RESEARCH

Evaluation of the First Year of a Pilot Program in Community Pharmacy: HIV/AIDS Medication Therapy Management for Medi-Cal Beneficiaries

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ABSTRACT

BACKGROUND: The advent of combined antiretroviral therapy (ART) has increased treatment effectiveness but created new challenges for patients infected with human immunodeficiency virus (HIV) and for community pharmacists managing patients' drug therapy. The ability of pharmacist-provided medication therapy management (MTM) services to increase medication adherence, improve health outcomes, and reduce overall medical costs has been demonstrated in community pharmacies for chronic diseases such as diabetes and hypertension. However, the effectiveness of pharmacist-provided MTM services in HIV/acquired immune deficiency syndrome (AIDS) has not been well studied. In January 2005, a pilot program to evaluate MTM services for patients with HIV/AIDS began in California, allowing 10 HIV/AIDS specialty pharmacies to receive compensation for the MTM services that they provided to HIV/AIDS patients.

OBJECTIVES: To examine the first year of the HIV/AIDS pharmacy MTM compensation pilot program, which described and compared pilot and non-pilot pharmacies with respect to (a) patient characteristics; (b) intermediate outcomes including type and number of ART medication regimens used, rates of adherence and excess medication fills for ART, use of contraindicated ART regimens, and occurrence of opportunistic infections; and (c) pharmacy and medical costs.

METHODS: This was a cohort study examining 2005 Medi-Cal pharmacy and medical claims data for patients with HIV/AIDS who were served by pilot pharmacies versus other pharmacies. The HIV/AIDS patients were Medi-Cal beneficiaries aged 18 years or older as of January 1, 2005, who were continuously enrolled from January 1, 2004, through December 31, 2005, and diagnosed with HIV/AIDS, identified by receipt of at least 1 ART prescription and at least 1 medical claim with a diagnosis (primary or secondary) of HIV/AIDS (ICD-9-CM code 042.0) during both the index period (the year before pilot program implementation, 2004) and the intervention period (the study year, 2005). The only difference in the inclusion criteria for the 2 cohorts was that the pilot pharmacy patients were required to have filled 50% or more of their antiretroviral prescriptions in 2005 at 1 of the 10 pilot pharmacies. Adherence was defined as a medication possession ratio (MPR) of 80%-120% and excess medication fills as MPR greater than 120%. Comparisons were made between groups using bivariate statistics (Pearson chi-square for categorical variables and t-tests for continuous variables). For comparisons of costs, generalized linear models assuming a gamma distribution and log link function were used; predictor variables for the models included age, gender, race/ethnicity, and dual coverage under Medicare.

RESULTS: A total of 7,018 HIV/AIDS patients in the Medi-Cal population were identified as meeting the study criteria. Of these, 19.3% (n=1,353) were pilot pharmacy patients. The demographic profile of pilot pharmacy patients was similar, but not identical, to that of patients receiving medications at other pharmacies. A larger percentage of pilot pharmacy patients were on protease inhibitor-based ART medication regimens (63.8% vs. 54.8%, $P<0.001$), remained on a single type of ART therapy throughout the study year (56.8% vs. 34.2%, $P<0.001$), and were classified as adherent (56.3% vs. 38.1%, $P<0.001$), compared with other pharmacy patients. Fewer pilot pharmacy patients used contraindicated regimens (11.6% vs. 16.6%, $P<0.001$) or had excess medication fills (19.7% vs. 44.8%, $P<0.001$). The rate of opportunistic infections did not differ significantly between groups (28.2% vs. 26.1%, $P=0.121$). The total mean (standard error) annual health care cost per patient was 10% higher in pilot pharmacies than in other pharmacies ($40,596 [$889] vs. $36,937 [$479], $P=0.001$); driven by use of (a) medications (primarily non-ART medications) and (b) mental health services. Payment from the California Department of Health Care Services for MTM services averaged $1,014 per pilot pharmacy study patient.

CONCLUSION: Study findings for the first year of the MTM program suggest that the pilot pharmacy patients received more appropriate HIV treatment. The degree to which these differences are affected by self-selection of patients into the pilot pharmacies is unknown. Longer-term outcomes and costs of the pilot program will be examined when data for subsequent years are available.

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What is already known about this subject

- The only 2 published studies related to pharmacist-provided MTM services in HIV/AIDS patients both concluded that pharmacist-led interventions had a positive effect on clinical outcomes. However, these studies were small and based in specialized HIV clinics, not community pharmacies.
- A chart review study demonstrated improved medication adherence (refilling prescriptions on average every 31 vs. 50 days) and a significantly greater reduction in viral load at 6 and 12 months after initiating therapy (both comparisons $P<0.05$) for patients with HIV/AIDS who attended a pharmacist-led medication adherence clinic (n=80) than for patients not attending.
- A prospective study of patients (n=34) attending a pharmacist-managed drug optimization clinic reported significant improvement from baseline in CD4+ T-lymphocyte counts (mean [SD] improvement 54 [78] cells per cubic millimeter [mm^3], $P<0.001$) and viral loads (mean reduction 1.02 $\log_{10}$ copies per milliliter [mL], $P=0.004$). However, that study lacked a comparison group.
- Larger studies using pharmacy records have demonstrated that improved adherence was correlated with reduced viral load; for example, for each 10% increase in adherence rate, viral load decreased by 0.12 $\log_{10}$ copies per mL (95% confidence interval [CI] = 0.01-0.23 $\log_{10}$ copies per mL), and when adherence fell below 95%, the percentage of patients with viral load below 400 copies per mL fell below 60%.

