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Research Brief

TO: Representative Mia Costello
FROM: Tim Spengler, Legislative Analyst
DATE: January 28, 2013
RE: Costs Associated with Mediset, a Medication Management Service
LRS Report 13.129

You were interested in the costs associated with the Mediset medication management system in Alaska. Additionally, you asked for information on potential ramifications for Alaska if proposed regulation changes, which pertain to certain Medicaid payment rates, are implemented. You also asked for reports or studies on the implications of medication non-compliance.

Briefly, a number of individuals in Alaska, many of whom are frail and elderly, have medical needs so complex that they must take up to a dozen or more medications daily. Certain pharmacies in the state specialize in providing comprehensive pharmacy care that aims to increase medication compliance for such individuals.[1] The Alaska Department of Health and Social Services (DHSS) estimates the additional fee for the Mediset service costs the state a total of about $200,000 annually. In addition to the usual pharmacy dispensing fee paid for traditional services, these pharmacies, called Mediset pharmacies, currently receive an extra fee. This Mediset fee would be eliminated under regulations currently under consideration.

Mediset Basics

Mediset is a medication management service that is provided by some Alaska pharmacies.[2] Mediset pharmacies package, deliver, and monitor medications for individuals with significant medication needs and are, as such, directly involved with the patients adherence to their prescribed medication plans. The oversight provided by these pharmacies aims to help patients—who are often taking numerous medications daily—stay medication compliant.

Individuals using Mediset services include the frail and elderly, those with serious mental illnesses, disabilities, and those residing in group homes. The term "mediset" refers to the actual compliance packaging—designed to increase patient medication adherence—in which a client's pills are arranged in an organized, easy-to-understand manner; however, in this report, "Mediset," will refer to the packaging, delivery, and monitoring services provided by clinical pharmacies.

According to the Alaska Department of Health and Social Services (DHSS), there are currently five pharmacies in the state submitting claims as Mediset pharmacies: Geneva Woods (Anchorage), Geneva Woods (Wasilla), Anchorage Mediset Pharmacy, Susitna Medical Services (Wasilla), and Frontier Medical (Anchorage).[3] All these pharmacies specialize in Mediset services and a large majority of their clients receive their medications in this way. In each of the last five years, these five pharmacies have served a total of around 2,500 individuals enrolled in Alaska Medicaid, according to DHSS. Over 30 other pharmacies around the state provide some sort of Mediset services but only as a small fraction of their business. These other pharmacies are not eligible for the Mediset fee that the above-listed pharmacies receive.

In addition to the usual pharmacy dispensing fees that any pharmacy would receive, Mediset pharmacies are currently reimbursed by Alaska Medicaid an additional five dollars per claim (per prescription) to be billed not more than once per

[1] Medication compliance or medication adherence refers to whether patients take their medications as prescribed (e.g., twice daily), as well as whether they continue to take a prescribed medication.

[2] Similar services are available throughout the United States although often these services go by different names. All provide the same basic clinical-pharmacy medication management services; according to the Alaska Department of Health and Social Services (DHSS), it is not typical for other states to pay an additional "Mediset" fee—on top of the usual dispensing fee—to pharmacies providing such services as is currently the case in Alaska. Wilda Laughlin, DHSS legislative liaison, (907) 465-1613, was our department contact for this report.

[3] The Alaska Native Medical Center—Mediset Pharmacy, has submitted claims in the past but did not submit any claims in 2012.

week.[4] These added fees would be eliminated if Medicaid payment regulation changes like those proposed in September 2012 are adopted. It should be noted that, according to DHSS, the current standard medication dispensing fees for all pharmacies paid by Alaska Medicaid are, on average, the highest in the country among fee-for-service Medicaid programs.

In order to receive medication management services through a Mediset pharmacy, an individual in the Alaska Medicaid program must have a doctor's order for the service based on patient's needs. Others clients can request this service, but their pharmacies will not be eligible for the additional Mediset fee from Medicaid unless they meet the criteria as set out in 7 AAC 145.410.

Total payments (which include both drug costs and dispensing fees) made by Alaska Medicaid to the five Mediset pharmacies for calendar years 2008 through 2011 averaged roughly $11 to $12 million per year. In 2012, payments went down to around $6.6 million as the result of numerous name brand drugs losing patent protection and being replaced by generics, as well as Alaska implementing regulations regarding maximum allowable costs for drugs. Also, dispensing fees decreased for all state pharmacies due to a September 2011 regulation change that limited dispensing fees to no more than one per recipient per medication per 28 days. (This did not pertain to Mediset fees, which are separate from traditional dispensing fees.) Prior to this change there was no such limit.

Attachment A is a table provided by DHSS that disaggregates the total payments made to the Mediset pharmacies by Alaska Medicaid over the last five years as well as the total payments made to all state pharmacies. The table also shows payments made for the dispensing fees alone, and the percentage of dollars spent on Mediset pharmacies compared to all state pharmacies. In 2012 for example, Medicaid payments to the Mediset pharmacies totaled around ten percent of the total payments made to all state pharmacies.[5]

Possible Impacts of Proposed Mediset Regulation Changes

Regulations proposed in September 2012 would eliminate the fee, five dollars per claim, which Mediset pharmacies currently receive from Medicaid.[6] Pharmacies could conceivably continue to provide Mediset services, but they would receive the usual fee that all pharmacies receive for dispensing medications in a traditional way. According to DHSS, the state would realize savings (or the funds could be redirected) of approximately $200,000 a year under such a change. Below is an excerpt from a document provided to us from DHSS regarding the proposed regulation changes.

> The September 2012 proposed regulations included many revisions to the current reimbursement methodology and were not specifically aimed at pharmacies dispensing medications in adherence assistance packaging. It is estimated that the total annual savings of the entire package, including impacts to mediset specializing pharmacies, would be about $1-$2 million. The mediset change would account for only about $200,000 of that amount.

We provide, as Attachment B, correspondence from DHSS that addresses your various Mediset-related questions. The department's response includes information on costs, number of Alaskans served, number of Mediset pharmacies, and information pertaining to possible regulation changes. In their response, the department relates that it anticipates that recipients will not lose access to medically necessary pharmacy services, including the use of adherence assistance packaging, if regulations are promulgated to eliminate Mediset fees.

Notwithstanding the savings estimated by DHSS, and the department's belief that sufficient pharmacy services will continue, concerns have been raised, primarily in the Mediset pharmacy and assisted living communities, regarding the potential long-

[4] For example, the additional Mediset fee for an individual served through a Mediset pharmacy who takes five medications a day would be $25 a week.

[5] When looking at the table, it is important to note that Mediset fees are included in the total payment figures, not the dispensing fee figures.

[6] The DHSS hosted a public meeting on pharmacy coverage and reimbursement on January 11th, 2013. As a result of this, the department must effectively start the regulation process anew by re-noticing the potential regulations and accepting public comments. The regulation specifically pertaining to Mediset fees is 7 AAC 145.410.

term costs of eliminating Mediset fees. A common concern is that should such a regulatory change be made, Mediset pharmacies would likely be unable to continue providing their clinical pharmacy services for many Alaska Medicaid recipients. In essence, they would be getting reimbursed for dispensing medications at the rate of a traditional pharmacy while providing services that require far more time and packaging expense.

Various entities in the state have voiced concerns regarding the potential changes to the Mediset regulation including the Geneva Woods Pharmacy, a provider of Mediset services with locations in Anchorage and Wasilla; Marlow Manor, an assisted living facility for seniors in Anchorage; and the ARC of Anchorage, which serves individuals with disabilities. We also spoke with a number of Juneau pharmacists and who were similarly concerned about the effects of such regulations on medication compliance, even though they are not employed in Mediset pharmacies.

The Geneva Woods Pharmacy recently produced a white paper in which they articulate its concerns for the proposed regulation changes. The concerns include the following:

- Medication compliance for at-risk individuals would decrease, resulting in increased medical interventions;
- Group homes for the mentally ill, disabled, or frail and elderly will find it difficult to manage medications for their residents with myriad needs, and
- Increased medication waste and abuse will occur.

We provide the pharmacies entire white paper as Attachment C.

Studies and Articles Regarding the Medical and Fiscal Implications of Medication Non-Compliance

Because of Alaska's limited skilled nursing and mental health facilities, assisted living facilities (ALHs) and group homes accommodate a significant percentage of the state's most vulnerable population. According to our review, without the medication management provided by Mediset pharmacies many of these entities would likely need to increase their reimbursement rates to cover this vital service. Another risk of eliminating the Mediset fee pertains to homebound and other individuals with complex medication needs who would be at a higher risk for medication non-compliance, which can result in more serious medical issues and potential increased costs for the state.

According to our review of the subject, a hallmark of medication management systems like Mediset is that they significantly increase a patient's compliance to his or her medication regime. Numerous studies also show that when individuals are non-compliant with their medications, they are far more likely to experience a costly avoidable hospitalization. Non-compliance can also lead to death.

The studies, briefs, and articles that we identified pertaining to medication non-compliance and clinical pharmacy services—a number from professional entities such as the American Medical Association, and some from magazines such as the *Atlantic*—frequently contained the same core messages or results, namely that non-compliance is costly both in terms of the human suffering it exacerbates and the financial burdens it causes, and how Mediset-like services can increase compliance. Below we provide some highlights regarding what we gleaned from our review noting in parenthesizes the source of the information. We include the source documents, as well a number of others, as Attachment D. Please note that some of these documents are copyrighted and are provided for your personal and individual use

- Medication non-adherence is a significant health care issue; studies show the annual cost of around $290 billion in the U.S. in avoidable medical spending. ("State of the States: Adherence Report," *CVS Caremark*, 2012)[7]

- A comprehensive pharmacy program composed of patient education and custom blister-packed medications was associated with substantial and sustained improvements in medication adherence among elderly patients receiving complex medication regimens and could lead to meaningful improvements in health outcomes especially among the at-risk elderly population. ("Effects of a Pharmacy Care Program on Medication Adherence," *American Medical Association*, November 13, 2006).

[7] Various studies that we reviewed estimated the costs associated with medication non-compliance at around this $290 billon mark.

- Thirty two million Americans use three or more medications daily and 75 percent of adults are non-adherent in some way. (Key Stats on Medication Adherence, *PhRMA*, 2011)

- In a recent poll, 51 percent of individuals 65 years old and older take at least five different prescription drugs regularly and one in four take 10-19 pills each day. Fifty seven percent polled report that they forget to take their medications (*New England Healthcare Institute*).[8]
- A Mediset-type program that provides medications in a package that identifies the day each dose is intended to be taken, and provides information on proper self-administration, can improve treatment adherence and outcomes in elderly patients. ("Impact of Medication Packaging on Adherence and Treatment Outcomes in Older Ambulatory Patients," *Journal of the American Pharmacists Association*, January/February 2008).

- Over two decades of research studies indicate that modern medication packaging solutions increase medication adherence rates significantly. (*Healthcare Compliance Packaging Council* report, which uses many sources including the World Health Organization, the American Heart Journal, and the Institutes for Medicine, 2011).

- Pharmacy-based medication management systems can reduce medication management issues, address problems as they arise, and reduce nursing home admissions of community dwelling, nursing home–eligible patients. ("Impact of a Medication Management System on Nursing Home Admission Rate," American Journal of Geriatric Pharmacology, February 2011).

- The role of a comprehensive pharmacy care program (such as Mediset) is critical in promoting medication adherence for the reduction of healthcare costs and the prevention of chronic disease progression. ("Effects of a Pharmacy-Care Program on Adherence and Outcomes," *The American Journal of Pharmacy Benefits*, January/February, 2012).

- Failure to follow prescriptions causes around 125,000 deaths a year and up to ten percent of all hospitalizations. Blister packs (Mediset) have been shown to boost compliance. ("The $289 Billion Cost of Medication Noncompliance, and What to Do About It," *The Atlantic*, source the *Annals of Internal Medicine*, September 2013).

- Inadequate implementation of treatment can have devastating effects including causing three times as many doctor visits and an additional $2,000 of healthcare costs per year compared to patients who follow their treatment plan ("Cost of Patient Noncompliance, Allan Showalter, MD, 2006).

Given the information above, it is not surprising that clinical pharmacy services, such as those that Mediset pharmacies in Alaska provide, are increasing in popularity throughout the country.[9] Jurisdictions are seeking to keep their citizens healthy and to reduce costs pertaining to hospitalization and medication waste. According to the information we reviewed, medication management systems can ultimately lead to lower healthcare costs and better outcomes.

We hope this is helpful. If you have questions or need additional information, please let us know.

[8] Other studies suggest that at least 50 percent of patients do not take their medicines as prescribed.

[9] Information on the rise of clinical pharmacies and medication management programs are documented in a number of sources including *www.allhealth.org/briefingmaterials/BiotechHealthcareSpecialtyPharmacies-416.pdf* and *www.accp.com/docs/positions/whitePapers/RewardsAdvancements.pdf*

Attachment A

Table on Payment to Mediset Pharmacies 2008-2012, DHSS, January 24, 2013

Alaska Medicaid Payments to Mediset Pharmacies, 2008-2012

	CY-2008		CY-2009		CY-2010		CY-2011		CY-2012	
Provider	Total Payment (Includes Dispensing Fee)	Dispensing Fee	Total Payment (Includes Dispensing Fee)	Dispensing Fee	Total Payment (Includes Dispensing Fee)	Dispensing Fee	Total Payment (Includes Dispensing Fee)	Dispensing Fee	Total Payment (Includes Dispensing Fee)	Dispensing Fee
Geneva Woods (Anchorage)	$ 5,905,724	$ 1,598,853	$ 5,055,047	$ 1,563,614	$ 4,631,017	$ 1,427,148	$ 4,104,844	$ 972,292	$ 2,150,327	$ 347,078
Geneva Woods (Wasilla)	$ 2,323,496	$ 565,849	$ 2,309,419	$ 547,433	$ 2,381,315	$ 601,364	$ 2,142,452	$ 425,313	$ 1,332,704	$ 158,848
Anchorage Mediset Pharmacy (Anchorage)	$ 3,594,921	$ 633,371	$ 3,640,545	$ 676,255	$ 3,923,248	$ 715,253	$ 4,296,718	$ 595,989	$ 2,392,815	$ 239,091
Susitna Mediset Services (Wasilla)	$ 191,656	$ 29,289	$ 738,157	$ 117,996	$ 629,160	$ 156,097	$ 763,889	$ 158,129	$ 536,680	$ 90,445
Alaska Native Medical Center - Mediset Pharmacy	N/A	N/A	N/A	N/A	N/A	N/A	$ 2,197	$ 440	$ -	$ -
Frontier Medical Pharmacy (Anchorage)*	N/A	N/A	N/A	N/A	$ 36,233	$ 9,933	$ 154,550	$ 28,600	$ 249,215	$ 46,664
Hewitt's Drug (Anchorage)*	$ 113,855	$ 23,961	$ 51,762	$ 18,947	N/A	N/A	N/A	N/A	N/A	N/A
Totals (Mediset Pharmacies above)	$ 12,129,653	$ 2,851,323	$ 11,794,929	$ 2,924,245	$ 11,600,973	$ 2,909,794	$ 11,464,649	$ 2,180,762	$ 6,661,742	$ 882,126
Totals (Total claims from all pharmacies)	$ 74,280,449	$ 7,666,338	$ 79,330,876	$ 8,052,495	$ 83,547,655	$ 8,608,451	$ 86,036,571	$ 8,701,307	$ 69,645,123	$ 8,705,090
Percentage of Costs due to Mediset Pharmacies (above)	16.3%	37.2%	14.9%	36.3%	13.9%	33.8%	13.3%	25.1%	9.6%	10.1%

Notes: *Hewitt's Drug closed in 2009 and the former owners opened Frontier in 2010. 2008 Data only contains data from 1/18/2008 through12/31/2008.
Source: Provided on January 24, 2013, by Wilda Laughlin (907) 465-1613, legislative liaison, Alaska Department of Health and Social Services.

Attachment B

Document from DHSS regarding Mediset, January 24, 2013

(Provided by DHSS legislative liason, Wilda Laughlin, 1/24/13)

Question 1: What has the Mediset program cost the state in each of the past 10 years?

Answer 1: Alaska Medicaid does not have a separate or defined benefit, service, or mediset program. Pharmacists can dispense medications in adherence assistance packaging (a.k.a. "medisets") based on the prescribers order's and the recipient's needs. The percent of prescriptions dispensed in medisets varies greatly from one pharmacy to the next with some pharmacies dispensing the majority of prescriptions in adherence assistance packaging and other pharmacies dispensing no prescriptions in adherence assistance packaging. Reimbursement for dispensing medications was revised in September 2011 at which time a separate "mediset fee" was incorporated into the payment methodology and only payable to qualifying "mediset pharmacies" for eligible recipients. Prior to September 2011 a separate dispensing fee was paid each time a prescription was dispensed, regardless of how it was packaged for dispensing, and the revisions in September 2011 limited the number of dispensing fees to no more than 1 every 28 days per medication strength per pharmacy.

While no separate mediset program exists there have been a number of pharmacies that have specialized in dispensing medications in adherence assistance packaging. The attached TABLE 1 has a breakdown of the payments made to these pharmacies for calendar years 2008 through 2012. The claims processing query system only maintains the most recent 5 years of data; older data can be retrieved but takes several weeks to acquire via ad hoc report requests. Between 2008 and 2012 the percent of total pharmacy claims payments made to the 5 primary mediset pharmacies accounted for 9.6%-16.3% of the pharmacy program costs and 10.1%-37.2% of the costs associated with the dispensing fees. Costs in both categories were highest in the oldest years and have decreased in recent years.

It is important to note that TABLE 1 only represents data for the pharmacies known to have specialized in this service. Pharmacies offering this service to a small portion of their patient base were not included because a prescription that was dispensed as a mediset is differentiable from a non-mediset prescription based on claims data alone.

Question 2: For each of the past 10 years, how many people has the program served?

