUSIONS

Despite advances in the understanding of HIV infection and many new treatment options, maintaining adherence remains an integral part of disease management. It was theorized that ongoing pharmacist intervention would result in cost savings and would maintain a high level of adherence indefinitely. In this study, a comprehensive pharmacy-care program was associated with substantial and sustained improvements in medication adherence, CD4 cell counts, and viral loads among HIV patients receiving HAART. The improved pharmacy services were provided at no additional cost to the patient or the insurance carrier. Continued intervention is necessary and this project demonstrated that it is financially sustainable. Furthermore, the results support the conclusion that incorporating a pharmacist-managed medication program into clinical practice may allow for the early identification of subjects destined to experience virological failure because of poor adherence.

This enhanced pharmacist-care program provides 1 model of primary healthcare delivery that improves the management of patients taking HAART. Studies in many other settings have demonstrated that a pharmacy-care program led to clinically meaningful improvements in patients with high blood pressure, high cholesterol, diabetes, and asthma. Healthcare professionals, health system administrators, government agencies, and policy makers all might consider emphasizing the importance of pharmacists in promoting medication adherence for the reduction of healthcare costs and the prevention of chronic-disease progression.

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