What this study adds

- To our knowledge, this is the first large-scale evaluation of an MTM program in HIV/AIDS patients.
- Among Medi-Cal patients diagnosed with HIV/AIDS and using ART, patients of pilot MTM pharmacies (those filling 50% or more of their ART prescriptions at pharmacies that were reimbursed for MTM services) were more likely to use protease inhibitor-based ART medication regimens (63.8% vs. 54.8%, $P<0.001$) and to remain on a single type of ART regimen throughout the study year (56.8% vs. 34.2%, $P<0.001$), compared with patients using other pharmacies.
- More pilot pharmacy patients were classified as adherent (56.3% vs. 38.1%, $P<0.001$) and fewer pilot pharmacy patients were on contraindicated regimens (11.6% vs. 16.6%, $P<0.001$), compared with other pharmacy patients. However, the rate of opportunistic infections did not differ significantly between groups (28.2% vs. 26.1%, $P=0.121$) during the study year.
- The total mean [SD] annual health care cost per patient was 10% higher in pilot pharmacies ($40,596 [$889] vs. $36,937 [$479], $P=0.001$); driven by use of medications (primarily non-ART medications) and mental health services.

The advent of combined antiretroviral therapy (ART) has increased treatment effectiveness but created new challenges for patients infected with human immunodeficiency virus (HIV) and for community pharmacists managing patients' drug therapy. Combined ART generally consists of 3 or more HIV drugs taken together from at least 2 of the 3 main drug classes; protease inhibitors (PI), nonnucleoside reverse transcriptase inhibitors (NNRTI); and nucleoside or nucleotide reverse transcriptase inhibitors (N(t)RTI).[1] Because the virus can develop resistance against any 1 drug given alone, at least 3 or more drugs, usually from 2 or more different classes, must be used at the same time. Treatment regimens containing a PI are typically among the most potent and/or durable against the virus, but often have the least tolerable side effects. Complex ART regimens contain multiple drugs with various dosing schedules, undesirable side effect profiles, and different storage requirements for many of the medications.[2] Strict adherence to HIV drug therapy has been shown to be crucial to achieving optimal therapeutic outcomes such as reduced viral load, reduction of drug resistance, and improved survival.[3-5]

The potential of pharmacist-provided medication therapy management (MTM) services to increase medication adherence, improve health outcomes, and reduce overall medical costs has been demonstrated in community pharmacies for chronic diseases such as diabetes and hypertension.[6,7] However, the effectiveness of pharmacist-provided MTM services in HIV/acquired immune deficiency syndrome (AIDS) has not been well studied. A review of the literature found only 2 studies that described the type of MTM services provided by a pharmacist and assessed outcomes. Both studies were conducted in HIV outpatient clinics. The first, a chart review study, demonstrated improved medication adherence (refilling prescriptions on average every 31 vs. 50 days, $P<0.05$) and a significantly greater reduction in viral load at 6 and 12 months ($P<0.05$) after initiating therapy for patients attending a pharmacist-led medication adherence clinic and at least 1 educational session from the clinical pharmacist (n=80) versus those not attending (n for comparison group not reported).[8] The second, a prospective study of patients (n=34) who had an extensive history of treatment and attended a pharmacist-managed drug optimization clinic, reported significant improvement from baseline in CD4+ T-lymphocyte counts (mean [SD] improvement 54 [78] cells per cubic millimeter [mm^3]; $P<0.001$) and viral loads (mean reduction 1.02 $\log_{10}$ copies per milliliter [mL]; $P=0.004$).[9] A significant decrease in the mean drug-related toxicity score was also observed among patients experiencing drug-related toxicities (n=25, mean [SD] reduction of 1.0 [0.8] on the 4-point Radiation Therapy Oncology Group common toxicity scale, $P<0.001$). However, that study lacked a comparison group.

Although not including a MTM services component, several studies have shown significant correlation between improved medication adherence, as measured by pharmacy data, and reduced viral load.[10-12] For example, Grossberg et al. reported that, for each 10% increase in adherence rate, viral load decreased by 0.12 $\log_{10}$ copies per mL (95% confidence interval=0.01-0.23 $\log_{10}$ copies per mL) and Fairley et al. reported that, when adherence fell below 95%, the percentage of patients with viral load consistently below 400 copies per mL fell below 60%.[11,12] It is reasonable to expect that the provision of MTM services would increase adherence, as it has in other disease states, and thus reduce viral load. However, barriers to the delivery of specialized counseling services to enhance adherence in HIV/AIDS patients in community pharmacy settings have also been recognized. For example, in a statewide survey of pharmacists in North Carolina, 59% of community pharmacist respondents indicated that they did not have enough time to provide adherence counseling to their HIV/AIDS patients.[13]