Answer 2: Alaska Medicaid does not have a separate or defined benefit, service, or mediset program. Pharmacists can dispense medications in adherence assistance packaging (a.k.a. "medisets") based on the prescribers order's and the recipient's needs. The number of recipients services by pharmacies know to specialize in mediset services between 2008 and 2012 is listed below. Recipients were counted if 1 or more prescription claim was received from one or more of the pharmacies specializing in dispensing medications in adherence assistance packaging listed in TABLE 1:

Year	**# of Recipients**
2008	2,494
2009	2,505
2010	2,478

2011	2,634
2012	2,611

Question 3: How many Mediset pharmacies are currently operating in Alaska and where are they located?

Answer 3: The pharmacies know to specialize in dispensing medications in medisets are identified in TABLE 1. Currently there are 5 pharmacies submitting claims as mediset pharmacies and a 6th (Alaska Native Medical Center – Medset Pharmacy) is known to provide this service but has not submitted any claims in 2012. One pharmacy, Hewitt's Drug, closed in 2009 but re-opened as a different business in 2010 as Frontier Medical Pharmacy.

Additional pharmacies provide mediset services but as a fraction of their overall line of business. The 2012 Cost of Dispensing Survey found that 32 pharmacies in the state provide unit dose services and 33 pharmacies dispense medications to long-term care facilities. Specific locations of the pharmacies identified in the 2012 Cost of Dispensing Survey are not know but they are all located within the state of Alaska as only in-state pharmacies were surveyed.

Question 4: If the proposed Mediset regulation changes (reducing the reimbursement rates for Mediset pharmacies, etc.) go into effect, what savings does the department expect to reap annually?

Answer 4: The September 2012 proposed regulations included many revisions to the current reimbursement methodology and were not specifically aimed at pharmacies dispensing medications in adherence assistance packaging. It is estimated that the total annual savings of the entire package, including impacts to mediset specializing pharmacies, would be about $1-$2 million. The mediset change would account for only about $200,000 of that amount.

Question 5: Does the department have any concerns regarding potential long term issues with changing Mediset regulations such as increased medication non-compliance, which may lead to increased hospitalizations and emergency room visits, wasted medication due to frequent prescription changes, drug abuse by those the medication was not prescribed for, or increased hardship for elderly and/or mentally ill patients?

Answer 5: The Department does not anticipate recipients would lose access to necessary and medically necessary pharmacy services, including the use of adherence assistance packaging. The Department does not anticipate there would be associated negative health impacts as access to pharmacy services would continue. The Department has analyzed claims data from all pharmacies and mediset specializing pharmacies and does not anticipate there to be increased waste.

Question 6: If there is any additional information you would like to provide regarding this topic that may be illuminating for the legislator please do so.

Answer 6: It is important to highlight the Department has not proposed preventing pharmacies from dispensing medications in adherence assistance packaging, only reforming the manner in which the Department reimburses pharmacies for dispensing medications. The current dispensing fees paid by Alaska Medicaid are the highest in the country amongst fee for service Medicaid programs and the proposed dispensing fees in the September 2012 proposed regulations would also have been the highest in the country. The payment of a weekly dispensing fee or separate mediset or unit dose fee is not a common practice within the profession. Many of the proposed changes in the September 2012 proposed regulations are in response to changing federal program requirements and are consistent with changing reimbursement structures within the profession and similar, albeit slightly higher, than the aggregate reimbursement rates for other Medicaid and commercial 3rd party payers.

Attachment C

White paper regarding proposed Medicaid payment regulations, Geneva Woods Pharmacy

NOTICE: Critical Changes for Medicaid Recipients

"It was once said that the moral test of government is how that government treats those who are in the dawn of life, the children; those who are in the twilight of life, the elderly; and those who are in the shadows of life, the sick, the needy and the handicapped."

-Hubert H. Humphrey

PROPOSED CHANGES TO REGULATIONS 7AAC 105,120,145,160

(Specific reference to Pharmacy Reimbursement Sections 120 and 145)

These proposed changes will:

- *Significantly impact the **care** for the medically fragile Medicaid Recipients*
- *Pose a public **safety** issue for the Alaskan Community*
- *Increase overall **cost** of Alaska's Healthcare*
- *Put Alaskan **jobs** and Independent Pharmacies at risk*

A Historical Perspective on Alaskan Pharmacies, Recent Proposed Regulation Changes and the Adverse Effects on Pharmacies, Medicaid Recipients and the Health Care Community prepared by Geneva Woods Pharmacy, Inc.

INTRODUCTION

This paper will provide information and a historical perspective on the accepted standards of practice that Alaska pharmacies have been operating under for the past 20 years. It will also describe the most recently proposed regulation changes and the effect they will have on pharmacies, Alaska Medicaid recipients and care providers. This paper will outline indications that the regulations create an uneven commerce playing field for Alaska based business and will likely lead to Alaska jobs and commerce being exported to large-scale pharmacy providers in the lower 48 states. While the regulation change is clearly targeting drug cost reductions, in reality the result will be increased overall health care costs.

HISTORICAL PERSPECTIVE

"Geneva Woods Pharmacy's current Mediset model was created in collaboration with the Alaska Division of Health Care Services to support the Independent Living Community"

The state of Alaska Legislature made a conscientious decision to become an institutionalized free state. The late 80's brought about greater independence and choice for people receiving services in Alaska. "Institutionalized" living was not considered the pathway for independent living and was considered an expensive alternative to community living. The state of Alaska began researching their options to become an "institutional free" state. The State of Alaska was instrumental in supporting community inclusion initiatives to allow individuals experiencing a disability, vulnerable Alaskans and seniors the ability to reside in their community and have choices over their quality of life. Living environments were expanded to include independent living, home ownership and assisted living homes. The availability of pharmacy programs and medical equipment and supplies were considered necessary services for individuals to reside in their community. Local companies such as Geneva Woods Pharmacy, created a service model, at the request of the state of Alaska, to support these individuals in their homes and community. In 1997, the last official institution, Harborview Medical closed. Alaska now was institution free and was seen as an innovative leader in the community inclusion movement.

THE IMPACT OF THE CHANGES

Proposed Regulation	Current Regulation	Effect of Proposed Regulation	Recommendations
7 AAC 145.410 All language recognizing Mediset services and the associated fees for dispensing, preparing, packaging and managing the Mediset program have been repealed.	A Mediset fee of $5.00 per claim to be billed not more than once every seven days will be paid to a Mediset Pharmacy for a recipient living in a congregate living home; a recipient of Home and Community Based Waiver Services; a Recipient eligible for Medicaid under a category in 7AAC 100.002 (b) or (d), who is Blind, Disabled, a Recipient who is an adult experiencing a Serious Mental Illness, or a Recipient who is a child experiencing a Severe Emotional Disturbance. Individuals that currently meet the diagnosis criteria as identified above, currently receive weekly medication boxes (Mediset). This weekly monitoring of their medications assists with medication regimen compliance, decreased medication waste, and medication safety. The pharmacy staff is directly involved with adherence to the prescribed medication plan and oversight of drug interactions. Due to the fact that we dispense only a 7 day supply at a time, a change or discontinuation of a medication can be made without destroying a 30 day supply of unused medication. This is a cost savings for the state. Medication safety also is very important. Instead of having a 30 day supply of narcotics in the medication cabinet, the facilities and vulnerable adults only stock 7 days therefore eliminating the risk of theft and misuse.	Mediset Pharmacies will receive the same reimbursement per prescription as a retail or mail order pharmacy with no recognition of the higher cost to provide these specialty services. The change in fee equates to a 73% reduction in dispense fees since 9/1/2011 and a 14% reduction in drug reimbursement. It appears that Alaska Medicaid does not value services that provide care for our most vulnerable Medicaid recipients. The risks of the elimination of this program include the non-compliance of medication management resulting in higher cost medical intervention; the inability for ALH's or group homes to manage medications for the residences resulting in increase reimbursement requirements to ALH's and group homes to cover medication management; the inability to respond to frequent medication changes thus resulting in higher costs of drugs due to wasted medications; larger volumes of controlled substances accessible to misuse and illegal distribution resulting in an unnecessary public safety hazard.	Repeal change in dispensing fee for Mediset services that were enacted on 9/01/11. Implement a fair dispense fee ($16.75 per dispensing of medication) that covers the increase cost of medication management, oversight, packaging, fulfillment and delivery of the medications (identified by physicians) to be included in compliance dose packaging.

Proposed Regulation	Current Regulation	Effect of Proposed Regulation	Recommendations
7 AAC 145.410 Proposed regulation calculates the dispense fee based on the dispensing pharmacies location on the road system. (8) "Pharmacy located on the road system" means a pharmacy that is physically located in a city, town, or village that is directly or indirectly connected to Anchorage by road.	Current dispensing fees are paid based on the volume of prescriptions dispensed per year.	This term is ambiguous and has previously been rejected as such. It is established that the Alaska Marine Highway is considered part of the road system as is the Dalton Highway.	What is the intent of the department? Recommendation is to identify locations by zones, zip codes or destination or a method to fairly compensate all community pharmacies in an equitable way.
7 AAC 145.410. Under the proposed regulation, out-of-state Pharmacies would now receive $13.36 per prescription.	The dispensing fee for an out-of state pharmacy is $3.50 per prescription	The **out-of-state pharmacies** (Non-Alaskan) would automatically get a $9.86 increase (**386% increase)** while the local Alaskan Pharmacies with similar volumes in retail pharmacy receive a $1.24 increase. In addition, the Mediset Pharmacies take over a 60% reduction in fees. The proposed regulation gives advantages to out-of-state pharmacies and penalizes Alaskan owned and operated pharmacies. We strongly believe that local pharmacies can better serve our communities.	Why is the State of Alaska rewarding out-of-state pharmacies with disproportionate increases in dispensing while penalizing some Alaskan pharmacies? Is the State of Alaska making a choice to provide for our Alaskan Medicaid recipients outside of Alaska? We request this language be removed.
7 AAC 145.400 The proposed regulations provides for a drug reimbursement of WAC (Wholesale acquisition costs) +1%. Payment is set for the lowest of acquisition costs, FUL, AAC, SMAC plus dispensing fee. **Language related to reconsideration of a SMAC price for a drug is repealed**	The current payment methodology is WAC (Wholesale Acquisition Cost) +8%. Reconsideration of a SMAC price for a drug is available with specific provisions.	At minimum this will result in a 7% reduction in drug reimbursement. This is in addition to an average 7% reduction in Sept. 2011. WAC does not allow for the additional cost of transporting drugs to Alaska. Some drugs are reimbursed below the pharmacy costs of acquisition, yet a request for reconsideration is no longer available, if this regulation is enacted.	No change to current regulation pricing methodology. Place change on hold pending changes anticipated from CMS.

Proposed Regulation	Current Regulation	Effect of Proposed Regulation	Recommendations
7AAC 120.110 The department may designate one or more enrolled pharmacy providers for the purchase of specialty drugs through a contract for services under AS 36.30.	Current regulations do not provide any specialty pharmacy contracts.	The department has control over the drug formulary; the reimbursement of drugs and the amount of dispense fee or per diem. There is a significant investment to provide specialty pharmacy. What is the intent of the department? Is it to contract with out-of-state pharmacies?	The department has been deficient in providing a published formulary for specialty drugs. A remediation system is needed to allow requests to use drugs not on the Preferred Drug List or when an alternate drug is needed in the instance of a national shortage situation. Also a process is needed in which a pharmacy can be instructed by Megellan which NDCs will be covered. Alaska specialty drug services should allow any willing provider to participate and not be outsourced to one or two providers.
7AAC 145.400 (e) reconsideration language is eliminated.	Current regulation affords a process to ask Medicaid to reconsider its reimbursement position in those cases where reimbursement is less than actual cost paid for the drug. This occurs frequently when the Medicaid formulary drug is in short supply nationally and the only alternative is a more expensive option.	This will limit access for Medicaid recipients. Pharmacies should not be expected to dispense medications and get a reimbursement amount that is less than the cost of the drug.	Reinstate the reconsideration process.
7AAC 145.400 Dispensing fees for infusion prescription are being eliminated.	Reimbursement for prescriptions in Alaska includes cost of drug at WAC +8% and a dispensing fee. The fee is based on a "volume based" equation developed by Alaska State Medicaid.	The time it takes pharmacy staff to accept new patients into service, (these are frequently complex medical patients) perform initial drug regimen review and monitor patient clinical status regularly throughout the entire therapy period without getting a dispensing fee will be cost prohibitive.	Reinstate a dispensing fee for all infusion prescriptions.

Proposed Regulation	Current Regulation	Effect of Proposed Regulation	Recommendations
7 AAC 145.400 The term "freight cost" has been eliminated and replaced with postage up to $16 per prescription for package.	The department has provided for reasonable and necessary postage for freight costs incurred in the delivery of the prescription from the dispensing pharmacy to the recipient.	Many patients including, but not limited to patients in rural Alaska and the southeast require Intravenous medications not readily available in their community. Transported pharmacy infusion medication requires temperature controlled measures and must be delivered within 12-24 hours. The average cost to ship a controlled package from Anchorage to Juneau is about $55.00. The inability to receive properly handled home infusion medications puts patients at risk. Lack of these medications would result in admittance to the local hospital or emergency room at a significant cost to the Medicaid system.	Regular mail is not an option. We recommend that reimbursement for reasonable and necessary freight costs to the dispensing pharmacy be reinstated.

CLARIFICATION QUESTIONS:

1. Has there been a medication management assessment to determine how these proposed regulations will affect the recipients that reside in assisted living home and congregate living facilities?
2. Has there been an assessment to determine how the reduced pharmacy reimbursements will impact in-state-service providers, access to quality services, and the general health, welfare, and safety of program recipients?
3. When will the Preferred Drug List for injectable and specialty medications be available?
4. What process will be used for remediation if needed medications are not on the Preferred Drug List?
5. Will there be a designated specialty pharmacy in every community?
6. What criteria will be followed in awarding a contract for specialty pharmacy services?
7. Have you been in discussions with or met with pharmacies that might respond to a request for contract to be awarded a sole source contract for specialty pharmacies?
8. Despite the availability of an exhaustive study, paid for by DHSS, recommending a new dispensing fee of $16.75 per prescription, why has DHSS chosen to ignore these recommendations and instead are proposing a dispensing fee of only $13.36?
9. When NADAC (National Average Drug Acquisition Cost) is implemented, will Alaska, like Oregon and Alabama continue to determine a State appropriate AAC (Actual Acquisition Cost) and not rely on a national AAC generated through NADAC?

OUR PERSPECTIVE

Geneva Woods Pharmacy has been providing pharmacy and medical supplies to the Alaskan community for over 35 years. We are an Alaskan owned company which employs 185 full time employees. We have worked collaboratively with the state of Alaska and the Division of Health Care Services over the past 20 years to design programs to support the intended mission of the State Senior Services Division. Their mission states it is "*to promote health, well being and safety for individuals with disabilities, seniors and vulnerable adults by facilitating access to quality services and supports that foster independence, personal choice and dignity."* We have been deeply affected by the recently proposed regulations regarding pharmacy reimbursement, specifically to the Mediset division. We are unable to understand or explain the rationale that would support a decision of this magnitude. Eliminating the short-cycle Mediset program for the division's most vulnerable recipients is fiscally and socially irresponsible and carries significant negative health consequences. It is our belief that those responsible for these regulations do not understand the benefits and cost-savings associated with recipients receiving a Mediset or the broad scale impact of these changes on the assisted living home community or patients in need of home infusion therapy. It also is our position that the current administration does not understand the cost to pharmacies to provide a clinical support model Mediset pharmacy program.

It appears there is a rush to implement a complex regulation change of this magnitude. Specialty pharmacies incur substantial cost to provide and support a clinical model. We are concerned that these regulations will not only cause harm to those affected, it will also cause a negative impact for Alaskan jobs and harm Alaska based small business.

Geneva Woods Pharmacy recognizes the goals and strategic position of the State of Alaska Division of Health Care Services. The following statements reflect DHSS and direction.

Integrated Health & Wellness

We are focused on improving the health status of all Alaskans. It is necessary to continue bridging both policy and practice gaps that have traditionally existed between primary health care and behavioral health care. We need to prevent, intervene early, treat and help people recover from substance abuse as much as we need to screen, diagnose and treat chronic disease and mental health conditions. We desire to see a healthier Alaska, and believe the following strategies will bring us closer to this reality:

- *Promoting prevention and healthy life choices*
- *Integrating primary care with behavioral health*
- *Detecting and controlling the spread of infectious diseases*
- *Promoting diagnostic, treatment and recovery services*
- *Improving emergency response and preparedness*
- *Promoting rural infrastructure development*

Health Care Access and Delivery

The department is taking steps to improve access to quality health care in Alaska. Alaska Medicaid provides health insurance coverage to approximately 18 percent of Alaska's population. As in other states, Alaska's Medicaid program is challenged to meet increasing costs and demands for services. We believe the following strategies will allow for systemic improvements in both access and service delivery:

- *Promoting technology for sustainable and effective health care delivery.*
- *Supporting workforce development*
- *Enhancing management of high cost health needs*
- *Improving quality and access of care for underserved populations*
- *Promoting rural infrastructure development*

Sustainable Long-Term Care Delivery System

We are striving to improve long-term care service delivery. Alaska has successfully begun making more services available in homes and communities thereby delaying or avoiding higher cost and more restrictive institutional care for many individuals. There is still work to be done to improve access in rural and remote areas of our state and improve standardization of quality care across the continuum, in order to assure the health and welfare of these citizens. We believe the following strategies are vital to achieving this outcome:

•Identifying and coordinating health and welfare needs
•Promoting a service array that meets the needs of those requiring long-term care services
•Developing an integrated and comprehensive model of care
•Promoting rural infrastructure development

Partnerships

Priorities

Safe and Responsible Families and Communities

We are working to improve family and community safety and responsibility. When our neighbors struggle, appropriate supports should be in place to prevent progressively worsening circumstances. Our citizens, from infants to elders, deserve to feel safe, supported and ultimately empowered to become successful, contributing Alaskans. It takes strong families to build strong communities. We believe the following strategies will advance safety and responsibility in Alaskan families and communities:

• Providing effective and timely protective services
• Strengthening programs addressing family violence prevention
• Targeting suicide prevention efforts to communities in need
• Integrating and coordinating services to families
• Establishing community partnerships to identify and solve health problems.
• Promoting rural infrastructure development

While much of our attention is outwardly focused, we are committed to efficient and effective service delivery internal to the department. We believe we serve the public best by: integrating and coordinating our services, maximizing resources for effective service delivery, promoting accountability, strategically leveraging technology and implementing sound health policy decisions.

CONCLUSION

In summary, the proposed regulations will have far reaching and devastating implications. ***Prior to the Pharmacy regulation change on 9/1/2011, the estimated cost to provide the Mediset program, including the weekly dispensing clinical model was $1,435,000.00. This is only 0.056% of the total DHSS Budget!*** Patient safety, service-related costs, access to care and the elimination of Alaska-based jobs will be affected. In addition, increasing drug waste and decreasing controls over prescription medications will impact public safety.

The proposed regulations are inconsistent with the state mandated prescription dispensing survey results and recommendations and directly oppose the direction being taken by CMS related to short cycle dispensing (Section 3310 of the Patient and Affordable Care Act). CMS understands the value of short cycle dispensing and medication management.

It is believed that these implications have not been adequately assessed. In addition, and in many cases, these regulations are in direct conflict with consultant recommendations found in the recent dispensing survey conducted by the Alaska Department of Health & Social Services.

It is further believed that it is in the best interest of the State, Medicaid recipients, the assisted living home community and independent pharmacy interests to reject the proposed regulations. Before proceeding further, the Department needs to (while) assuring recipient access to needed services (especially for our most vulnerable citizens); address recipient and community safety; and that Alaska owned pharmacy providers-which are local employers- remain a viable business model within the state.

Attachment D

When the Patient Is 'Noncompliant', New York Times, November 15, 2012

Effects of a Pharmacy-Care Program on Adherence and Outcomes, American Journal of Pharmacy Benefits • January/February 2012

Thinking Outside the Pillbox, New England Healthcare Institute – August 2009

Effect of a Pharmacy Care Program on Medication Adherence and Persistence, Blood Pressure, and Low-Density Lipoprotein Cholesterol, American Medical Association, 2006

Patient Compliance, Medication Adherence, and Medication Non-Adherence, Statistics & References, epill.com

What is Medication Adherence Patient Compliance and Non-Adherence? epill.com

Impact of medication packaging on adherence and treatment outcomes in older ambulatory patients, Journal of the American Pharmacists Association, Jan/Feb 2008

Two-Plus Decades of Research Studies Support Improved Patient Adherence with Calendarized, Compliance-Promoting Packaging, Healthcare Compliance Packaging Council, 2011

Medication Therapy Management: 10 Years of Experience in a Large Integrated Health Care System, Journal of Managed Care Pharmacy, April 2010

Impact of a Medication Management System on Nursing Home Admission Rate in a Community-Dwelling Nursing Home–Eligible Medicaid Population, American Journal of Geriatric Pharmacology, February 2011

Offsetting Effects of Prescription Drug Use on Medicare's Spending for Medical Services, Congressional Budget Office, November 2012

Various Relevant Articles, various sources

http://well.blogs.nytimes.com/2012/11/15/when-the-patient-is-noncompliant/

DOCTORS NOVEMBER 15, 2012, 11:44 AM196 Comments

When the Patient Is ‘Noncompliant’

By DANIELLE OFRI, M.D.

“A 63-year-old man with hypertension, elevated cholesterol and diabetes,” the intern recited as he presented the case to me in clinic. He read the list of seven medications the patient was prescribed. “But he’s noncompliant,” the intern added.

“Noncompliant” is doctor-shorthand for patients who don’t take their medications or follow medical recommendations. It’s one of those quasi-English-quasi-medical terms, loaded with implications and stereotypes.

Joon Park

As soon as a patient is described as noncompliant, it’s as though a black mark is branded on the chart. “This one’s trouble,” flashes into most doctors’ minds, even ones who don’t want to think that way about their patients. And like the child in school who is tagged early on as a troublemaker, the label can stick around forever.

Despite efforts to change the term to the slightly more accurate “nonadherent,” the word “noncompliant” remains firmly entrenched in the medical lexicon. No matter what it’s called, however, it’s an enormous problem. Experts estimate that some 50 percent of patients do not take their medicines as prescribed or follow doctors’ recommendations.

When I address this issue with my patients, I – like most doctors — typically ask the basic question, "Are you taking your medications?" and then write down "Yes" or "No." But a recent article in The Annals of Internal Medicine made me rethink that approach.

"It's an immense oversimplification" to reduce compliance to whether or not a patient swallows a pill, says the author, Dr. John Steiner, a researcher at Kaiser Permanente in Colorado.

To illustrate his point, he constructed a chart for a theoretical 67-year-old patient with diabetes, hypertension and high cholesterol and tabulated what it would take to be "adherent" with all medical recommendations.

Besides obtaining five prescriptions and getting to the pharmacy to fill them (and that's assuming no hassles with the insurance company, and that the patient actually has insurance), the patient would also be expected to cut down on salt and fat at each meal, exercise three or four times per week, make it to doctors' appointments, get blood tests before each appointment, check blood sugar, get flu shots – on top of remembering to take the morning pills and then the evening pills each and every day.

Added up, that's more than 3,000 behaviors to attend to, each year, to be truly adherent to all of the doctor's recommendations. Viewed in that light, one can see how difficult it is for a patient to remain fully compliant.

Even if they do succeed in some areas — cutting out salt and taking their blood pressure pills, for example — they may still get chided by their doctors for not exercising, or for missing a colonoscopy appointment.

I once did a small experiment with a group of medical students. We wrote up prescriptions for a number of common medications—metformin, lasix, albuterol, lisinopril, ranitidine. I handed each student two prescriptions and two boxes of Tic Tacs, and instructed them to take the "medicines" for a week. When we met for our next session, I asked them how they did, and they all had abashed expressions on their faces. Not one was able to take every single pill as directed for seven days.

"Be compassionate," Dr. Steiner advises doctors. "Understand what a complicated balancing act it is for patients."

Doctors and patients need to work together to figure out what is reasonable and realistic, prioritizing which measures are most important. For one patient, taking the diabetes pills might be more crucial than trying to quit smoking. For another, treating the depression is more critical than treating the

cholesterol. A water pill may be out of the question for a taxi driver on the road all day; a low-salt diet may be impossible for someone living in a homeless shelter.

“Improving adherence is a team sport,” Dr. Steiner adds. Input from nurses, care managers, social workers and pharmacists is critical.

When I discuss the complicated nuances of adherence with my students, I often offer up the example of my grandmother. A thrifty, no-nonsense woman, she routinely sliced all her pills in half. Whatever the doctor prescribed for blood pressure, cholesterol and heart disease — she took only half the dose. If I suggested she take the pills as instructed, she’d wave me off with, “What do those doctors know, anyway?”

She died suddenly in her home, at age 87, most likely of a massive heart attack. It was a painful loss for all of us. Had she taken her medicines at the appropriate doses, she might have survived the heart attack. But then maybe she would have died a slower and more painful death from some other ailment. Her biggest fear had always been ending up dependent in a nursing home, and by luck or design, she was able to avoid that. Perhaps there was some wisdom in her “noncompliance.”

Danielle Ofri is an associate professor of medicine at New York University School of Medicine and editor in chief of the Bellevue Literary Review. Her most recent book is “Medicine in Translation: Journeys With My Patients.”

Original Research

At a Glance

Effects of a Pharmacy-Care Program on Adherence and Outcomes

Patrick J. Dunham, BSEE; and Jeffrey M. Karkula, RPh, BSPharm

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 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 nonadherence 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.

PRACTICAL IMPLICATIONS

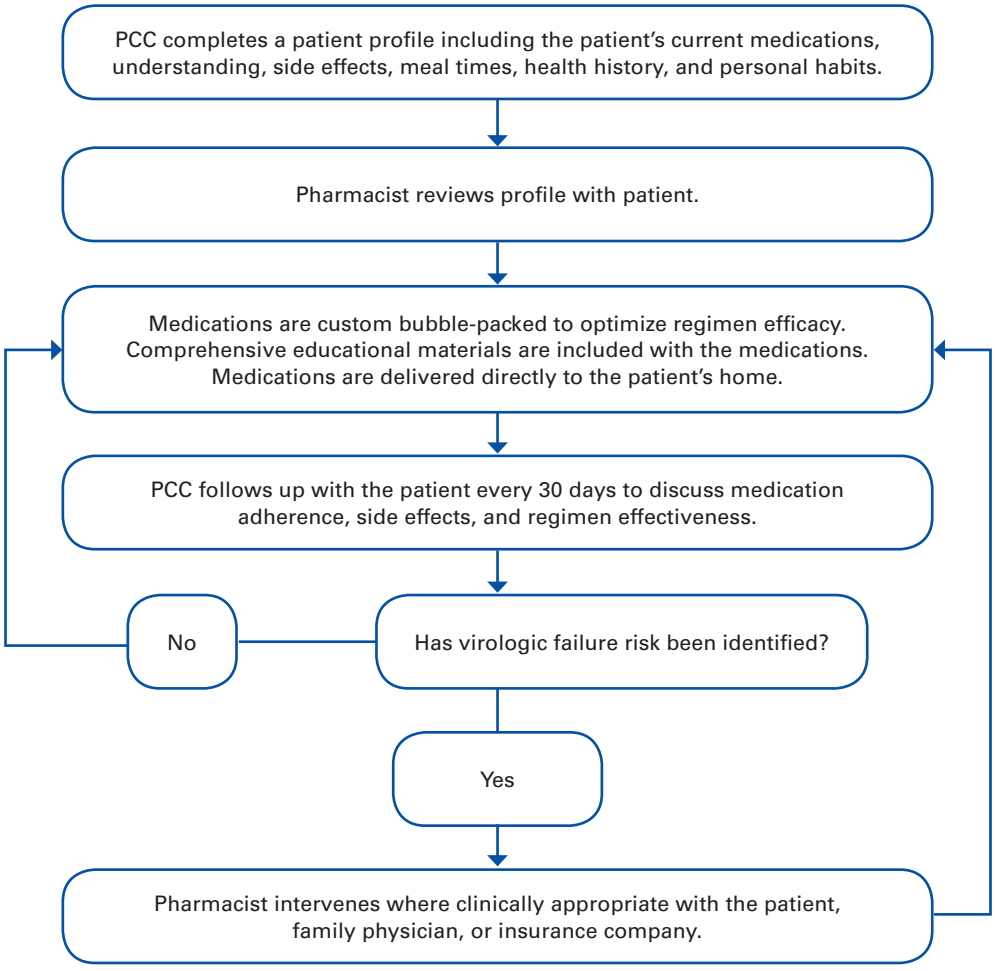
Any discussion of appropriate human immunodeficiency virus therapy must take into consideration the extent of the provided pharmacy services which can best achieve the goals of adherence and improved outcomes.

- 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.

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.[13] 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**.

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.

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 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.

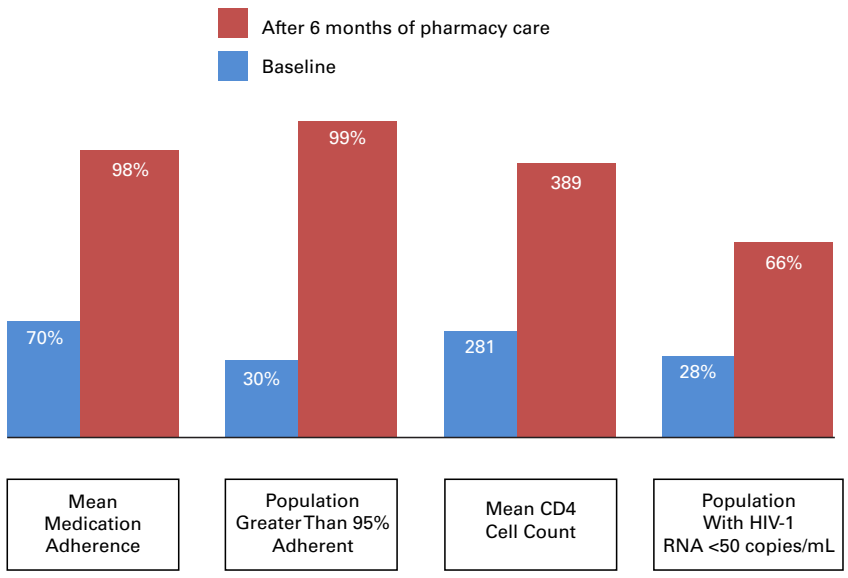
If intervention was necessary, the clinical pharmacist contacted the prescriber, provided clinical recommendations to solve the drug therapy problem identified, documented their activities, and followed up directly with the patient to ensure the problems were resolved. The process repeated every 30 days 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

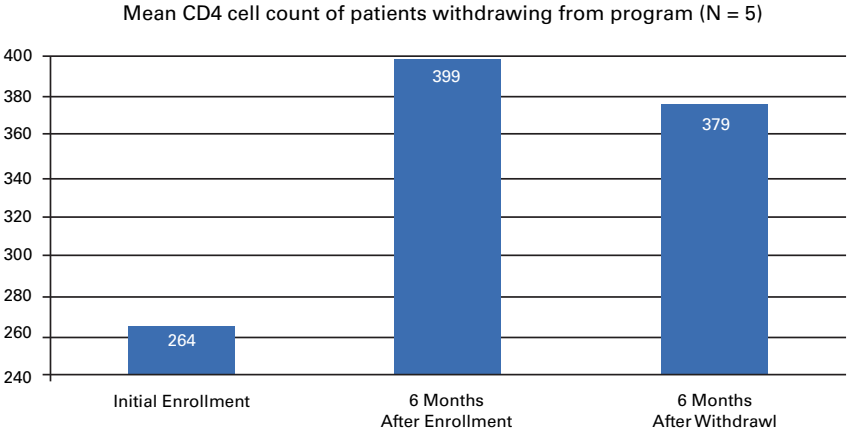
Mean medication adherence was calculated from the medication possession ratio (MPR) (supplies of medication received relative to amount prescribed) by using prescription dispensing records from the specialty pharmacy. MPR has been widely used and validated as a proxy for drug adherence.[14]

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/μL) 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**.

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.

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/µL) 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 studies[18] 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**.

Figure 4. Mean Costs of HIV Care in 2003 Stratified by CD4 Cell Count[14]

CD4 Stratum (cells/µL)	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.

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 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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REFERENCES

1. Bender B, Rand C. Medication non-adherence and asthma treatment cost. *Curr Opin Allergy Clin Immunol*. 2004;4(3):191-195.

2. Rantucci M. *Pharmacists Talking with Patients*. Baltimore, MD: Lippincott, Williams & Wilkins; 2006:41-45.

3. Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA*. 2006;296(6): 679-690.

4. Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JS. The impact of adherence on CD4 cell count responses among HIV-infected patients. *J Acquir Immune Defic Syndr*. 2004;35(3):261-268.

5. Horizons/Population Council, International Centre for Reproductive Health and the Coast Province General Hospital, Mombasa. *Adherence to Antiretroviral Therapy in Adults: A Guide for Trainers*. Mombasa-Kenya: 2004; Module 1:14-22.

6. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med*. 2000;133(1): 21-30.

7. Gross R, Yip B, Lo Re V 3rd, et al. A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression. *J Infect Dis*. 2006;194(8):1108-1114.

8. Malone DC, Abarca J, Skrepnek GH, et al. Pharmacist workload and pharmacy characteristics associated with the dispensing of potentially clinically important drug-drug interactions. *Med Care*. 2007;45(5):456-462.

9. Wisenberg B. Pharmacy benefits managers promote low-cost generics, adherence to drug plans. *Wall Street Journal*. September 17, 2008.

10. *Pharmacy Satisfaction Digest*. Wilson Health Information. 2008;1:4-7.

11. Haskard-Zolnierek KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care*. 2009;47(8):826-834.

12. Chernew ME, Shah MR, Wegh A, et al. Impact of decreasing copayments on medication adherence within a disease management environment. *Health Aff (Millwood)*. 2008;27(1):103-112.

13. Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents*. Department of Health and Human Services. December 1, 2009;1-161.

14. Sikka R, Xia F, Aubert R. Estimating medication persistency using administrative claims data. *Am J Manag Care*. 2005;11(7):449-457.

15. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA*. 2006;296(21):2563-2571.

16. Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med*. 2007;146(10):714-725.

17. Chen RY, Accortt NA, Westfall AO, et al. Distribution of health care expenditures for HIV-infected patients. *Clin Infect Dis*. 2006;42(7):1003-1010.

18. Gebo K, Fleishman J, Conviser R, et al. Contemporary costs of HIV healthcare in the HAART era. Poster presented at: 13th Conference on Retroviruses and Opportunistic Infections. February 5-8, 2006; Denver, CO.

19. Liu H, Golin CE, Miller LG, et al. A comparison study of multiple measures of adherence to HIV protease inhibitors. *Ann Intern Med*. 2001;134(10):968-977. ajpb

Thinking Outside the Pillbox

A System-wide Approach to Improving Patient Medication Adherence for Chronic Disease

A NEHI Research Brief – August 2009

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About the Initiative:

NEHI's project takes a unique, system-wide and multi-stakeholder approach to addressing patient medication adherence, a key issue in the treatment of chronic disease. The goals of the initiative are to first identify and then test strategies that will improve the health of patients with chronic disease and create cost savings.

Introduction

In its 2007 report, "Waste and Inefficiency in the Health Care System – Clinical Care: A Comprehensive Analysis in Support of System-wide Improvements," the New England Healthcare Institute estimated that a full third of the $2.4 trillion spent on health care in the U.S. could be eliminated without reducing the quality of care. The overuse and misuse of medical services and unwarranted practice variation across the country account for much of this waste.

Poor medication adherence – another source of health care inefficiency

Poor medication adherence is increasingly recognized as another significant source of waste in our health care system. Poor adherence often leads to preventable worsening of disease, posing serious and unnecessary health risks, particularly for patients with chronic illnesses. An estimated one third to one half of all patients in the U.S. do not take their medications as prescribed by their doctors.[1] Nonadherence has been shown to result in $100 billion each year in excess hospitalizations alone.[2] NEHI estimates that nonadherence along with suboptimal prescribing, drug administration, and diagnosis could result in as much as $290 billion per year in avoidable medical spending or 13 percent of total health care expenditures.