Pilot Program Description

In January 2005, a pilot program to compensate and evaluate community pharmacy-based MTM services for patients with HIV/AIDS began in the state of California. This program, under Welfare and Institutions Code Section 14199-14199.3, allowed 10 HIV/AIDS specialty pharmacies in the state to receive compensation for the MTM services that they provided to HIV/AIDS Medi-Cal patients. The California Department of Health Care Services (DHCS) provided pilot pharmacies $9.50 per prescription dispensed to a Medi-Cal beneficiary for the 3-year term of the pilot program. The DHCS selected the 10 pilot pharmacies based on the requirements of the legislation authorizing the pilot.[14] The first 10 pharmacies that applied and met the following criteria

were selected: (a) patient population comprising 90% or more of persons with HIV/AIDS, (b) had the ability to immediately provide specialized services rendered by a qualified pharmacist or other health care provider operating within his or her scope of practice, and (c) had pharmacists and other qualified health care providers to identify patients who should receive MTM services. Specialized services were defined as being distinct from generalized patient education and information activities already required by law and provided for in the professional dispensing fee. These services (a) were to be patient specific and individualized services provided directly by a pharmacist to the patient or, in limited circumstances, the patient's caregiver, and (b) involved face-to-face interaction between the patient or caregiver and the pharmacist during delivery of MTM services. The possible types of MTM services outlined in the legislation were based on the definition of MTM services published by the American Pharmacists Association.[15] Patients of pilot pharmacies chose to patronize pilot pharmacies either through their own selection process and/or based on physician referral; these decisions were made independent of this study.

Following up on previous work suggesting a potential impact of pharmacist-provided MTM services on adherence and viral load in HIV/AIDS patients who were treated in the community setting,[8,9] the California HIV/AIDS pharmacy MTM services pilot program provided an opportunity to investigate a broader range of outcomes using a larger sample of patients with HIV/AIDS. The California study examined patients receiving care at pharmacies providing a wide range of MTM services and compared their outcomes with those of similar patients at other pharmacies throughout the state.

Study Objectives

The purpose of this study was to examine the first year of the HIV/AIDS pharmacy MTM services compensation pilot program. The study used pharmacy and medical claims data to describe and compare patients filling prescriptions at pilot (MTM) versus other pharmacies with respect to (a) patient characteristics; (b) intermediate outcomes, including the number and type of ART medication regimens, rates of adherence and excessive fills, use of contraindicated ART regimens, and occurrence of opportunistic infections; and (c) pharmacy and medical costs.

Methods

Description of the Intervention

The intervention in this study was participation in the DHCS compensation pilot program for MTM services. The program required that participating pharmacies be able to immediately offer MTM services; therefore, pharmacies selected for the pilot compensation program had been offering a range of MTM services before participating. Although the specific services that each pilot pharmacy must provide were not defined, all pilot pharmacies offered services to (a) manage adverse drug reactions and medication side effects; (b) evaluate patient ability to adhere to medication regimens, in consultation with physicians and case managers; and (c) tailor drug regimens to accommodate specific patient needs.[16] Each pharmacy worked with patients and/or their physicians according to their own practice norms, and further details were not available to the researchers.

Outcome Measures

Provision of MTM services in pilot pharmacies was expected to (a) improve adherence to ART regimens, (b) result in more rational ART medication strategies (e.g., fewer contraindicated regimens, fewer medication changes per year which can decrease likelihood of developing drug resistance), (c) decrease occurrence of opportunistic infections, and (d) reduce costs through more rational medication usage and reduced need for medical services. Ten outcome measures were assessed (Table 1).

Study Design and Patient Selection

This was a cohort study examining 2005 Medi-Cal pharmacy and medical claims data for patients with HIV/AIDS served by pilot pharmacies versus other pharmacies. All study procedures were approved by the University of California San Diego and the DHCS Human Research Protection Programs. The study group, pilot pharmacy HIV/AIDS patients, consisted of Medi-Cal beneficiaries aged 18 years or older as of January 1, 2005, who were continuously enrolled from January 1, 2004, through December 31, 2005, and diagnosed with HIV/AIDS, identified by receipt of at least 1 prescription for ART and at least 1 medical claim with an HIV/AIDS-related diagnosis (primary or secondary) *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 042.0 during both the index period (from January 1 through December 31, 2004) and the study period (from January 1 through December 31, 2005). The ART medications are shown in Appendix A.

Patients were identified as pilot pharmacy patients if they had filled 50% or more of their ART prescriptions in 2005 at 1 of the 10 pilot pharmacies. Comparison group patients met the same inclusion and exclusion criteria as study patients, except that they were not identified as having filled 50% or more of their ART prescriptions in 2005 at 1 of the 10 pilot pharmacies. Individuals enrolled in managed care plans were excluded because paid claims are not generated for Medi-Cal participants enrolled in managed care.

Data Analysis

Descriptive statistics were calculated for all variables. Frequency distributions were used to describe categorical variables, and means, medians, standard deviations, and ranges were used for continuous variables. Gender, dual coverage under Medicare, race/ethnicity, ART adherence and ART medication category were expressed as percentages, and differences between groups (pilot versus other pharmacy patients) were assessed using the Pearson

TABLE 1 Outcome Measures (2005)

Variable	Description
Number of pharmacy visits	Number of days patient visited pharmacy to fill ART prescription or prescriptions
ART adherence level (MPR)	MPR = ∑ number days supply ART for year / 365.25 days Nonadherent: MPR < 50% Partially adherent: MPR 50% - 79% Adherent: MPR 80% - 120% Excess fills: MPR > 120% Calculated using medication with highest days supply on day when multiple prescriptions were filled to avoid double counting of days
ART medication regimen strategy	Categories are mutually exclusive and are assigned the therapy with the greatest number of days supplied during the year (see drug list in Appendix A) - Only 1 N(t)RTI - Multiple N(t)RTI - N(t)RTI + NNRTI - N(t)RTI + PI ± NNRTI
Contraindicated ART regimen[a]	- amprenavir + fosamprenavir - atazanavir + indinavir - zalcitabine in regimen - emtricitabine + lamivudine - stavudine + zidovudine - didanosine + stavudine - saquinavir alone - Only a single class NRTI/NtRTI regimen - Only mono or dual therapy with NRTI/NtRTI - Only triple therapy NRTI/NtRTI - except if abacavir + zidovudine + lamivudine or tenofovir + zidovudine + lamivudine
Number of ART medication regimen strategies	Number ART regimen strategies = ∑ regimen strategies - Regimen strategies: each prescription fill categorized as a single ART, multiple ART, NNRTI, or protease inhibitor regimen strategy - Regimen strategies counted only once: (e.g. if patient switched from single ART to NNRTI and back to ART, number of regimen strategies = 2)
Opportunistic infection	See list in Appendix B
Total medication cost	Paid claims amount for all prescription medications
ART medication cost	Paid claims amount for antiretroviral therapy medications (single agent or in combination)
Non-ART medication cost	= Total medication cost − ART medication cost
Medical costs[b]	Paid claims amounts for: Inpatient Hospital outpatient (includes emergency department) Outpatient Mental health Laboratory/X-ray AIDS Waiver Program[c]

[a] *DHHS Panel on Antiretroviral Guidelines for Adult and Adolescents (2008).*[21]

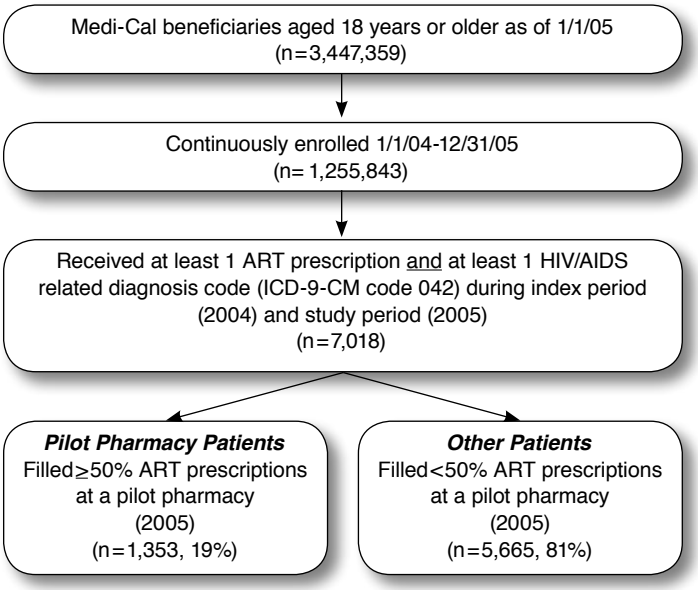
[b] *Medical costs were assigned to service categories using codes indicating type of service (i.e., Medi-Cal vendor codes).*

[c] *Under contract with the Department of Health Care Services agencies to provide home and community-based services as an alternative to nursing facility care or hospitalization.*

ART = antiretroviral therapy; MPR = medication possession ratio; N(t)RTI = nucleoside or nucleotide reverse transcriptase inhibitors; NNRTI = non-nucleoside reverse transcriptase inhibitors; PI = protease inhibitor.

chi-square test. Age and number of pharmacy visits to fill ART prescriptions were expressed as means, and differences between groups were assessed using t-tests. Differences in costs were analyzed using generalized linear models assuming a gamma distribution and log link function; predictor variables for the models included age, gender, race/ethnicity, and dual coverage under Medicare.[17,18] Standardized estimates of costs were calculated for pilot and nonpilot pharmacies. Standard errors were calculated using the nonparametric bootstrap, and *P* values were calculated using the percentile method. DHCS payments to pilot pharmacies, $9.50 per prescription dispensed for any medication (not just ART drugs), were not included in the cost estimates and are presented separately. Statistical significance was set at $P<0.05$. All statistical analyses were performed using Stata version 9.2 (Stata Corp., College Station, TX).

FIGURE 1 Patient Selection From Medi-Cal Claims Database



ART = antiretroviral therapy; HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Results

Medi-Cal HIV/AIDS Patients (Pilot and Other Pharmacy Patients Combined)

The study population consisted of 7,018 patients meeting the study inclusion criteria (Figure 1). Patients had a mean (SD) age of 46.5 (8.8) years, were predominantly male (80.1%), and slightly more than one-half (53.3%) had dual coverage with Medicare during 2005. The largest proportion of patients was white (46.2%), with African-American and Latino patients comprising 25.9% and 19.5% of the population, respectively.

The mean (SD) number of pharmacy visits to fill ART prescriptions during 2005 was 14.4 (8.0). More than 80% of fills were for a 30-day supply. Approximately 18% of patients were either nonadherent or only partially adherent to their ART medications. Almost equal proportions were adherent (41.6%) or had excess fills (40.0%). When classified by the type and number of ART medications received, the largest percentage (56.5%) of patients were taking a PI-based regimen (N(t)RTIs + PI ± NNRTI). The remainder of patients were on regimens not containing a PI; an NNRTI-based regimen (N(t)RTIs + NNRTI) (29.9%) or less potent multiple N(t)RTIs (11.4%). A small percentage (2.2%) of patients were on a single N(t)RTI, a treatment strategy that is not recommended.