A problem with many symptoms

Precise definitions of medication adherence vary, but the World Health Organization provides an all-encompassing description of poor adherence: any deviation from the prescribed course of medical treatment. Indicators of poor medication adherence range from a patient's failure to pick up or renew prescriptions, to failure to take prescribed medicine at the prescribed dosage level or at the prescribed interval, to failed persistence and the abandonment of a medication regimen altogether.

Solutions must address many barriers

There are many barriers to medication adherence. Cost, side effects, the challenge of managing multiple prescriptions (polypharmacy), patients' understanding of their disease, forgetfulness, cultural and belief systems, imperfect drug regimens, patients' ability to navigate

the health care system, cognitive impairments, a reduced sense of urgency due to asymptomatic conditions ("I don't feel sick – I don't need the medicine"): all these and more are important barriers to sustained drug adherence.

Adherence and Chronic Disease: Scope of the Problem

Today, more than one half of all Americans live with at least one chronic condition.[3] This percentage is anticipated to rise substantially in coming years as our population ages and health risks such as obesity continue to rise.

Chronic disease and poor adherence are linked

In general, adherence rates are lower among patients with chronic conditions than among those with acute conditions. Likewise, medication persistence – the length of time a patient continues to take a prescribed drug - tends to be very low for those with chronic illness. Studies have shown a significant drop in adherence shortly after a drug is prescribed. Among a large cohort of patients with coronary artery disease, over 25 percent of patients discontinued drug therapy within 6 months.[4] Another study of patients receiving statin drugs found that while adherence was nearly 80 percent within the first three months of treatment, adherence dropped to 56 percent within 6 months and only one in four patients had an adherence level of 80 percent or greater after five years.[5]

Poor adherence leads to poor outcomes

Reaching the improved health outcomes that prescription drugs offer depends on patients following their drug regimens. Patients with chronic disease are particularly vulnerable to poor health outcomes if they do not adhere closely to their medications, with a resultant increase in need for both outpatient medical care and hospitalizations. In a recent study of diabetes and heart disease patients, nonadherent patients had significantly higher mortality rates than adherent patients (12.1 percent versus 6.7 percent) [6] A large observational study of patients with diabetes, hypertension, high cholesterol and congestive heart failure found that for all four conditions, hospitalization rates were significantly higher for patients with low medication adherence.[7] Among diabetes patients, the one-year risk of hospitalization was 13 percent for patients with high adherence and 30 percent for patients with low adherence. Similarly, hypertension patients with high adherence had a 19 percent risk of hospitalization compared to a 28 percent risk for patients with low adherence.

Poor adherence also leads to increased medical costs

This increased risk of hospitalizations due to poor health outcomes translates to significant excess costs. Several studies have found that overall health care costs are much higher for patients with poor adherence. For example, among diabetes patients, those with high levels of adherence had total annual health care costs of $8,886 while patients with low levels of adherence had almost twice the total annual health care costs totaling $16,498.[8]

The system-wide costs of poor adherence are enormous: In 2001, Ernst and Grizzle estimated the annual cost of "drug-related morbidity" in the ambulatory care setting to be

$177 billion, an estimate that encompassed poor adherence, as well as suboptimal prescribing, drug administration, and diagnosis. NEHI has updated this estimate, adjusting the average costs and number of medical events to reflect more current data. NEHI now estimates that the current cost of drug-related morbidity, including poor adherence, to be as much as $290 billion annually. A detailed explanation of NEHI's analysis is available in Appendix I. To put this in context: for a typical mid-sized employer with $10 million in claims, poor adherence may generate avoidable health care spending of about $1 million.

The relevance of adherence policy to U.S. health care reform

Since 75 percent of U.S. health care spending now goes to the treatment of chronic disease, poor adherence should be seen as a serious roadblock to improved efficiency in the health care system, as well as a threat to public health.[9] The debate in Washington over national health care reform provides an ideal opportunity for policymakers to assess the evidence for effective adherence promotion and to link appropriate strategies to the larger goals of health care reform. Several of the major objectives of health care reform are directly relevant to adherence promotion, including payment reform (especially a transition to outcomes-based payments), widespread adoption of health care information technologies, primary care reform and care coordination.

Adherence Initiatives: The Landscape

New initiatives to promote medication adherence have increased as chronic disease management has become a national priority. Improved adherence is a goal of the 2003 Medicare Modernization Act that created the Medicare Part D drug benefit. The legislation promotes creation of Medication Therapy Management services that utilize professional pharmacists to counsel targeted Medicare beneficiaries on their prescription use. Adherence is also an implicit goal of well-known initiatives in chronic care such as the Asheville Project and the Ten-City Challenge of the American Pharmacists Association Foundation (both for diabetes management), and the Medicare disease management pilot program.

Much of the innovation in adherence efforts is not yet scientifically controlled

Some initiatives such as the Medicare demonstration projects have been designed as randomized controlled trials, but a great many of the adherence initiatives now underway in the field are not designed as trials. They are designed primarily to demonstrate the capabilities of specific health care providers in promoting adherence or to demonstrate the utilization of new tools and technologies. For example, the pharmacy profession and the pharmacy industry have developed new tools (such as patient assessment tools) and new initiatives that expand the role of pharmacists and pharmacies in improving adherence. The movement among many corporations towards proactive patient/consumer health management and the use of value-based insurance design (VBID) is demonstrating the use of financial incentives to promote healthier behaviors, including medication adherence. The new generation of Internet, health information technology and communications

technologies have inspired a host of new inventions and entrepreneurial start-ups designed to provide medication adherence prompts and monitoring capability to patients and caregivers.

Research Findings

Literature Review: Findings from Controlled Trials

An examination of findings from randomized, controlled trials provides some suggestive evidence on broad categories of interventions that have proven effective in improving adherence. NEHI derived findings from seven previously performed reviews and a total 40 peer-reviewed studies relevant to adherence among the chronically ill. Appendix II includes a list of the reviews we identified.

Simplified drug regimens
Modifying a patient's drug regimen to reduce the number of pills a patient is required to take at each dose is one way to address adherence. One study found that among hypertension patients, those who took once-daily therapy had 11 percent better adherence (as defined by the percentage of correct doses) than those who took twice-daily therapy.[10] Similar improvements were seen among patients with high cholesterol. Patients prescribed to take their medication twice daily had 10 percent better adherence (as measured by pill counts) than patients with a four times daily dosing schedule.[11]

Patient education
Providing patients with appropriate education has been shown to improve adherence. Education materials generally attempt to provide patients with information about their disease, useful background information on their medications and how they work, and the importance of adherence. Materials may come in the form of educational sessions, videos or written material. One study found that among elderly patients with three or more medications, visits by a pharmacist to provide education improved adherence by nearly 12 percent (adherence defined as the percentage of correct doses).[12] Another study found that providing depression patients with multiple forms of educational materials improved pharmacy refills (a proxy for adherence) by 25 percent.[13]

Case management
While case management comes in many forms, some approaches have been successful in improving medication adherence. Key elements of case management may include instructing patients on how to recognize symptoms and side effects, regular phone calls to monitor and prompt adherence, and regular reviews of clinical reports to check on outcomes and to spot adherence failures. For example, among diabetes patients, those who received bi-weekly automated assessment calls and self-care training by a nurse had 21 percent better adherence (as measured by self report of missed doses) than those patients who received usual care.[14]

Discharge counseling
Patients who receive counseling immediately preceding and/or following a discharge from the hospital are more apt to adhere. Interventions often include in-hospital discharge counseling by a pharmacist or nurse, as well as post-discharge home visits to provide pharmaceutical counseling. One study found that among elderly patients with more than three medications, adherence improved by 43 percent (as defined by self-report of "never missing a dose") among patients who received pharmacist counseling before and after hospital discharge, compared to patients who did not receive the intervention. [15]

Pharmaceutical counseling
Another successful intervention to improve adherence is counseling by community pharmacists. The details of the counseling may vary but likely include a review of the medication list, assessment of patient knowledge about their condition and medications, education on adherence strategies, and suggestions for lifestyle changes to decrease symptoms. One study of patients with heart failure found that among patients who received monthly pharmacist counseling, non-adherence (defined as percentage of missed daily doses) was less than half of that observed among the usual care patients.[16] Similarly, another study of patients with heart failure found that pharmaceutical counseling combined with dose simplification increased adherence by 46 percent ('adherent' defined as medication possession ratios between 80 and 120 percent).[17]

Limitations of the Literature Review
Findings from the literature come with important qualifications and limitations. Very few of the conducted studies are of high methodological quality. Even within the peer reviewed literature, sample sizes tend to be small and follow-up periods are short. Measurements of adherence vary across studies and the focus of studies is often very narrow – focusing on one disease among a specific population. Interventions often include multiple components, making it difficult to determine the exact impact of individual elements of the intervention. Studies examining similar interventions often found conflicting results, making it difficult to draw conclusions about the impact of specific or discrete interventions.

Findings from Expert Interviews: Three Pillars of Improved Adherence

NEHI and analysts from Avalere Health interviewed and examined a total of 34 adherence programs and experts in the field. The interviews provided insights into current initiatives that serve as 'living laboratories' for new adherence practices. A full list of interviews is available in Appendix III.

Findings from the interviews suggest three pillars of improved adherence (see Figure 1). It is important to note that while presented in the following order, these three pillars do not necessarily need to be addressed in this order. Additionally, the relationship between these pillars is not necessarily linear either and for many patients it is important to address and re-address these pillars several times along their care and regimen continuum.

Designing the right medication regimen for the individual patient

The design of a medically appropriate drug regimen for each individual patient is a crucial factor in sustained medication adherence. Medication appropriateness should be considered in the context of all other prescriptions and medical orders to which the patient is subject – not always an easy task when patients have multiple prescriptions written by multiple prescribers. Some experts interviewed by NEHI claim that prescribers could reduce non-adherence to only 10-15 percent simply by getting the correct drug regimen in place.

Reducing drug cost barriers

Out-of-pocket drug costs exert a powerful influence on adherence that is largely independent of other behavior-related factors. The impact of out-of-pocket drug costs has likely increased in recent months. Recent survey data from the Kaiser Family Foundation and the National Business Group on Health suggest that poor adherence has increased since the recession in 2008.[18,19]

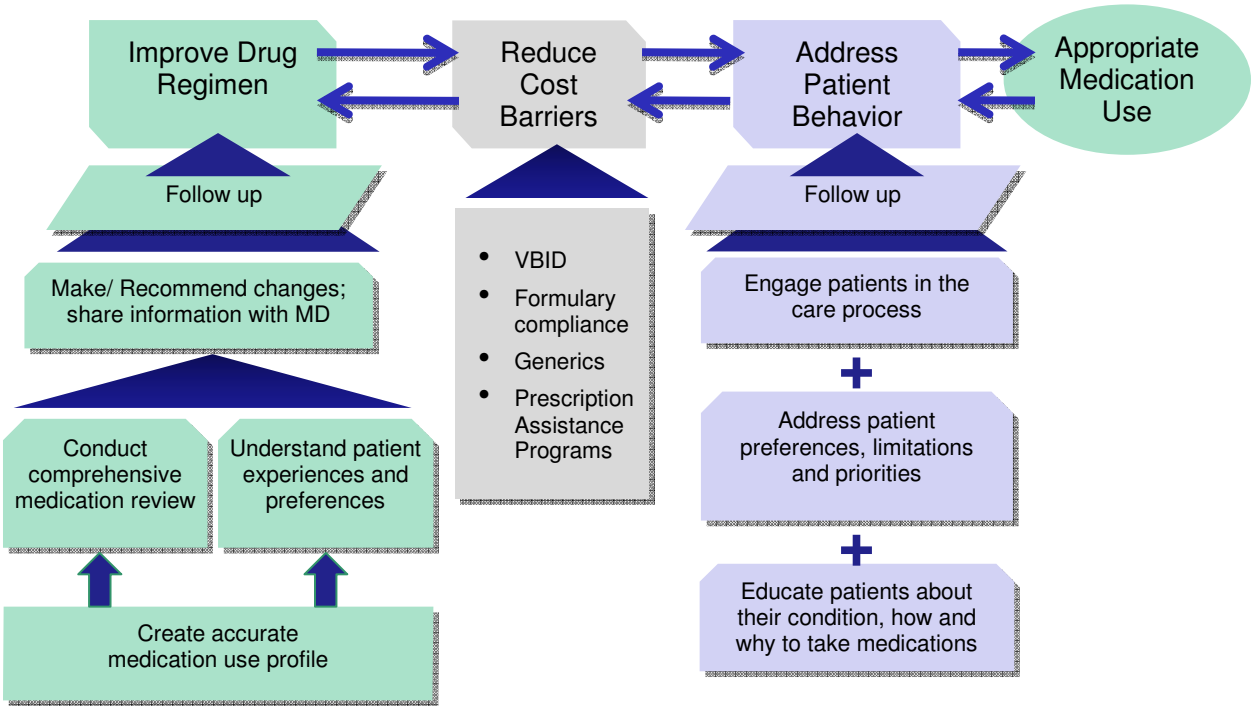
Economists confirm a strong price elasticity of demand between drug costs and adherence (higher costs lead to lower adherence). Many corporations are now seeking to improve adherence and reduce unnecessary medical spending by employing value-based insurance design (VBID) plans that lower employee contributions and out-of-pocket costs for cost effective medications for chronic disease. Experts suggest that lowering medication co-payments for specific chronic conditions can be linked to improved medication possession ratios.

Addressing the behaviors and preferences of individual patients

Experts stress that patients not only vary across a continuum of knowledge (their health literacy, their understanding of their disease and so on), they vary across a continuum of willingness and ability to adhere as well. This variability among patients also extends to patients' proclivity to persist in adherence over time – thus a successful adherence strategy must provide continuity of care and follow-up. The odds that an adherence strategy will be successful are related to how well the strategy can first identify the varying needs of individual patients, and then match services accordingly. An ideal adherence strategy should be patient-centered and holistic taking into account everything from lifestyle to cultural and belief systems.

As a result, promising adherence strategies are invariably multi-component strategies. They do not rely on single 'silver bullet' interventions but typically involve a suite of interventions or services. For example, in many of the programs studied by NEHI, interventions involve one-on-one patient interviews with health care professionals, patient education and follow-up reminder systems.

Figure 1. Three Pillars of Improved Adherence



Source: Avalere Health, NEHI Analysis

Design Principles for Adherence Interventions

Findings from the expert interviews suggest a number of key design principles for medication adherence interventions.

Patient-centered
Adherence interventions should utilize direct contacts with the patient (face-to-face, through telephone or other contact) and should tailor the overall intervention to meet the patient's preferences and address the patient's readiness to adhere to and persist with prescribed medication.

A holistic view of the patient
Adherence interventions should be built around an understanding of the patient's overall medical condition, particularly reconciliation with the patient's full set of prescription drug orders.

Multiple components
Successful interventions should pull together and integrate a complete set of tools and incentives that achieve an optimal drug regimen, overcome cost barriers and address behavior factors unique to each patient.

Physician support and engagement
While interventions may rely on services delivered outside the physician practice (such as pharmacy-based counseling or medication reconciliation), interventions should engage directly with the prescribing physician. Interventions should support the physician with accurate and complete information on the patient and, with appropriate privacy safeguards, gain access to patient data from the doctor that may prove important to the overall intervention.

Continuity of care and follow-up
Follow-up care is crucial if interventions are to overcome the propensity of many patients to drop treatment (failure to persist). Interventions should support patients as they undergo transitions, such as hospital discharges, that may disrupt adherence or reduce the patient's sense of urgency to adhere.

Data and data infrastructure
Few of the design principles outlined here can succeed without making timely and complete data available to patients, physicians and other providers when they need it. Data on patients and on relevant medications must be available at the point of prescription and at every point of patient follow-up. Lack of complete and timely data will hinder the ability of health care providers to identify and track non-adherent patients.

Targeting and stratifying key populations
An ideal, system-wide approach to medication adherence would entail "mass customization" of adherence interventions. Infrastructure would be put in place to serve great numbers of chronically ill or at-risk patients in highly individualized ways. As a practical matter, promising adherence interventions rely heavily on targeting that identifies those patient populations most at risk and most likely to avoid serious illness through improved adherence. Promising interventions also stratify target populations in order to match an appropriate mix of services, from "low-touch" services to "high-touch" services," and thus achieve the highest level of cost effectiveness.

Levers to Improve Adherence: Choices for Policymakers

In the course of our research NEHI identified broad categories of actions that can improve patient adherence, categories we refer to as "levers" to improve adherence. None represent a single, discrete intervention; they must be used in some combination with each other. However, each one represents a fairly discrete investment decision for decisionmakers such as health plans, employers and government agencies. The key decision for policymakers is on which levers to focus, how to weigh the utilization of one lever against others and how the introduction of each should be sequenced within an overall strategy for adherence. NEHI presented these levers to a multi-stakeholder expert panel and audience and asked them to vote on the levers that they would invest in to see the greatest improvement in adherence. Four levers rose to the top: appropriate care teams, patient engagement and education, payment reform and health information

technology. While the remaining six levers received only a small portion of the vote, they are still important and viable options to consider.

Most Promising Levers as Identified by Expert Roundtable

Use of health professionals: assembling appropriate care teams
The adherence process begins with the individual patient and with the prescribing physician. Research and expert interviews underscored the limitations faced by physicians today in promoting adherence, including too-brief encounters with patients, inadequate information on which to act, and limited reimbursement for "cognitive services" like counseling.

As a result, adherence initiatives point in two directions; 1) they provide further support to physicians through physician extenders; or 2) they provide new support outside the physician practice to fill the void in promoting and managing patient medication adherence. Pharmacists and pharmacy researchers have been especially active in the last decade in developing new tools and techniques for meeting the adherence challenge. For example, Medication Therapy Management (MTM) strategies have been largely developed by the pharmacy profession.

Whether an initiative involves providing support to physicians within the phyisician's office or outside the office, such efforts will involve the establishment of some form of care team. There is certainly room for team members from within the traditional physician practice as well as outside.

Programs are using many variants of care teams, but the most fundamental variables relative to care teams are the locus of care and how the care is delivered.