Total annual medication cost per patient averaged (SD) $25,254 ($18,692). The largest proportion of total medication cost was for ART, which averaged $16,195 ($8,217) per patient. The difference between total and ART cost was attributable to non-ART outpatient medications.

TABLE 2 HIV/AIDS Patient Demographics (2005)

	Pilot Pharmacies	Other Pharmacies	*P* Value[a]
Number of pharmacies	10	2,103	N/A
Number (%) study patients	1,353 (19.3)	5,665 (80.7)	N/A
Mean [SD] (range) age in years	46.0 [8.9] (18-77)	46.7 [8.7] (18–87)	0.016
Number (%) male	1,032 (76.3)	4,589 (81.0)	<0.001
Number (%) dual Medicare coverage[b]	657 (48.6)	3,059 (54.4)	<0.001
Race/ethnicity number (%)			
Non-Latino White	603 (44.6)	2,637 (46.5)	0.189
African American	398 (29.4)	1,426 (25.2)	0.001
Latino	238 (17.6)	1,128 (19.9)	0.050
Other race/ethnicity	114 (8.4)	474 (8.4)	0.944

[a]*P value for Pearson chi-square test for categorical variables (sex, Medicare coverage, and race/ethnicity) and t-test for age.*
[b]*Patients also had Medicare coverage for at least 1 month during the year.*
HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome.

Pilot Versus Other Pharmacy Patients

Approximately 20% of the study population received the majority of their prescription medications at a pilot pharmacy in 2005 (Table 2). Compared with nonpilot pharmacy patients, pilot pharmacy patients were slightly younger (mean 46.0 vs. 46.7 years, P=0.016). The proportion of pilot pharmacy patients who were male (76.3%) or had dual Medicare coverage (48.6%) was less than in the nonpilot pharmacy group (81.0% and 54.4%, respectively; P<0.001). The pilot pharmacy group had a larger proportion of African-American patients, compared with the nonpilot group (29.4% vs. 25.2%, respectively; P=0.001), and a smaller percentage of Latino patients (17.6% vs. 19.9%, respectively; P=0.050).

Patients of pilot pharmacies had a greater mean [SD] number of pharmacy visits to fill ART prescriptions, compared with nonpilot pharmacy patients (15.4 [10.5] vs. 14.1 [7.3], respectively; P<0.001); however, the median number of visits was 13 in both groups (Table 3). Comparing patients in the pilot pharmacy group with those served by other pharmacies, the percentage of patients classified as adherent was significantly greater (56.3% vs. 38.1%, P<0.001) and the percentage of patients with excess fills was much smaller (19.7% vs. 44.8%, P<0.001). A significantly greater number of pilot pharmacy patients were classified as nonadherent or partially adherent, compared with other pharmacy patients, although the magnitude of difference was 4 percentage points or less (P<0.001).

A significantly greater percentage of pilot pharmacy patients

TABLE 3 Prescription Medication Use in 2005

	Pilot Pharmacies (n = 10)	Other Pharmacies (n = 2,103)	*P* Value[a]
Number of patients	1,353	5,665	
Pharmacy visits with ART prescriptions[b] Mean [SD] median (range)	15.4 [10.5] 13 (1 – 62)	14.1 [7.3] 13 (1 – 101)	< 0.001
Number (%) of patients by category			
ART adherence level			
Adherent (MPR 80% - 120%)	762 (56.3)	2,157 (38.1)	< 0.001
Partially adherent (MPR 50%-79%)	158 (11.7)	443 (7.8)	< 0.001
Non-adherent (MPR < 50%)	166 (12.3)	525 (9.3)	0.001
Excess fills (MPR > 120%)	267 (19.7)	2,540 (44.8)	< 0.001
ART medication regimen strategies			
Only 1 N(t)RTI	13 (1.0)	138 (2.4)	0.001
Multiple N(t)RTI	120 (8.9)	681 (12.0)	0.001
N(t)RTI + NNRTI	357 (26.4)	1,743 (30.8)	0.002
N(t)RTI + PI ± NNRTI	863 (63.8)	3,103 (54.8)	< 0.001
Used at least 1 contraindicated ART regimen	157 (11.6)	943 (16.6)	< 0.001
Count of ART medication regimen strategies used			
1 strategy	768 (56.8)	1,938 (34.2)	< 0.001
2 strategies	439 (32.4)	2,372 (41.9)	
3 or more strategies	146 (10.8)	1,355 (23.9)	
At least 1 opportunistic infection	381 (28.2)	1,478 (26.1)	0.121

[a]*P values for Pearson chi-square test for categorical variables and t-test for continuous variables.*

[b]*Number of visits that included the filling of at least 1 ART prescription.*

ART = antiretroviral therapy; MPR = medication possession ratio; N(t)RTI = nucleoside or nucleotide reverse transcriptase inhibitors; NNRTI = nonnucleoside reverse transcriptase inhibitors; PI = protease inhibitor; SD = standard deviation.

TABLE 4 Generalized Linear Model Analyses: Pharmacy and Medical Cost Per Patient in 2005 Standardized to the Underlying Population Characteristics

Mean [SE] cost ($)	Pilot Pharmacies	Other Pharmacies	*P* Value[a]
Total medication cost	27,816 [538]	24,651 [234]	<0.001
ART medication cost	16,657 [212]	16,087 [112]	0.022
Non-ART medication cost	11,142 [432]	8,565 [205]	<0.001
Inpatient cost	5,561 [585]	5,698 [338]	0.855
Hospital outpatient cost	459 [47]	472 [20]	0.769
Outpatient cost	1,119 [54]	1,046 [26]	0.203
Mental health cost	686 [57]	467 [26]	0.002
Laboratory and X-ray cost	211 [20]	194 [7]	0.455
AIDS	1,472 [99]	1,354 [41]	0.251
Other	3,299 [188]	3,091 [94]	0.380
Total	40,596 [889]	36,937 [479]	0.001

[a]*Deviance statistics not shown; these are available from the author upon request.*

AIDS = acquired immune deficiency syndrome; ART = antiretroviral therapy; SE = standard error.

(63.8%) were on a PI-based ART regimen (N(t)RTIs + PI ± NNRTI), compared with other pharmacy patients (54.8%), *P*<0.001 (Table 3). The percentage of pilot pharmacy patients on less potent combination regimens was significantly smaller for each category as compared with other pharmacy patients. A significantly smaller percentage of pilot pharmacy patients (1.0%) were on the nonrecommended single N(t)RTI treatment strategy, compared with other pharmacy patients (2.4%; *P*<0.001).

A smaller percentage of pilot pharmacy patients were on contraindicated ART regimens as compared with other pharmacy patients (11.6% vs. 16.6%, respectively; *P*<0.001) (Table 3). Identified contraindications included all of those screened (Table 1), except that no patients had stavudine plus zidovudine, or saquinavir as a single agent. Pilot pharmacy patients were also significantly less likely to change their medication regimen strategy compared with patients in other pharmacies (*P*<0.001). For example, 56.8% of pilot pharmacy patients were able to remain on one ART regimen strategy throughout the year, compared with only 34.2% of other pharmacy patients. Almost one-quarter of other pharmacy patients used 3 or more regimen strategies during the study year, compared with only 10.8% of the pilot pharmacy patients. No significant difference in the number of patients experiencing opportunistic infections was detected between pilot and other pharmacy patients (*P*=0.121).

The mean (standard error [SE]) total medication cost per patient was greater in the pilot group ($27,816 [$538]) than in the other pharmacy group ($24,651 [$234]), *P*<0.001, Table 4). This difference was largely attributable to a 30% greater cost for non-ART medications ($11,142 [$432] vs. $8,565 [$205], respectively; *P*<0.001) and less attributable to a small difference in ART medication cost ($16,657 [$212] vs. $16,087 [$112], respectively; *P*=0.022). Examination of expenditures for a subset of non-ART medications (medication categories with costs exceeding $500 per patient in 2005 in either the pilot or other pharmacy group) revealed that pilot pharmacy patients had appreciably higher annual costs for several therapeutic categories, compared with other pharmacy patients—for example, analgesics, gastrointestinal agents (primarily antiemetics), and blood products (Table 5). The pilot pharmacy patients also had significantly higher mental health medical services costs per patient than did the other pharmacy patients ($686 [$57] vs. $467 [$26], respectively, *P*=0.002; Table 4). No other medical cost differences were statistically significant. Higher medication (non-ART and ART) and mental health services resulted in a higher average total cost per patient in the pilot pharmacy group ($40,596 [$889]) than in the other pharmacy group ($36,937 [$479], *P*=0.001).

TABLE 5 Selected Non-ART Medication Costs Per Patient by Therapeutic Category - (2005)[a]

Mean [SD] Median Cost	Pilot Pharmacies	Other Pharmacies	Difference (%) Pilot vs. Other	*P* Value[b]
Analgesics	$1,902 [8,287] 34	$670 [2,842] 19	$1,232 183.9%	<0.001
Gastrointestinal (e.g., antiemetic/antivertigo, gastric acid secretion reducers)	$1,860 [4,816] 77	$1,285 [3,618] 41	$575 44.7%	<0.001
Blood (e.g., hematinics, heparin)	$851 [4,270] 0	$594 [3,246] 0	$257 43.3%	0.014
Psychotherapeutic drugs (e.g., antipsychotics, atypical, dopamine, serotonin antagonists)	$1,177 [2,194] 204	$993 [2,123] 100	$184 18.5%	0.004
Anticonvulsants	$569 [1,278] 0	$482 [199] 0	$87 18.0%	0.018
Anti-infectives/miscellaneous	$1,367 [4,069] 107	$1,179 [3,960] 104	$188 15.9%	0.119
Hormones	$606 [2,436] 0	$704 [3,261] 0	($98) -13.94%	0.294

[a]*Categories exceeding $500 per patient in 2005 in either pilot or other pharmacy group.*
[b]*Assessed using t-test.*
ART = antiretroviral therapy.

In addition, the California DHCS paid $2,730,053 to pilot pharmacies for MTM services provided in 2005 to all Medi-Cal beneficiaries using these pharmacies (n=14,896 patients [including 1,353 study patients] with 287,374 prescription claims; $9.50 × 287,374 prescription claims). The average annual DHCS payment per Medi-Cal beneficiary using pilot pharmacies was $183.27 ($2,730,053 per 14,896 unduplicated Medi-Cal beneficiaries in the pilot pharmacies in 2005). Considering study patients only, the average annual DHCS payment for MTM services per pilot pharmacy study patient was $1,014 ([144,352 prescription claims × $9.50] per 1,353 study patients).