Care teams may be centered:

> Within the physician or medical practice, as exemplified by the patient medical home.
>
> Outside the physician or medical practice, as exemplified by interventions led by pharmacists or pharmacies, such as the Asheville Project, in which pharmacists play a leading role in monitoring and counseling diabetics. Other interventions outside the phyisican or medical practice include those led by third parties, such as health coaching or disease management services led by nurses and other care managers, which may be retained directly by employers or health care payers.

And care team services may be delivered:

- On a face-to-face basis.
- Through telephone-based alternatives, such as call center-based services (utilizing nurses, pharmacists or other professionals), automated voice responses, and/or Web-based services.

The profusion of care team models raises important issues for policymakers. For example, if physician office care teams prove effective, how will physicians make the investments necessary to create care teams? If care teams outside the physician office are effective, then how will the efforts of these teams coordinate with physicians and other clinicians? Finally, experts have noted that providers at all levels are not sufficiently trained to address adherence issues. Thus, how will the care teams of the future be trained to most effectively improve medication adherence?

Some answers to these questions lie in how care teams will utilize tools, incentives and enabling technologies that undergird promising adherence strategies.

Patient Engagement and Education

Experts distinguish between patient "activation," which refers primarily to assessment of the patient, and patient engagement and education, which motivates the patient over time to sustain adherence. Many experts emphasize the importance of ensuring that the patient understands his or her disease, the role and function of their medication, and the importance of good adherence. These interactions should take into account the patient's level of health literacy, as well as language and cultural factors.

Much of the current work that applies patient engagement and education tools to adherence comes out of the pharmacy sector. A leading example is applied motivational interviewing (MI). Experts describe MI as "directive, patient-centered counseling designed to motivate patients for change by helping them recognize and resolve the discrepancy between their behavior, personal goals and values."[20] A recent study found that patients who underwent MI maintained their medication adherence levels over time, compared to a significant decline in adherence among patients who received usual care.[21]

Payment Reform/Pay-for-Performance or Outcomes

Improved adherence is directly relevant to the growing health policy debate over reform of physician and provider reimbursement. The ongoing debate focuses on realigning current health care reimbursement incentives away from rewarding volume (fee-for-service reimbursements) and towards rewarding good outcomes, of which medication adherence may qualify as either a means toward that end or an endpoint itself. Performance-based or global service reimbursements could also serve the purpose of creating incentives for investments that will facilitate adherence, including investment in new staff, adherence-related tools and enabling technologies such as clinical decision support, electronic prescribing and electronic medical records. Given the emerging role of non-physicians such as pharmacists in adherence promotion, payment reform to promote adherence could be extended to non-physicians as well. Currently, community pharmacists are not reimbursed for patient counseling (beyond limited MTM programs) which leaves these providers with little incentive to provide additional adherence-related services.

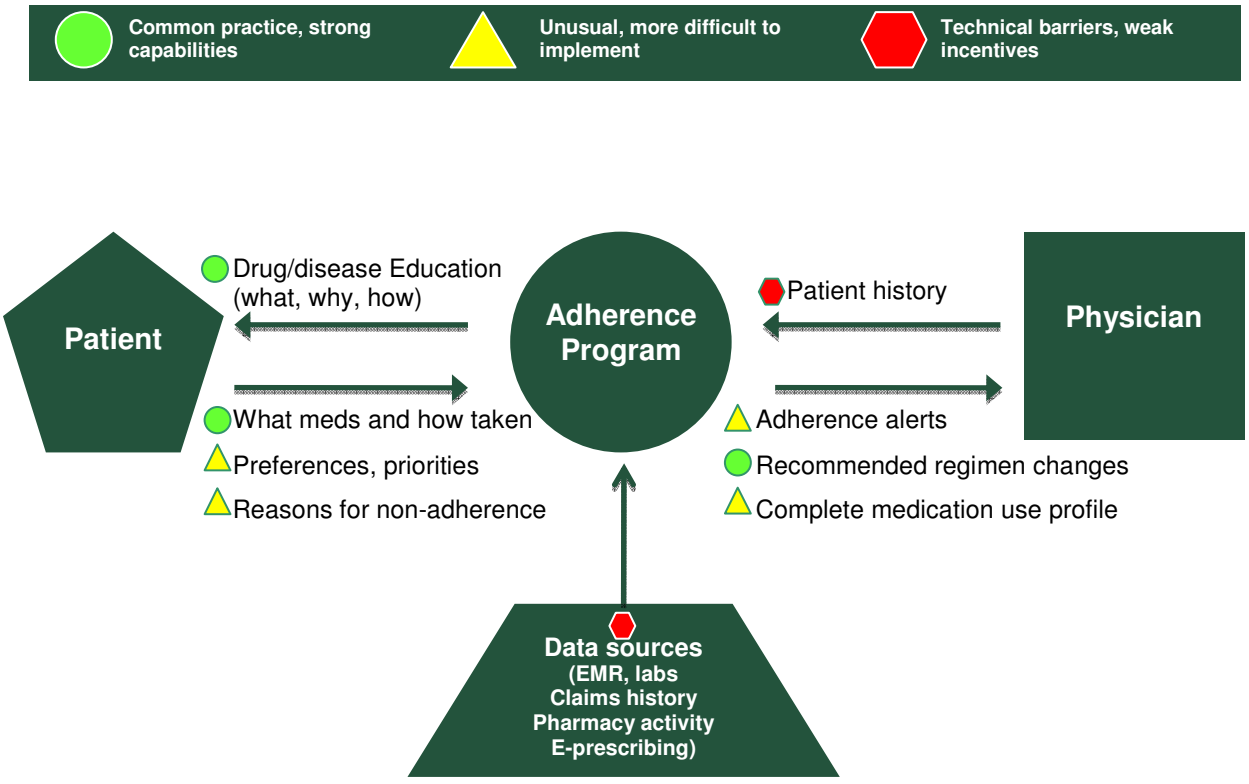
Health Information Technology (Health IT)

Secure, reliable and robust information flows are essential to improved adherence: patients, caregivers, physicians, pharmacists and other professionals need information at the right time and the right place across the medication adherence process. Data is needed to improve physician prescribing decisions and provider follow up, including data on appropriate drug regimens, patient medical and prescribing history, and pharmacy data on medication pick-up and refills. Supporting technologies include electronic health records, e-prescribing and clinical decision support systems.

When used with appropriate security and privacy safeguards, patient data and pertinent pharmacological data is also useful to other stakeholders, including employers and health plans looking to design targeted adherence programs. Accurate and timely data is particularly important as a patient moves throughout the health care system and care is provided by professionals other than the patient's primary care physicians, such as occurs during hospitalizations and/or visits to specialists.

Despite the importance of these data flows, there are significant gaps in how data is currently shared. Figure 2 outlines how adherence-related data moves throughout the health care system, where and between which players data is currently shared as common practice, where data sharing is more difficult to implement and is not as common, and where data flows are inhibited by technical barriers and weak incentives.

Figure 2. Critical Information Flows



Source: Avalere Health, NEHI Analysis

Additional Tools, Incentives and Technologies to Improve Adherence

Medication Reconciliation and Regimen-setting

Some experts believe that a great portion of non-adherence could be corrected if doctors had a comprehensive and accurate medication list of what medications patients are taking and what they should be taking and could tailor a patient's regimen to their preferences and priorities. Given the high number of patients on multiple prescriptions, reconciliation of new drug orders with old orders is essential. While it is not necessarily a new technique, medication reconciliation has assumed new importance as an increasing number of patients are prescribed multiple prescription medicines, often by multiple prescribing physicians. A recent study found that multiple providers increased the risk of an adverse drug event, many of which may be related to poor adherence. Each additional provider prescribing medications increased the odds of such an event by 29 percent.[22]

Doctors are frequently at a disadvantage in reconciling medications, as multiple prescriptions are often prescribed by multiple doctors who may or may not communicate with each other. Yet reconciliation can be as straightforward as asking patients to bring all their medications in a paper bag for the doctor or pharmacist to review. A more systematic approach to medication reconciliation and good regimen design will require use of other levers identified below, including the circulation of timely and accurate data through health information technology and supportive payment policies that allow doctors or other providers – including pharmacists – to review patient medication regimens. Medication Therapy Management (MTM) programs have focused on this aspect of adherence improvement, but have important limitations. MTM programs are only for Medicare and Medicaid patients with very complex regimens, provide counseling only once a year, and follow-up is not required.

Patient Assessment

Adherence experts emphasize that understanding the needs, preferences and medication history of the individual patient is critical to improving adherence. Patient assessment begins with understanding a patient's existing and complete prescription history so that a patient's overall prescription regimen can be reviewed and optimized.

Patient assessment techniques extend to issues of patient behavior and patient preferences. An increasing number of psychometric tools and surveys allow health care teams to predict a patient's likely adherence patterns or assess the patient's readiness to change adherence behaviors. For example, the "Adherence Estimator" developed by Colleen McHorney and others at Merck and Company is a three-item test that measures "intentional non-adherence," specifically medication non-fulfillment and non-persistence.[23] Also, "patient activation" tools have been pioneered by Dr. Judith Hibbard and colleagues at the University of Oregon. "Activation" refers to the patient's ability and willingness to take on the role of

managing their health and health care.[24] The Patient Activation Measure (PAM) determines a patient's knowledge, skill and confidence in managing their health. Research has shown that a patient's level of activation correlates with adherence. As such, some providers are now administering the PAM, both online and in the physician's office, as a screening tool to identify patients who are likely to be nonadherent. Once providers have this information, they may choose to provide the patient with additional services or refer them to another program. Assessment of the patient's level of "activation" may extend to his or her ability to pay for prescription medicine and hence to the prescriber's ability to make the drug regimen affordable for the patient. For instance, based on a patient's level of "activation" a provider may choose to prescribe a simplified drug regimen, recommend a patient assistance program, start a patient on a generic form of a drug or recommend the use of mail order.

Plan Design/Value-based Insurance Design

Employers in the U.S. are increasingly taking a new approach to managing health care benefit costs by designing health insurance benefit programs that provide employees with incentives to utilize preventive medicine and wellness services. Adherence is an implicit goal of many such programs, and could well become an explicit goal if employers and health care payers gain greater confidence in the effectiveness of adherence interventions. Value-based insurance design (VBID) programs reduce employee cost sharing for high value services that prevent or encourage good management of chronic diseases. Accordingly, many employers are offering to reduce employees' costs for highly effective medications for specific chronic conditions such as diabetes and asthma.

Other Employer-sponsored Incentives

Adoption of VBID plans is one manifestation of a larger movement among employers and health care payers to utilize direct financial incentives to promote preventive medicine and healthier lifestyles. Current practices include differential premium contribution levels for employees who participate in wellness activities or maintain good behaviors, and one-time or annual rewards for specific activities (many employers offer rewards for employees who self-administer a Health Risk Assessment). Other incentives are designed to reward adherence among employees/patients enrolled in specific disease management programs, or to provide employees with enhanced benefits in exchange for participation in activities, such as health coaching, that promote adherence and other health goals.

Redirecting Manufacturer Rebates

Pharmaceutical manufacturers engage in direct negotiations with purchasers (health plans, pharmacy benefit managers, some employers) to provide access to specific drugs for specific tiers on a drug formulary. Interest is growing among some manufacturers in securing placement of drugs on health plan formularies and linking discounts and rebates for the drugs to improved adherence among patients. From the manufacturer's standpoint the cost of discounts and rebates will be offset

by increased revenues resulting from improved adherence. For example, Merck and Cigna recently announced a new deal under which Merck will provide discounts on its diabetes drugs to Cigna if the health insurer's diabetic members adhere to their diabetes medications. This approach is a 'lever of levers' in that it could provide financing for direct adherence initiatives deployed downstream, among patients, physicians, pharmacists and others.

Another way to redirect manufacturer rebates is to provide rebates/other financial incentives directly to the patient. These financial incentives could come in the form of reduced health insurance premiums or co-payments for patients adherence closely to their medications.

Technologies for Reminders and Monitoring

Technologies to facilitate adherence have greatly increased in recent years, enabled in part by Internet, cellular telephone and automated voice advances. The new technologies create new capabilities to remind patients to take medications at prescribed times and to monitor adherence from remote locations. Examples include customizable messaging systems that contact patients by phone, email or text message, electronic pill bottles and caps, electronic medication dispensers and boxes, mobile phone applications, and in-home monitoring devices. Many of these technologies also have the capability to transmit data back to the provider's office and/or pharmacy as well as to place prescription refill requests. Some technology vendors are linking products to call centers that provide patients with immediate access to health care professionals.

Conclusion

Patient medication adherence is a complex problem for which no simple and over-arching solutions have yet appeared. Promising approaches have emerged in peer-reviewed literature and in targeted initiatives and programs that appear in different areas within the health care system. But questions remain as to whether even the most promising approaches can be scaled-up to a point where major advances in adherence can occur throughout the system.

A fundamental question is whether poor adherence can and should be addressed as a stand-alone issue, or whether it is best addressed more indirectly by intensifying effort on other health policy reforms and calibrating those reforms so as to promote adherence. For example, fundamental payment reform that rewards outcomes should have the effect of promoting adherence. A strong nationwide investment in health IT should have the effect of providing patients and clinicians with information they currently lack to devise appropriate drug regimens and provide adequate follow-up. The ongoing movement to improve health care quality by tracking metrics of quality should encompass metrics of adherence.

What is needed now is greater awareness of the adherence crisis, a careful effort to make adherence a goal and a measure of progress for U.S. health care reform, and new effort to generate data on scalable, real-world solutions. NEHI looks forward to educating public and private policymakers on the scope of the adherence crisis, and on sound, data-based findings from tested adherence interventions in the months ahead.

About the New England Healthcare Institute

The New England Healthcare Institute (NEHI) is a nonprofit, health policy institute focused on enabling innovation that will improve health care quality and lower health care costs. Working in partnership with members from across the health care system, NEHI brings an objective, collaborative and fresh voice to health policy. We combine the collective vision of our diverse membership and our independent, evidence-based research to move ideas into action.

Appendix I: Estimated Cost of Poor Adherence

We sought to update the annual cost of drug-related morbidity and mortality using the model developed by Johnson and Bootman in 1995 and updated by Ernst and Grizzle in 2000. As in the 2000 update, we used the same decision-analytic model design and probability data, but changed the estimated average costs and number of medical events to reflect more current data. Whenever possible we used data from the same year, primarily 2007; some data was used from 2004, 2006 and 2008. Because earlier data was used, the total figure may be an underestimate.

The study estimated the likelihood of a patient experiencing one or more drug-related problem (DRP) in the ambulatory care setting and the cost of the subsequent negative outcomes. Specifically, DRPs included untreated indication, improper drug selection, subtherapeutic dosage, failure to receive drugs, overdosage, adverse drug events, drug interactions, and drug use without indication. The study did not delineate poor adherence from other DRPs, so the estimate includes the overall impact of all DRPs. There are five possible negative outcomes in the Johnson and Bootman model that create additional costs to the system (the two that do not are death and no treatment): an additional physician visit, additional treatment, ED visit, hospital admission or LTC admission. We replicated the Johnson and Bootman method for determining the number of events by multiplying the cumulative conditional probabilities for each of the six outcomes by the 2008 number of total physician visits estimated by the CDC, which was 901,954,000. The results of this calculation are listed in the table.

Whenever possible, cost updates came from the same sources used by Ernst and Grizzle. The average cost of a hospital admission, $17,271, was determined by dividing total hospital revenue in 2007 by the total number of admissions in the same year, figures obtained from the American Hospital Association. The average cost of a physician visit, from the Agency for Healthcare Research and Quality (AHRQ), was $155 in 2004, $46 more than in 2000. The average cost of an ED visit, $993, was also obtained from 2006 AHRQ data. Using 2007 Kaiser Family Foundation data to divide total reported sales by the total number of prescriptions sold, the average prescription cost was updated from $42 to approximately $58. Finally, the average cost of a long-term care admission was updated using 2008 data from the U.S. Department of Health and Human Services. The average daily expenditures on nursing homes and assisted living facilities were averaged and multiplied by the average length of stay, producing a figure of $13,761, which is $4,272 more than the 2000 reported figure.

The updated cost estimate, approximately $289 billion, was obtained by multiplying the number of events for each possible outcome by each respective cost estimate. This is a rough estimate of the increase in costs between 2000 and 2008, and is intended to be used as such.

Summary of Cost of Illness for Drug-Related Morbidity and Mortality				
	No. of Events (millions)	**Cost per Event**	**Total Cost (billions)**	**% Increase Since 2000**
Total Physician Visits	156.9	$155	$24.2	57%
Total Hospital Admissions	11.5	$17,271	$197.8	61%
Total ED Visits	23.5	$993	$23.3	24%
Total LTC Facility Admissions	4.3	$13,761	$58.8	56%
Total Additional Prescriptions	100.3	$58,49	$5.9	60%
Total Deaths	1.1	--	--	--
Total	**--**	**--**	**$289.0**	**161%**

Appendix II: Review Articles

Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews 2008(2).

Higgins N, Regan C. A systematic review of the effectiveness of interventions to help older people adhere to medication regimes. Age Ageing 2004 May;33(3):224-9.

Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007 Mar 26;167(6):540-50.

Krueger KP, Berger BA, Felkey B. Medication adherence and persistence: a comprehensive review. Adv Ther 2005 Jul-Aug;22(4):313-56.

McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. JAMA 2002 Dec 11;288(22):2868-79.

Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005 Aug 4;353(5):487-97.

Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. Am J Health Syst Pharm 2003 Apr 1;60(7):657-65.