Discussion

This article describes the initial evaluation of a novel community pharmacy-based MTM compensation program for patients enrolled in Medi-Cal and diagnosed with HIV/AIDS. To our knowledge, this is the first large-scale MTM program and evaluation of its kind in patients with HIV/AIDS. The results showed that a larger percentage of pilot pharmacy patients were on PI-based ART medication regimens. Although these regimens often have more side effects, pilot pharmacy patients had a greater adherence rate and fewer ART regimen changes than did nonpilot pharmacy patients. Fewer pilot pharmacy patients were on contraindicated regimens or had excess medication fills. The rate of opportunistic infections did not differ significantly between groups. The total annual cost per patient was 10% higher in pilot pharmacies. The difference was attributable to higher medication costs (largely non-ART) and greater use of mental health services by pilot pharmacy patients. Payment from California DHCS for MTM services averaged $1,014 per pilot pharmacy study patient ($183 per patient considering all patients using pilot pharmacies).

The greater percentage of adherent patients in pilot pharmacies is consistent with findings from the Cantwell-McNelis and James (2002) study of HIV/AIDS patients attending a pharmacist-led medication adherence clinic that demonstrated improved medication adherence and decreased viral load for patients attending the clinic over a 1-year period versus those not attending.[8] Although our study was not able to include clinical outcomes (e.g., viral load) it would be reasonable to expect that the improved adherence observed in pilot pharmacy patients will translate to improved clinical outcomes given the results of large studies using pharmacy records that have demonstrated that improved adherence is correlated with reduced viral load.[10-12]

In the present study, the age, gender, and race/ethnicity mix of the entire study population of HIV/AIDS Medi-Cal patients was fairly similar to that observed in 2 studies of California HIV/AIDS patients; one (Purdum et al., 2004) described the HIV/AIDS population of Kaiser California and another an HIV/AIDS nurse case-management program with pharmacy support in the inner city of San Francisco.[19,20] Thus, our overall study population appears to be similar to that in California. In the present study, the pilot pharmacy group was slightly younger, had a lower percentage of males and Medicare dual-eligible patients, and a higher percentage of African-American patients than did the cohort of patients filling ART prescriptions at other pharmacies. Although these differences were statistically significant the magnitude of difference for each was small. Therefore, the demographic profile of HIV/AIDS patients receiving medications at pilot pharmacies was generally similar to that of HIV/AIDS patients receiving medications at nonpilot pharmacies across the state.

The proportion of patients experiencing opportunistic infections during this study year was low, and similar, for both groups.

The proportion of patients who were partially adherent or nonadherent in both groups is troublesome because these patients are at greater risk of developing resistance that could affect their longer-term therapy options. Future evaluation will investigate if the rates of opportunistic infections and nonadherence change during the subsequent 2 years of the pilot program.

One finding deserves special emphasis. The majority of pilot pharmacy patients remained on a single type of medication regimen strategy for the year studied, compared with patients of other pharmacies, who changed their medication regimen type more often. Even though combined ART treatment has proven effective against HIV, one of the key limitations is that the virus becomes resistant to the available drugs. The more drugs and the more drug classes that a patient is exposed to increases the likelihood of developing drug resistance. Patients who need to switch regimens often (either due to lack of efficacy or intolerance or inability to manage side effects) are essentially exhausting their future treatment options and will not remain as healthy or live as long as patients who are successful on a single regimen for as long as possible. Because the pilot pharmacy patients were able to use and stay on a potent PI-based regimen more often than the patients filling ART prescriptions at other pharmacies, the expectation is that the pilot pharmacy patients will maintain their health and live longer.

The average total cost per patient in the pilot pharmacy group was approximately 10% greater than in the other pharmacy group. Medi-Cal was the only payer in the study; therefore reimbursement rates for services and products were equal between groups (although minor variation can occur because of differences in claim amounts submitted). Thus, differences in expenditures reflected differences in utilization rates or mix of products and services. The higher cost was attributable to greater utilization of medications (largely non-ART) and mental health services.

Although statistically significant, the magnitude of difference in average ART medication cost per patient between pilot and other pharmacies was small, $570 per patient per year (3.5%). However, pilot-pharmacy patients had a greater number of pharmacy visits to fill prescriptions and higher total medication cost due mostly to non-ART medication usage. Pilot patients used more antiemetics, analgesics and anticonvulsants. These medications are commonly used in HIV/AIDS patients to treat side effects of ART medications such as nausea and pain of peripheral neuropathy. This finding is consistent with that of March et al. who reported a positive effect of pharmacist MTM services on medication side effects, expressed in their study as a reduction in drug-related toxicities.[9] In addition to treating side effects, the pilot pharmacy patients appear to receive more medications for psychiatric comorbidities, which is consistent with the increased expenditures on mental health services. These findings suggest that the pilot pharmacy patients may receive more appropriate HIV treatment and perhaps more comprehensive medical access and care for their other conditions, often related to their primary therapy.

There remains a need to determine the ultimate long-term benefit of patients being more adherent on appropriate combined ART regimens and using more non-ART medications and mental health services over several years. Possible savings in more costly inpatient care will be investigated when data for subsequent years of the pilot program are available. These longer-term data also will allow investigation of the cost-effectiveness of the $9.50 per prescription payments for MTM services by the California DHCS. However, with the advent of Medicare Part D, the dual-eligible Medicare patients will no longer receive medications through Medi-Cal and thus will not be available for follow-up. However, the results of this pilot may help Medicare Part D plans understand the value of community pharmacists providing MTM services to HIV/AIDS patients; especially Medicare Special Needs Plans focusing on this patient population.

Limitations

The foremost limitation of this study is that it is an evaluation of an ongoing program and may be subject to selection bias due to nonrandom assignment of HIV/AIDS patients to pharmacies. If patients who fill their prescriptions at pilot pharmacies are different from patients who fill their prescriptions at other pharmacies, then the pilot pharmacy estimated effect will include both the true pilot program effect and the baseline differential between patients. Although the 2 patient groups appeared to be similar with regard to observable variables (e.g., age, gender), nonobservable variables (e.g., willingness to follow treatment protocols, possible physician referral of more complicated patients to pilot pharmacies) may differ between groups and affect conclusions. Second, it is possible that some of the other (comparison cohort) pharmacies provided some of the same services as the pilot pharmacies, because only the first 10 pharmacies meeting program criteria were enrolled in the pilot compensation program.

Third, an inherent limitation to this analysis is its reliance on Medi-Cal retrospective claims data that do not include clinical outcomes such as viral load and CD4 counts.

Fourth, our results are relevant to California but may not reflect what would occur with a similar MTM program in patient populations with different demographic or disease characteristics. Fifth, comparison of patient outcomes and costs before and after MTM services were initiated by pilot pharmacies was not possible because the pilot pharmacies provided MTM-like specialty services for varying amounts of time before receiving the compensation from the pilot program. Finally, this was an analysis of only the first year of the pharmacy compensation pilot program. Claims data from subsequent years of the pilot program are being sought to determine whether observed differences in outcomes and treatment costs continue to be observed over the 3-year period of the pilot program.

Conclusions

Patients at pilot pharmacies appear to benefit from more specialized and patient-specific MTM services offered by pilot pharmacies. Pilot pharmacy patients were on more potent ART regimens, had higher medication adherence rates, fewer excess fills, and fewer contraindicated regimens than nonpilot pharmacy patients. Importantly, more pilot pharmacy patients remained on a single type of ART regimen throughout the study year, which decreases the likelihood of developing drug resistance and enhances the ability to maintain health over a longer period of time. Total cost per patient was 10% higher in pilot pharmacies, with the higher cost attributed to non-ART medications and mental health services. Longer-term outcomes and costs of the pilot program will be examined when data for subsequent years are available.

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DISCLOSURES

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APPENDIX A Alphabetical List of Antiretroviral Therapy (ART) Medications by Category

Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (N(t)RTI)
Abacavir sulfate
Abacavir sulfate/lamivudine
Abacavir/lamivudine/zidovudine
Didanosine/magnesium/Al NaCB/sodium citrate
Didanosine
Didanosine/calcium carbonate/magnesium
Didanosine/sodium citrate
Emtricitabine
Lamivudine
Lamivudine/zidovudine
Stavudine
Zalcitabine
Zidovudine
Tenofovir disoproxil fumarate
Emtricitabine/tenofovir
Nonnucleoside Reverse Transcriptase Inhibitors
Delavirdine mesylate
Efavirenz
Nevirapine
Protease Inhibitors
Amprenavir/vitamin E
Amprenavir/vitamin E/propylene glycol
Atazanavir sulfate
Fosamprenavir calcium
Indinavir sulfate
Nelfinavir mesylate
Ritonavir
Ritonavir/lopinavir
Saquinavir
Saquinavir mesylate
Tipranavir
Fusion Inhibitor
Enfuvirtide

APPENDIX B Opportunistic Infections and ICD-9-CM Codes

Opportunistic Infections	ICD-9-CM code
Pneumocystis jiroveci pneumonia (PCP)	136.3
Toxoplasma gondii encephalitis	130.0
Cryptosporidosis	007.4
microsporidiosis	136.8
Mycobacterium tuberculosis	010-018
Mycobacterium avium complex disease	031.0, 031.2
Bacterial pneumonia	482.9, 482.89
Salmonellosis	003.0, 003.1
Campylobacter *jejuni* infections	008.43
Shigellosis	004.9
Bartonella infections	088.0
Treponema pallidum infections (syphilis)	091-097
Candidiasis	112
Cryptococcus neoformans meningitis	117.5
Histoplasma capsulatum infections	115.0
Coccidiodomycosis	114
Invasive aspergillosis	117.3
Cytomegalovirus (CMV) disease	078.5
Herpes Simplex virus (HSV) disease	054
Varicella zoster virus (VZV) disease	052.9
Human papilloma virus (HPV) disease	079.4
Hepatitis C virus (HCV) disease	070.41, 070.51, V02.62, 070.54, 070.44, 070.70, 070.71
Hepatitis B virus (HBV) disease	070.30, 070.2, 070.32, 070.22, V02.61, 070.21, 070.31, 070.23, 070.33
Penicillosis	117.3
Leishmansiasis	085
Paracoccidioidomycosis	116.1
Isospora belli infections	007.2
Chagas disease (American trypanosomiasis)	086.0-086.2

ICD = International Classification of Diseases, Ninth Revision, Clinical Modification