Appendix III: Expert Interviews

Programs and Organizations Examined and Analyzed

Amgen
Blue Cross Blue Shield of Massachusetts
BlueCross BlueShield of South Carolina
Boston Scientific
Community Care of North Carolina
Continua Health Alliance
CVS Caremark
EMC Corporation
Geisinger Health System
Group Health
Innovation Rx
Kaiser Permanente
Kerr Drugs
Medco
Medication Management, LLC
Medication Management Systems
Novartis
Outcomes
Partners HealthCare
Mount Sinai Hospital, Chicago
Surescripts
Thomson Reuters
Varolii
Vitality

Additional Experts Consulted

Bruce Bagley, MD, *Director, Quality Improvement,* American Academy of Family Physicians

Bruce Berger, PhD, *Professor and Department Head, Pharmacy Care Systems,* Auburn University Harrison School of Pharmacy

Ray Bullman, *Executive Vice President,* National Council on Patient Information and Education

Michael E. Chernew, PhD, *Professor of Health Care Policy, Department of Health Care Policy,* Harvard Medical School

Mark Fendrick, MD, *Professor, Division of General Medicine, Department of Internal Medicine and Department of Health Management and Policy,* University of Michigan

Brian Haynes, MD, PhD, *Professor, Department of Clinical Epidemiology and Biostatistics; Chief, Health Information Research Unit,* McMaster University

Judith Hibbard, PhD, *Senior Researcher, Institute for Policy Research and Innovation; Professor, Department of Planning, Public Policy & Management,* University of Oregon

David Hom, *President,* David Hom, LLC

Eve Slater, MD, *Associate Clinical Professor of Medicine,* Columbia College of Physicians & Surgeons

Norrie Thomas, PhD, RPh, *Executive Vice President, Business Development,* HWB, Inc.

Notes and References

[1] Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005 Aug 4;353(5):487-97.
[2] *Ibid.*
[3] Robert Wood Johnson Foundation. Chronic conditions: Making the case for ongoing care. September 2004.
[4] Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. JAMA. 2002 Jul 24-31;288(4):462-7.
[5] Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. JAMA. 2002 Jul 24-31;288(4):455-61.
[6] Ho PM, Magid DJ, Masoudi FA, McClure DL, Rumsfeld JS. Adherence to cardioprotective medications and mortality among patients with diabetes and ischemic heart disease. BMC Cardiovasc Disord. 2006 Dec 15;6:48.
[7] Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care. 2005 Jun;43(6):521-30.
[8] *Ibid.*
[9] CDC. Chronic Disease. Available online: http://www.cdc.gov/nccdphp/overview.htm
[10] Mounier-Vehier C, Bernaud C, Carre A, Lequeuche B, Hotton JM, Charpentier JC. Compliance and antihypertensive efficacy of amlodipine compared with nifedipine slow-release. Am JHypertens. 1998;11(4 pt 1):478-486.
[11] Brown BG, Bardsley J, Poulin D, Hillger LA, Dowdy A, Maher VM, Zhao XQ, Albers JJ, Knopp RH. Moderate dose, three-drug therapy with niacin, lovastatin, and colestipol to reduce low-density lipoprotein cholesterol <100 mg/dl in patients with hyperlipidemia and coronary artery disease. Am J Cardiol. 1997 Jul 15;80(2):111-5.
[12] Lowe CJ, Raynor DK, Purvis J, Farrin A, Hudson J. Effects of a medicine review and education programme for older people in general practice. Br J Clin Pharmacol. 2000 Aug;50(2):172-5.
[13] Katon W, Rutter C, Ludman EJ, Von Korff M, Lin E, Simon G, Bush T, Walker E, Unützer J. A randomized trial of relapse prevention of depression in primary care. Arch Gen Psychiatry. 2001 Mar;58(3):241-7.
[14] Piette JD, Weinberger M, McPhee SJ, Mah CA, Kraemer FB, Crapo LM. Do automated calls with nurse follow-up improve self-care and glycemic control among vulnerable patients with diabetes? Am J Med. 2000 Jan;108(1):20-7.
[15] Lipton HL, Bird JA. The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial. Gerontologist. 1994 Jun;34(3):307-15.
[16] Bouvy ML, Heerdink ER, Urquhart J, Grobbee DE, Hoes AW, Leufkens HG. Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: a randomized controlled study. J Card Fail. 2003 Oct;9(5):404-11.
[17] Varma S, McElnay JC, Hughes CM, Passmore AP, Varma M. Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. Pharmacotherapy. 1999 Jul;19(7):860-9.
[18] Kaiser Family Foundation. Many Americans still delaying care, struggling to pay medical bills. April 2009
[19] National Business Group on Health. NBGH survey finds recession driving many American workers to make lifestyle changes to help control health care costs. May 27, 2009
[20] Rollnick S, Miller W. What is Motivational Interviewing? Behav Cogn Psychter 1995; 23:325-224.
[21] Ogedegbe G, Chaplin W, Schoenthaler A, Statman D, Berger D, Richardson T, Phillips E., et al. A practice-based trial of motivational interviewing and adherence in hypertensive African Americans. Am J Hypertens. 2008 Oct;21(10):1137-43. Epub 2008 Jul 24.
[22] Green JL, Hawley JN, Rask KJ. Is the number of prescribing physicians an independent risk factor for adverse drug events in an elderly outpatient population? Am J Geriatr Pharmacother. 2007 Mar;5(1):31-9.
[23] McHorney C. The adherence estimator: Abrief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. Current Medical Research and Opinions. 2009; 25(1):215-238.
[24] Hibbard J, Cunningham P. How engaged are consumers in their health and health care, and why does it matter? Res Briefs. 2008 Oct;(8):1-9.

ORIGINAL CONTRIBUTION

Effect of a Pharmacy Care Program on Medication Adherence and Persistence, Blood Pressure, and Low-Density Lipoprotein Cholesterol

A Randomized Controlled Trial

Jeannie K. Lee, PharmD
Karen A. Grace, PharmD
Allen J. Taylor, MD

Context Poor medication adherence diminishes the health benefits of pharmacotherapies. Elderly patients with coronary risk factors frequently require treatment with multiple medications, placing them at increased risk for nonadherence.

Objective To test the efficacy of a comprehensive pharmacy care program to improve medication adherence and its associated effects on blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C).

Design, Setting, and Patients A multiphase, prospective study with an observational phase and a randomized controlled trial conducted at the Walter Reed Army Medical Center of 200 community-based patients aged 65 years or older taking at least 4 chronic medications. The study was conducted from June 2004 to August 2006.

Intervention After a 2-month run-in phase (measurement of baseline adherence, BP, and LDL-C), patients entered a 6-month intervention phase (standardized medication education, regular follow-up by pharmacists, and medications dispensed in time-specific packs). Following the intervention phase, patients were randomized to continued pharmacy care vs usual care for an additional 6 months.

Main Outcome Measures Primary end point of the observation phase was change in the proportion of pills taken vs baseline; secondary end points were the associated changes in BP and LDL-C. Primary end point of the randomization phase was the between-group comparison of medication persistence.

Results A total of 200 elderly patients (77.1% men; mean [SD] age, 78 [8.3] years), taking a mean (SD) of 9 (3) chronic medications were enrolled. Coronary risk factors included drug-treated hypertension in 184 patients (91.5%) and drug-treated hyperlipidemia in 162 (80.6%). Mean (SD) baseline medication adherence was 61.2% (13.5%). After 6 months of intervention, medication adherence increased to 96.9% (5.2%; $P<.001$) and was associated with significant improvements in systolic BP (133.2 [14.9] to 129.9 [16.0] mm Hg; $P=.02$) and LDL-C (91.7 [26.1] to 86.8 [23.4] mg/dL; $P=.001$). Six months after randomization, the persistence of medication adherence decreased to 69.1% (16.4%) among those patients assigned to usual care, whereas it was sustained at 95.5% (7.7%) in pharmacy care ($P<.001$). This was associated with significant reductions in systolic BP in the pharmacy care group (−6.9 mm Hg; 95% CI, −10.7 to −3.1 mm Hg) vs the usual care group (−1.0 mm Hg; 95% CI, −5.9 to 3.9 mm Hg; $P=.04$), but no significant between-group differences in LDL-C levels or reductions.

Conclusions A pharmacy care program led to increases in medication adherence, medication persistence, and clinically meaningful reductions in BP, whereas discontinuation of the program was associated with decreased medication adherence and persistence.

Trial Registration clinicaltrials.gov Identifier: NCT00393419

JAMA. 2006;296:(doi:10.1001/jama.296.21.joc60162) www.jama.com

ADHERENCE TO CHRONIC PHARmacological therapies is poor,[1-3] leading to worsening disease severity and increased costs associated with higher hospital admission rates.[4,5] Barriers to medication adherence are numerous, but include the prescription of complex medication regimens, treatment of asymptomatic conditions, and convenience factors.[6] These factors are particularly prevalent among the elderly population, placing them at increased risk for medication nonadherence. Because approaches to improve adherence can be complex and labor intensive,[7] there are no accepted, fully effective strategies in widespread clinical use. Moreover, in elderly patients, effective strategies to improve adherence have not been investigated, and an effect on meaningful health outcomes has not been identified.

The Federal Study of Adherence to Medications in the Elderly (FAME) was a multiphase, single-center study of the efficacy of a comprehensive pharmacy care program, which included patient education and an adherence aid (medications custom-packaged in blister packs) to improve medication adherence among military health care beneficiaries aged 65 years

See related editorial.

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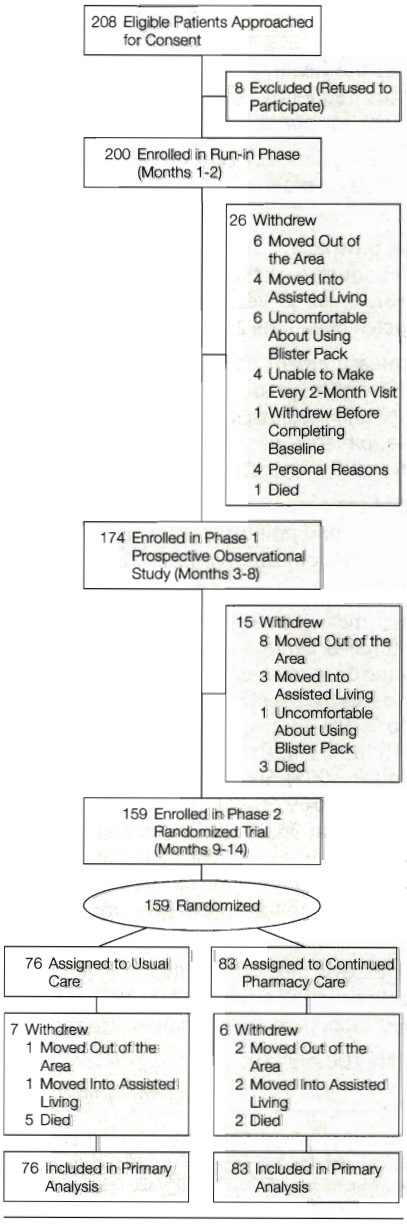
or older who were prescribed at least 4 chronic medications per day. We further tested the impact of this program on blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C), biomarkers of the efficacy of pharmacotherapy to lead to optimal cardiovascular health outcomes.

Figure 1. Flow of Patients Through the Study Protocol



METHODS

Study Population

The FAME trial follows the specifications of the revised CONSORT criteria.[8] This trial was a single-center study conducted at the Walter Reed Army Medical Center, a university-affiliated, suburban, tertiary care US military medical center. Eligible patients were recruited from the outpatient general medicine service and the Armed Forces Retirement Home, an affiliated retirement home of approximately 900 independently living military health care beneficiaries located in Washington, DC, and were elderly men and women (≥65 years) taking 4 or more chronic medications daily, a population selected as being at increased risk for medication nonadherence. Patients were excluded if they did not live independently (assisted living or nursing home residents were excluded) or in the presence of any serious medical condition for which 1-year survival was expected to be unlikely.

The Walter Reed Army Medical Center Department of Clinical Investigation, which is composed of the Clinical Investigation Committee, Human Use Committee, and the Central Investigative Regulatory Office, approved the study. Among 208 eligible patients approached for written informed consent, 200 patients volunteered to participate and 8 refused. Study patients were observed at the pharmacy clinics at both the Walter Reed Army Medical Center and Armed Forces Retirement Home. Study enrollment began on June 30, 2004, and was completed on July 6, 2005. The last follow-up visit occurred on August 30, 2006.

Study Design

The FAME study consisted of 3 phases (run-in phase, phase 1 [prospective, observational study], and phase 2 [randomized controlled trial]), with a follow-up period of 14 months. The flow of patients through the trial is shown in FIGURE 1. The intent was for all volunteers to participate in all 3 phases of the study.

During the run-in phase (initial visit through 2 months), data collection included baseline demographics, self-reported race according to categories of the US Census Bureau (for descriptive purposes), medication lists, measurement of baseline medication adherence (measured at both 1 and 2 months), BP (initial visit and 2 months), and LDL-C (initial visit and 2 months). Baseline medication adherence during the run-in phase was assessed for all chronic medications using pill counts, expressed as the percentage of pills taken relative to the number of pills that should have been taken.

During the run-in phase, no specific educational or adherence interventions were performed. Baseline medication adherence was defined as the mean value of the 1- and 2-month adherence assessments.

Baseline BP and LDL-C levels were measured twice (initial visit and 2 months), with the mean representing the baseline value for subsequent comparisons. For all time points (run-in phase, phase 1, and phase 2), the clinical pharmacist meeting with the patient used a calibrated, automated sphygmomanometer to obtain the BPs. Blood pressure was measured 3 times, each 2 minutes apart, in the seated position. Measured BP was calculated as the mean of the second and third BP values. Serum, collected for the measurement of LDL-C, was processed at a single laboratory located in Walter Reed Army Medical Center using a direct assay, eliminating the need for fasting. Other lipid values were not defined end points of our study and therefore were not measured. The rationale for this was the prevalent use of statins in clinical practice as the principle mode of therapy for hyperlipidemia aimed at reducing LDL-C.

Following successful completion of the run-in phase, all patients entered phase 1 (3-8 months), a prospective, observational study of a comprehensive pharmacy care program. The comprehensive pharmacy care program consisted of 3 elements, including individualized medication education (using standardized scripts), medications dispensed using an adherence aid (blister packs) (FIGURE 2), and regular fol-

low-up with clinical pharmacists every 2 months. Individualized educational interventions were performed to teach participants their drug names, indications, strengths, adverse effects, and usage instructions during each visit. The initial visit was scheduled for 1 hour. Subsequent visits (including adherence assessments, education as needed, and prescription refills) were scheduled for 30 minutes.

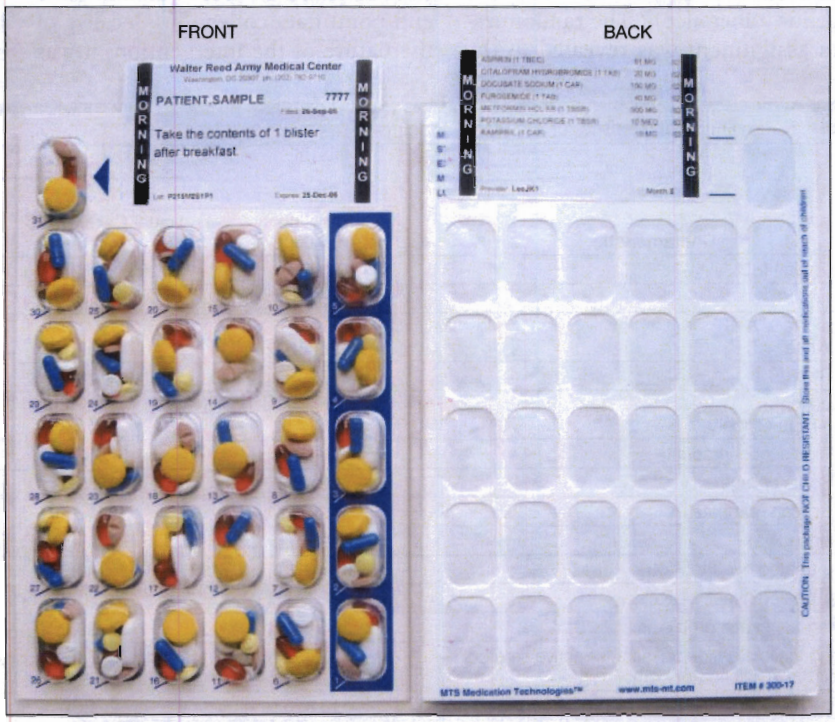
At the start of this phase, all pill bottles were confiscated and discarded. Thereafter, all medications were provided to patients in customized blister packs (Figure 2) filled by pharmacy technicians at the main outpatient pharmacy using a commercially available system and checked by clinical pharmacists. Each blister pack, with 31 numbered blisters, was labeled using a customized computer program to meet the standards of the prescriptions. Two blister packs per dosing time (a 2-month supply) were dispensed at each study visit. Patients were instructed to tape any medications not taken back into the blister pack, to account for any selective adherence.

During follow-up visits, blister-packed medications were counted, including medications not taken (taped back into the blister pack). Study personnel did not adjust medications or their dosages. At 3 times during this phase (4, 6, and 8 months), pill counts were performed, using the blister packs, for all participants. At the end of this phase (study month 8), repeat measurements of BP and LDL-C of the participants were performed.

Patients successfully completing phase 1 entered phase 2, a 6-month randomized clinical trial evaluating the relationship between the method of medication administration and sustained medication adherence (persistence). Patients were randomized in a 1:1 ratio to either a return to usual care or continued pharmacy care. Usual care was defined as returning to their baseline (prestudy) status of medication provision; however, medication education and blister-packed medications were not provided. At the end of phase 1, participants had none of their chronic medications. For the usual care group in phase 2, all medications were provided in new pill bottles with a 90-day supply and 1 refill prescription. Participants were directly provided their medications by study personnel; therefore, there was exact accounting of the prescription fill date. The proportion of pills taken, using these pill bottles, was assessed at the end of the study at 14 months when the patients randomized to the usual care group returned for the final study visit.

Patients randomized to the pharmacy care group continued to meet with clinical pharmacists every 2 months, as previously performed in phase 1 of the study, and were provided blister-packed medications and also continued medication education as needed. An assessment of the proportion of pills taken was measured using the blister packs at 10, 12, and 14 months for patients randomized to the continued pharmacy care group. Blood pressure and LDL-C were measured at the conclusion of phase 2 (study month 14) to note the associated changes in these outcome markers with the changes in medication adherence observed between the 2 randomized groups.

Figure 2. Sample Blister Pack of Medications for Morning



The multidose adherence package enables clear packaging and labeling of multiple medications in a disposable, punch card format. The translucent blister facilitates visual verification of the card content. This medication packaging organizes the patients' pills according to the daily dosing time and prevents them from working with multiple medication bottles. Patients received combinations of morning, noon, evening, or bedtime blister packs according to their regimen. Patients took the numbered blister that matched the day of the month.

Randomization

Patients were randomized to either usual care or continued pharmacy care in a 1:1 ratio using a computer-generated random number sequence. Allocation was concealed to both patients and the study personnel who enrolled participants by central control of the randomization sequence. Patients were randomized in blocks

based on the level of baseline medication adherence (above or below 55% baseline adherence).[9] The randomization assignment was revealed to the participants at the 8-month study visit (end of phase 1) after completing the end point data collection. Because of the nature of the intervention, it was not possible to blind either the participants or the clinical pharmacists assessing the outcomes to the study group assignment.

Table 1. Baseline Characteristics of the Elderly Patients*

Characteristic	Baseline (n = 200)	Phase 2: Randomization		P Value†
		Usual Care Group (n = 76)	Continued Pharmacy Care Group (n = 83)	
Age, mean (SD), y	78 (8.3)	78 (6.2)	77 (10.5)	.45
Men	155 (77.1)	56 (73.7)	62 (74.7)	.51
Race				
White	128 (63.7)	43 (56.6)	51 (61.4)	.24
Black	65 (32.3)	31 (40.8)	29 (34.9)	
Education				
<High school	15 (7.5)	9 (12.9)	3 (3.7)	.11
High school graduate	68 (33.8)	27 (38.6)	26 (32.1)	
Some college	63 (31.3)	21 (30.0)	32 (39.5)	
College graduate	43 (21.4)	13 (18.6)	20 (24.7)	
Unknown‡	11 (5.5)	6 (7.9)	2 (2.4)	
Drug-treated hypertension	184 (91.5)	69 (90.8)	77 (92.8)	.43
Drug-treated hyperlipidemia	162 (80.6)	61 (80.3)	69 (83.1)	.40
Having ≥4 health problems	115 (57.2)	38 (50.0)	52 (62.7)	.07
Taking tricyclic antidepressant, selective serotonin reuptake inhibitor, or both	33 (16.4)	6 (7.9)	17 (20.5)	.03
Taking medication for memory problems	13 (6.5)	2 (1.3)	6 (3.8)	.28
Medication practice at study entry				
Taking multiple doses (≥3 per d)	78 (38.8)	27 (35.5)	31 (37.3)	.47
Receiving help with taking medications	34 (16.9)	12 (15.8)	19 (22.9)	.18
Using pill box	117 (58.2)	37 (48.7)	51 (61.4)	.07
Using medication chart or list	40 (19.9)	10 (13.2)	22 (26.5)	.03
No. of chronic medications, mean (SD)	8.7 (3.1)	8.3 (2.8)	9.1 (3.2)	.12
Baseline medication adherence at completion of run-in phase (n = 179), mean (SD)	61.2 (13.5)	61.1 (14.1)	61.4 (13.0)	.88
Medications				
β-Blocker	95 (47.3)	43 (56.6)	48 (58.5)	.46
ACE inhibitor	101 (50.2)	39 (51.3)	55 (67.1)	.03
Calcium channel blocker	74 (36.8)	31 (40.8)	36 (43.9)	.41
Angiotensin II receptor blocker	22 (10.9)	13 (17.1)	7 (8.5)	.08
Clonidine	9 (4.5)	5 (6.6)	4 (4.9)	.45
Thiazide diuretic	52 (25.9)	24 (31.6)	25 (30.5)	.51
Furosemide	44 (21.9)	19 (25.0)	20 (24.4)	.54
Other antihypertensive agents§	31 (15.4)	11 (14.5)	18 (22.0)	.16
Statin	160 (80)	61 (80.3)	68 (81.9)	.79
Niacin	8 (4.0)	1 (1.3)	7 (8.5)	.04
Fibrate	1 (0.5)	1 (1.3)	0	.48
Ezetimibe	4 (2.0)	1 (1.3)	3 (3.7)	.34
Other antilipid agents‖	9 (4.5)	4 (5.3)	5 (6.1)	.55
Systolic BP, mean (SD), mm Hg	134.2 (18.6)	135.0 (20.3)	133.4 (17.6)	.60
Diastolic BP, mean (SD), mm Hg	71.4 (10.0)	71.4 (10.6)	71.7 (9.1)	.85
LDL-C, mean (SD), mg/dL	92.8 (30.4)	98.4 (33.6)	91.6 (30.5)	.18

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.
SI conversion: To convert LDL-C to mmol/L, multiply by 0.0259.
*Data are presented as number (percentage) unless otherwise specified.
†Usual care group vs continued pharmacy care group.
‡Patient refused to disclose.
§Hydralazine, doxazosin, and terazosin.
‖Fish oil and bile acid sequestrants.

Outcome Measures and End Points

The prespecified primary end point of phase 1 was the change in medication adherence from run-in to the 8-month adherence assessment. The prespecified secondary end points were the associated changes in BP and LDL-C from run-in to the 8-month point within subgroups of patients with either pharmacologically treated hypertension or hyperlipidemia. The prespecified primary end point of the phase 2 randomized trial was the persistence of mean medication adherence between the usual care and continued pharmacy care groups.

Statistical Analyses

Mean medication adherence was calculated as the proportion of medications taken for all chronic medications. Baseline characteristics between the usual care and continued pharmacy care groups were compared using t test or a χ^2 test, as appropriate. Changes in medication adherence, BP, and LDL-C for phase 1 were compared using paired t tests.

For the primary end point of phase 2, analyses were performed according to the intention-to-treat principle. Mean medication adherence between the 2 study groups (usual care and continued pharmacy care) were compared by using a t test for independent groups. Patients who did not complete the randomized trial (because of death or withdrawal) were analyzed by the imputation method of last observation carried forward, using the medication adherence level at the conclusion of phase 1.

To control for baseline differences between study groups, a multivariable analysis was performed for the randomized trial (phase 2) primary end point. The dependent variable for this analysis was the change in medication adherence between the end of phase 1 and the conclusion of phase 2. The independent variables were those baseline characteristics that had between-group comparisons with $P<.20$, in addition to the randomized trial group assignment and the baseline (run-in phase) medication adherence. As a prespecified analysis in phase 2, we tested the change in BP and LDL-C between the usual care and continued pharmacy care groups.

All analyses were conducted using SPSS version 13.0 (SPSS Inc, Chicago, Ill) by an investigator (A.J.T.). $P\leq.05$ was considered statistically significant, except for the dual primary end points (phase 1 and phase 2) for which statistical significance was set at $P\leq.025$ to correct for multiple comparisons.

RESULTS

Of the 200 study patients, 1 did not provide complete baseline assessments; therefore, 199 contributed to the data analysis (Figure 1). The mean (SD) age of the study patients was 78 (8.3) years (TABLE 1). Cardiovascular risk factors were prevalent, including drug-treated hypertension in 184 patients (91.5%) and drug-treated hyperlipidemia in 162 patients (80.6%). The patients took a mean (SD) of 9 (3) different chronic daily medications.

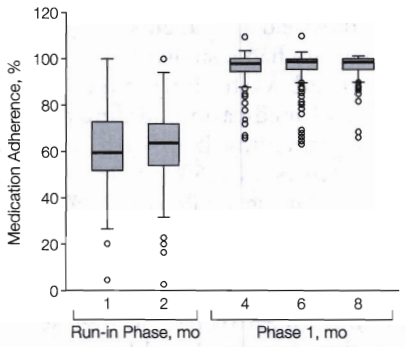
Mean (SD) baseline medication adherence at completion of run-in phase was 61.2% (13.5%). After initiation of the 6-month pharmacy care program, there was improvement in medication adherence (FIGURE 3) noted at the 4-month pharmacy visit. At 4, 6, and 8 months, medication adherence was 96% or higher. At the conclusion of phase 1 (8 months), the primary end point was met with a mean (SD) medication adherence of 96.9% (5.2%), representing an absolute change in adherence of 35.5% (95% confidence interval [CI], 31.2%-38.5%; $P<.001$). The proportion of patients in whom all chronic medications were taken with an adherence rate of at least 80%, a commonly accepted cut point for defining an acceptable level of medication adherence, increased from 5.0% to 98.7% ($P<.001$) (TABLE 2).

Improved adherence was associated with improvements in both secondary end points (BP and LDL-C). Among patients with drug-treated hypertension (n=184), mean (SD) systolic BP was reduced from 133.2 (14.9) mm Hg to 129.9 (16.0) mm Hg ($P=.02$). Diastolic BP was not significantly reduced. There was no change in the number of antihypertensive agents taken from baseline to the end of phase 1 (mean [SD], 2.52 [1.15] vs 2.55 [1.23]; $P=.68$). Among patients with drug-treated hyperlipidemia (n=162), mean (SD) LDL-C decreased from 91.7 (26.1) mg/dL (2.38 [0.68] mmol/L) to 86.8 (23.4) mg/dL (2.25 [0.61] mmol/L) ($P=.001$).

Following successful completion of phase 1 (n=159), patients were randomized to either continued pharmacy care (n=83) or were returned to their previous (baseline) method of medication administration (usual care; n=76). The characteristics of the 2 groups were similar with respect to age, sex, baseline medication adherence, and other baseline characteristics (Table 1).

For the primary end point of the randomized clinical trial (FIGURE 4), the continued pharmacy care group showed sustained mean (SD) medication adherence (95.5% [7.7%]), whereas medication adherence declined in the usual care group (69.1% [16.4%]; $P<.001$) (Table 2). However, medication adherence at the conclusion of phase 2 for the

Figure 3. Box Plot of Medication Adherence Across Time in Months of the Run-in Phase and Phase 1



The run-in phase includes months 1 and 2. Phase 1 is pharmacy care including education and blister-packed medications for months 4, 6, and 8. The heavy horizontal line represents the mean, the box represents interquartile range, whiskers represent 95% confidence intervals, and circles represent outliers. Medication adherence may exceed 100% when patients mistakenly take more medications than they should (duplicate consumption of medications).

usual care group was modestly higher than at study entry (run-in phase, 66.5% [14.0%] vs 61.1% [14.1%]; $P=.02$). At the end of the study, those elderly patients assigned to usual care had a similar frequency (compared with their baseline method of medication administration) of receiving help with their medications (11.6% vs 15.9%; $P=.58$) and using a pillbox (62.3% vs 49.3%; $P=.09$), but were more likely to use a medication chart (65.2% vs 13.0%; $P<.001$).

Multiple linear regression analysis controlling for baseline differences ($P<.20$) in the study groups showed that the assignment to usual care ($\beta=.81$; $P<.001$) and taking medications for psychiatric or memory problems ($\beta=.15$; $P=.007$) were independently related to the change in medication adherence during phase 2. A prespecified analysis of the associated changes in BP and lipid levels in the continued pharmacy care group showed significant reductions in systolic BP (−6.9 mm Hg; 95% CI, −10.7 to −3.1 mm Hg; $P=.04$ vs usual care) and diastolic BP (−2.5 mm Hg; 95% CI, −4.9 to −0.2 mm Hg; $P=.39$ vs usual care). The mean (SD) number of antihypertensive agents used was similar between treatment groups (continued pharmacy care vs usual care: 2.60 [1.23] vs 2.61 [1.14]; $P=.93$). The LDL-C was not further reduced from 9 to 14 months in the continued pharmacy care group and was not different between study groups.

Patients who did not complete the run-in phase, phase 1, and phase 2 were comparable with those patients who completed each phase with respect to all baseline characteristics as shown in Table 1, except dropouts after phases 1 and 2 were more likely to be men. Among patients who completed the study, compliance with study visits was 100% in that the study was the source of refill medications.

COMMENT

The National Council on Patient Information and Education has aptly termed medication nonadherence "America's other drug problem."[10] Furthermore, the problem of medication nonadherence poses an even greater risk among elderly patients in the United States,[11,12] among whom poor medication adherence is common, morbid, costly, and difficult to treat. Among the elderly, polypharmacy, the use of multiple medications resulting in complicated drug regimens, is an important barrier to medication adherence.[11]

The FAME study sought to investigate the effect of a comprehensive pharmacy care program composed of clinical pharmacist education and blister-packed medications on medication adherence in the elderly population and to associate this intervention to improved control of BP and LDL-C, 2 surrogates of clinical risk for cardiovascu-

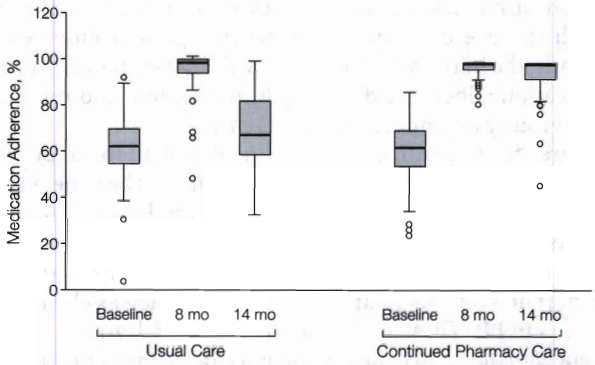
Table 2. Outcomes at 2 Months, 8 Months, and 14 Months

Outcomes	2 Months (Run-in Phase)	8 Months (End of Phase 1: Intervention)	*P* Value*	14 Months (End of Phase 2: Randomization) Usual Care Group	14 Months (End of Phase 2: Randomization) Continued Pharmacy Care Group	*P* Value†
All patients	(n = 179)	(n = 159)		(n = 76)	(n = 83)	
Medication adherence, %						
Mean (SD)	61.2 (13.5)	96.9 (5.2)	<.001	69.1 (16.4)	95.5 (7.7)	<.001
Median (range)	61.7 (4.0-92.0)	99.1 (66.0-100.0)		67.9 (33.0-97.0)	99.1 (47.0-100.0)	
≥80% Adherence to all medications, %	5.0	98.7	<.001	21.7‡	97.4‡	<.001
Patients with drug-treated hypertension	(n = 184)	(n = 142)		(n = 62)	(n = 73)	
Systolic BP, mm Hg						
Mean (SD)	133.2 (14.9)	129.9 (16.0)	.02	133.3 (21.5)	124.4 (14.0)	.005
Difference (95% CI)§		−3.3 (−6.0 to −0.6)		−1.0 (−5.9 to 3.9)	−6.9 (−10.7 to −3.1)	.04
P value‖				.69	.001	
Diastolic BP, mm Hg						
Mean (SD)	70.5 (9.2)	69.7 (10.5)	.30	68.6 (10.5)	67.5 (9.9)	.54
Difference (95% CI)§		−0.8 (−2.3 to 0.7)		−1.2 (−3.7 to 1.2)	−2.5 (−4.9 to −0.2)	.39
P value‖				.30	.04	
Patients with drug-treated hyperlipidemia	(n = 162)	(n = 122)		(n = 57)	(n = 64)	
LDL-C, mg/dL						
Mean (SD)	91.7 (26.1)	86.8 (23.4)	.001	88.4 (21.0)	87.5 (24.2)	.84
Difference (95% CI)§		−4.8 (−7.8 to −1.9)		−5.8 (−11.0 to −0.6)	−2.8 (−8.1 to 2.5)	.85
P value‖				.03	.30	

Abbreviations: BP, blood pressure; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol.
SI conversion: To convert LDL-C to mmol/L, multiply by 0.0259.
*Run-in phase vs end of phase 1 (intervention).
†Usual care group vs continued pharmacy care group.
‡For usual care group, 15 of 69 patients adhered to at least 80% of all medications; for continued pharmacy care group, 75 of 77 patients adhered.
§Compared with 2 months (run-in phase).
‖Either usual care group or continued pharmacy care group vs run-in phase.

lar outcomes. This study is the first clinical trial to specifically address medication nonadherence in the elderly population and is one of few randomized controlled studies to demonstrate improvement in both adherence and health outcomes with the use of reminder packing in a comprehensive pharmacy care program. These findings of marked improvements in rates of medication adherence to levels consistently at 96%, associated with reduced BP and LDL-C, and the requirement of continued pharmacy intervention for persistence of these changes provide a template for optimal delivery of complex medication regimens to elderly individuals for maximal benefit of prescribed pharmacological therapy.

Figure 4. Box Plot of Medication Adherence During the Randomized Trial (Phase 2) for the Continued Pharmacy Care and Usual Care Groups From Baseline and Final Medication Adherence Assessment



Baseline was at the end of the run-in phase (2 months), end of phase 1 was at 8 months, and final medication adherence assessment was at 14 months. The heavy horizontal line represents the mean, the box represents interquartile range, whiskers represent 95% confidence intervals, and circles represent outliers.

Medication nonadherence among older adults is a prevalent and costly problem. Among adults aged 65 years or older, the prevalence of patients with 2 or more chronic health problems is high (65%)[13] and leads to frequent use of multiple medications.[14,15] Predictably, the complexity of these regimens promotes medication nonadherence. Medication nonadherence is particularly problematic for asymptomatic conditions, such as hypertension and hyperlipidemia, despite a favorable tolerability profile of many medications used in their treatment. In a retrospective study[16] of 4053 patients aged 65 years or older prescribed medications for hypertension and hyperlipidemia, the adherence to both classes of medication decreased rapidly to 40.5% at the 3-month interval, and then to 32.7% at 6 months and thereafter stabilized.

Low adherence rates lead to increased adverse health outcomes, including increased ambulatory care visits, emergency department visits, and hospitalizations. In a claims database analysis, patients who were adherent and who had either hypertension or hyperlipidemia showed up to 50% lower all-cause hospitalization risks.[5] This problem may be magnified in the treatment of cardiovascular conditions, in which up to 50% of cardiovascular admissions may be attributable to nonadherence.[4] Furthermore, although drug costs for adherent patients are higher, overall health care costs related to fewer hospital admissions are substantially lower in patients who are adherent.[5,17]

In contrast with the extensive existing literature on the effectiveness of pharmacological interventions, few prospective trials of adherence interventions have been conducted, and evidence from randomized trials is scant.[18] These trials have provided little evidence to date that medication adherence can be consistently and durably improved within the resources typically available in clinical settings,[19-22] and that such interventions lead to improved health outcomes. In general, multicomponent interventions, including cognitive and behavioral characteristics, are believed to be most effective.[7] These recommendations are relevant to the study design of FAME, which included the provision of external cognitive supports involving education strategies (patient education and counseling) and a behavioral component focused on the mechanics of medication delivery (blister packs).

Patient education, regarded as an essential initial step to ensure medication adherence, has only a marginal and nondurable effect on medication-taking behavior.[19,20,22] Convenience packaging alone has not been adequately studied as an adherence aide. A meta-analysis of unit-of-use packaging suggested slight increases in medication adherence, but of 13 trials, only 7 reported statistically significant results[23] and most were of short duration (months). In comparison with simple studies of convenience packaging alone, 2 studies of complex intervention programs, involving provision of care at the worksite, special pill containers, reminders, self-monitoring, support groups, feedback, and reinforcement, reported positive effects on both adherence and clinical outcomes in patients with hypertension.[24,25]

We used a strategy of education, tailored medication provision, and the convenience of blister-packed medications, which led to a marked and sustained increase in medication adherence from 61% to 96%. The proportion of individuals who achieved a pill count exceeding 80% for all of their medications increased by 16-fold (from 5.0% to 98.7%), and these changes were associated with clinically meaningful reductions in BP and LDL-C.

The randomized controlled trial phase of FAME provides insight into the

required duration of a pharmacy care adherence program. Despite receiving 6 months of pharmacy care education and enculturation of medication adherence through the use of blister-packed medications, the initial marked increase in medication adherence did not persist in the group randomized to resume "usual care" for 6 months, although there was a modest increase over baseline adherence levels. In comparison, the group randomized to continued pharmacy care sustained high medication adherence and had further improvements in BP. These findings are consistent with the known transient effect of medication education and imply that the continued provision of blister-packed medications was a key component of the medication adherence program.

Based on our experience and consistent with the recommendations of others,[26] we suggest that medication adherence interventions should follow the FAME strategy of addressing underlying reasons for nonadherence, educating patients, providing serial follow-up, and promoting convenience through reminder packaging. In our experience, pharmacists are essential health care professionals in this process of evaluation and follow-up, underscoring the need for a teamwork approach to the problem of medication adherence.[26]

There are practical limitations to the wide-scale implementation of a comprehensive pharmacy care program that must be recognized and overcome to ensure its effectiveness for improving medication adherence. For the pharmacist, education, medication organization, and oversight of blister packing are all time intensive. Blister packing is particularly time-consuming due to the absence of automated systems to facilitate this key component of the program; therefore, the development of accurate, technological-based blister-packing systems is needed before such programs could be disseminated on a wide-scale basis. Moreover, given the pervasive and morbid effects of medication nonadherence, health care professionals, health systems, third-party payers, governmental agencies, and policy makers are all stakeholders in promoting greater emphasis on not simply the prescription or provision of medications, but also on medication adherence.[27]

Several limitations to our study are acknowledged. The generalizability of our results is limited to elderly patients taking multiple chronic medications and may not apply to specialized populations, such as elderly individuals in assisted living or those with memory problems. Our study did not evaluate formal measures of cognitive function. Our study design provides evidence on its global impact on adherence, BP, and LDL-C, but cannot distinguish the individual impact of its components (education vs blister packs). Although factorial design trials could provide such data, presently available data have been summarized and indicate that comprehensive programs are more effective than limited ones.[7] On a practical level, patient knowledge on the indications and proper use of medications plausibly should promote the beneficial impact of convenience aides like blister packs.

We studied BP and LDL-C as accepted surrogate clinical outcomes known to be associated with cardiovascular events. Practical performance of clinical outcome studies to measure the effect of adherence programs on hard clinical events (death, myocardial infarction, or stroke) are likely to be limited by large sample sizes and long durations.

The relationship between BP and LDL-C control and clinical outcomes has been established through both epidemiological and clinical treatment trials. For example, a 3-mm BP reduction, observed at the end of phase 1 of the FAME study, has been associated with a 5% reduction in coronary deaths and an 8% reduction in stroke deaths.[28-31] Each mg/dL reduction in LDL-C has been associated with an approximately 1% relative risk reduction for cardiovascular events.[30-32] Accordingly, among elderly, at-risk populations with high absolute event rates, the absolute population impact of improved BP and LDL-C control simply through improved medication adherence could be substantial.

Our study was conducted in a population of elderly US citizens eligible for health care at military medical treatment facilities as a federal health care benefit and who were treated with 4 or more chronic medications. This is consistent with survey data from older community living populations showing that 4 chronic medications is an average medication burden.[33,34] Thus, we think that our results should be generalizable to other elderly populations. However, within the military health care system, all medications are provided at no cost to the patient, thereby removing financial constraints as a barrier to adherence. This characteristic of the military health care system created an optimal environment for this study, but potentially limits the generalizability of our findings to clinical populations in which financial barriers to medication acquisition are present. In such populations, generic formulations and coverage plans such as the Medicare drug plan should be leveraged to remove financial barriers to adherence.[27] Alternatives to pill counts for adherence monitoring include systems such as electronic pill caps. Such systems provide a time and date stamp to bottle opening but are generally not widely available, are not available in our system, and are only considered an adjunct to pill counts.[35] Lastly, because of the nature of the intervention studied in this trial, blinding of participants and the research personnel was not possible.

CONCLUSIONS

In this study, a comprehensive pharmacy program composed of patient education and custom blister-packed medications was associated with substantial and sustained improvements in medication adherence among elderly patients receiving complex medication regimens. The association of improved medication adherence with re-

duced levels of BP and LDL-C suggests that such a program could lead to meaningful improvements in health outcomes. The results of the FAME study call for greater emphasis within health care delivery systems and policy organizations on the development and promotion of clinical programs to enhance medication adherence particularly among the at-risk elderly population.

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Study concept and design: Lee, Grace, Taylor.
Acquisition of data: Lee, Grace, Taylor.
Analysis and interpretation of data: Lee, Grace, Taylor.
Drafting of the manuscript: Lee, Grace, Taylor.
Critical revision of the manuscript for important intellectual content: Lee, Grace, Taylor.
Statistical analysis: Taylor.
Obtained funding: Lee, Taylor.
Administrative, technical, or material support: Lee, Grace, Taylor.
Study supervision: Grace, Taylor.

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REFERENCES

1. Blackburn DF, Dobson RT, Blackburn JL, Wilson TW. Cardiovascular morbidity associated with nonadherence to statin therapy. *Pharmacotherapy*. 2005; 25:1035-1043.
2. Abughosh SM, Kogut SJ, Andrade SE, Larrat P, Gurwitz JH. Persistence with lipid-lowering therapy: influence of the type of lipid-lowering agent and drug benefit plan option in elderly patients. *J Manag Care Pharm*. 2004;10:404-411.
3. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *JAMA*. 2002;288:462-467.
4. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med*. 1990; 150:841-845.
5. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43:521-530.
6. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487-497.
7. Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care*. 1998;36:1138-1161.
8. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA*. 2001;285:1987-1991.
9. Botelho RJ, Dudrak R. Home assessment of adherence to long-term medication in the elderly. *J Fam Pract*. 1992;35:61-65.
10. National Council on Patient Information and Education. *The Other Drug Problem: Statistics on Medicine Use and Compliance*. Bethesda, Md: National Council on Patient Information and Education; 1997.
11. Balkrishnan R. Predictors of medication adherence in the elderly. *Clin Ther*. 1998;20:764-771.
12. Gurwitz JH, Field TS, Harrold LR, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA*. 2003;289: 1107-1116.
13. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med*. 2002;162:2269-2276.
14. Flaherty JH, Perry HM III, Lynchard GS, Morley JE. Polypharmacy and hospitalization among older home care patients. *J Gerontol A Biol Sci Med Sci*. 2000;55:M554-M559.
15. Quinn ME, Johnson MA, Andress EL, McGinnis P, Ramesh M. Health characteristics of elderly personal care home residents. *J Adv Nurs*. 1999;30:410-417.
16. Chapman RH, Benner JS, Petrilla AA, et al. Predictors of adherence with antihypertensive and lipid-lowering therapy. *Arch Intern Med*. 2005;165:1147-1152.
17. Balkrishnan R, Rajagopalan R, Camacho FT, Huston SA, Murray FT, Anderson RT. Predictors of medication adherence and associated health care costs in an older population with type 2 diabetes mellitus: a longitudinal cohort study. *Clin Ther*. 2003;25:2958-2971.
18. Vik SA, Maxwell CJ, Hogan DB. Measurement, correlates, and health outcomes of medication adherence among seniors. *Ann Pharmacother*. 2004;38:303-312.
19. Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health Syst Pharm*. 2003;60:657-665.
20. Takiya LN, Peterson AM, Finley RS. Meta-analysis of interventions for medication adherence to antihypertensives. *Ann Pharmacother*. 2004;38:1617-1624.
21. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. *JAMA*. 2002;288:2868-2879.
22. Haynes RB, Yao X, Degani A, Kripalani S, Garg A, McDonald HP. Interventions to enhance medication adherence [update of: *Cochrane Database Syst Rev*. 2002;(2):CD000011]. *Cochrane Database Syst Rev*. 2005;(4):CD000011.
23. Connor J, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? a systematic review. *Bull World Health Organ*. 2004;82:935-939.
24. Haynes RB, Sackett DL, Gibson ES, et al. Improvement of medication compliance in uncontrolled hypertension. *Lancet*. 1976;1:1265-1268.
25. Logan AG, Milne BJ, Achber C, Campbell WP, Haynes RB. Work-site treatment of hypertension by specially trained nurses: a controlled trial. *Lancet*. 1979; 2:1175-1178.
26. Becker MH, Maiman LA. Strategies for enhancing patient compliance. *J Community Health*. 1980;6: 113-135.
27. Mojtabai R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff (Millwood)*. 2003;22:220-229.
28. Stamler J, Rose G, Stamler R, Elliott P, Dyer A, Marmot M. INTERSALT study findings: public health and medical care implications. *Hypertension*. 1989;14:570-577.
29. MacMahon S, Cutler JA, Stamler J. Antihypertensive drug treatment: potential, expected, and observed effects on stroke and on coronary heart disease. *Hypertension*. 1989;13:I45-I50.
30. Stamler J, Dyer AR, Shekelle RB, Neaton J, Stamler R. Relationship of baseline major risk factors to coronary and all-cause mortality, and to longevity: findings from long-term follow-up of Chicago cohorts. *Cardiology*. 1993;82:191-222.
31. Kannel WB, Neaton JD, Wentworth D, et al. Overall and coronary heart disease mortality rates in relation to major risk factors in 325,348 men screened for the MRFIT: Multiple Risk Factor Intervention Trial. *Am Heart J*. 1986;112:825-836.
32. Stamler J, Daviglus ML, Garside DB, Dyer AR, Greenland P, Neaton JD. Relationship of baseline serum cholesterol levels in 3 large cohorts of younger men to long-term coronary, cardiovascular, and all-cause mortality and to longevity. *JAMA*. 2000;284:311-318.
33. Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivela SL, Isoaho R. Use of medications and polypharmacy are increasing among the elderly. *J Clin Epidemiol*. 2002;55:809-817.
34. Hale WE, May FE, Marks RG, Stewart RB. Drug use in an ambulatory elderly population: a five-year update. *Drug Intell Clin Pharm*. 1987;21:530-535.
35. Lee JY, Kusek JW, Greene PG, et al. Assessing medication adherence by pill count and electronic monitoring in the African American Study of Kidney Disease and Hypertension (AASK) pilot study. *Am J Hypertens*. 1996;9:719-725.

Patient Compliance & Medication Adherence:

Patient Compliance
Medication Adherence
Medication Non-Adherence
Statistics & References

Compliance means taking the correct amount of the prescribed medicine at the proper time. See all e-pill Medication Reminders.

Key Stats on Medication Adherence (PhRMA 2011) | What is PDC? 'I Never Miss a Dose'?

- 32 million Americans use three or more medicines daily
- 75% of adults are non-adherent in one or more ways
- The economic impact of non-adherence is estimated to cost $100 billion annually

The average adherence rate (the degree to which patients correctly follow prescription instructions) for medicines taken only once daily is nearly 80 percent, compared to about 50 percent for treatments that must be taken 4 times a day. As many as 75 percent of patients (and 50 percent of chronically ill patients) fail to adhere to, or comply with physician prescribed treatment regimens.

CVS Report on Adherence PDF Rx Adherence

In a recent poll of U.S. individuals 65 years old and older who use medications, researches found that 51% take at least five different prescription drugs regularly, and one in four take between 10 and 19 pills each day. 57% of those polled admit that they forget to take their medications. Among those using five or more medications, 63% say they forget doses, compared to 51% among those who take fewer medicines. (10)

Drugs don't work in patients who don't take them

C. Everett Koop, MD

Remembering to take your medicine is the key to compliance. Medicine will be effective only when taken as prescribed by your physician. Professional Info

The Real Drug Problem: Forgetting to Take Them WSJ - Amy Dockser Marcus article
Good patient compliance and adherence means taking the right drugs, on time and in the proper doses. Distant Caregiving | Links | Professional info | e-pill Medication Reminder catalog | Help to select the right Medication Reminder

Patient Compliance: Medication non-compliance (non-adherence), the failure to take drugs on time in the dosages prescribed, is as dangerous and costly as many illnesses.

Want to Improve Patient Compliance? Five Tips for Generating Patient Satisfaction and Compliance

Get Medsmart: Despite the fact that medications can save or extend lives, the average patient fails to follow her/his pill prescription half the time.

The reasons behind this failure are varied; ranging from simple forgetfulness to confusion to ambivalence, but the problem costs an estimated $290 billion in emergency-room visits and other avoidable medical expenses in the United States (11).

Studies have shown than non-compliance causes 125,000 deaths annually in the US (2), leads to 10 to 25 percent of hospital and nursing home admissions, and is becoming an international epidemic. It is, in the words of The New York Times (1) the world's "other drug problem".

Negative Economic Effects of Non-Compliance

· 23% of nursing home admissions due to noncompliance(3). Cost $31.3 billion / 380,000 patients.

· 10% of hospital admissions due to noncompliance (4,5). Cost $15.2 billion / 3.5 million patients.

Prescriptions

· About 50% of the 2 billion prescriptions filled each year are not taken correctly (7).

· 1/3 of patients take all their medicine, 1/3 take some, 1/3 don't take any at all (Rx prescription never filled) (6).

Care Giving

· 25,000,000 nonprofessional caregivers in the US (8).

· 80% of nonprofessional caregivers are women (8).

· 80%-90% of people requiring care in the US receive it from family members or friends (9).

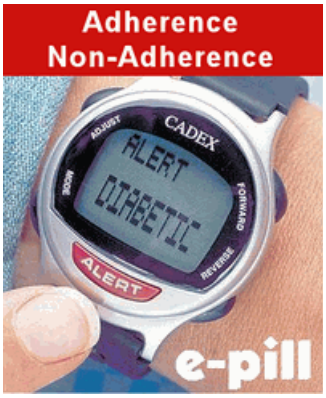
Merck Manual on ways to Improve Patient Compliance (Medication Reminders & Pillboxes)

World Health Organization. Adherence to Long-Term Therapies Adherence Report)

Bridge Medical. Medication Error References Medication Errors and Medication)

References
1. The New York Times June 2, 1998 2. Smith, D., Compliance Packaging: A Patient Education Tool, American Pharmacy, Vol. NS29, No 2 February 1989 3. Standberg, L.R., Drugs as a Reason for Nursing Home Admissions, American Health care Association Journal, 10,20 (1984). 4. Schering Report IX The Forgetful Patient: The High Cost of Improper Patient Compliance. 5. Oregon Department of Human Resources, A study of Long-Term Care in Oregon with Emphasis on the Elderly March 1981. 6. Hayes, R.B.NCPIE Prescription Month, October 1989 7. National Council for Patient Information and Education. 8. Rosalynn Carter Institute of Georgia Southwestern College. 9. Parade Magazine, 1/29/95. 10. Med Ad News February 2010 11. New England Healthcare Institute

Adherence: Medication Adherence and Patient Compliance



What is Medication Adherence Patient Compliance and Non-Adherence?

Adherence is simply taking your medications, or not taking them as the case may be, in any way that differs from the way your health care provider prescribed it to be taken. Non-Adherence (to the prescribed regimen) will result in consequences ranging from unpleasant side effects of the medication to exacerbated symptoms of the condition it was being used for, or even ineffectiveness of the medication. | Learn more about Patient Compliance | VIDEOs | All e-pill Devices |

Quick facts - Patient Compliance / Medication Adherence:

At any given time, regardless of age group, it is estimated up to 59% of those on five or more medications are in non-adherence.

- 11% of all hospital admissions are the result of prescription medication non-adherence .
- 23% of all nursing home admissions are due to failure to take medications accurately.

GOOD / POOR Adherence Adherence, which means taking the right amount of the prescribed medicine at the right time, is being recognized as a major problem in healthcare today. It is more costly and more serious than many major illnesses.

FACTS: (common non-adherence errors include):

- Forgetting to take your medicine.
- Taking the right medication at the wrong time.
- Taking the incorrect medication.
- Taking the incorrect dosage (too few or too many pills).
- Discontinuing taking your medication prematurely.
- Not filling or refilling a prescription.
- Double dosing- taking two pills to make up for a skipped one.
- Combining your medication with an inappropriate food or beverage.

More than 125,000 Americans die each year due to prescription medication non-adherence, twice the number killed in car accidents.

- Every day, prescription non-adherence costs more than $270 million in additional hospitalization and other medical costs.
- 90% of outpatients are taking prescribed medicines improperly, contributing to prolonged or additional illness.
- People who miss doses need 3 times as many doctor visits as others and face increased medical costs.

Almost 60% of the prescription medication non-adherence problems could be prevented by improving Adherence.

When a Doctor or PA writes a prescription:

- 1/3 of patients take the medicine as directed.
- 1/3 take some of the medicine.
- 1/3 never fill the prescription.

Who is at risk?

- Y_ or N_ Do you often forget to take their medication?
- Y_ or N_ Do you frequently skip dosages?
- Y_ or N_ Do you discontinue taking medications before the prescription has run out?
- Y_ or N_ Do you sometimes forget to refill your prescriptions?

Even ONE "YES" to any of these questions, puts you at serious risk for medication non-adherence health problems.

More about ADHERENCE: Medication factors (eg, duration, schedule, formulation, palatability, cost, and adverse effects) are clearly associated with adherence.

Longer duration of the medication regimen and increased complexity of the medication schedule represent risk factors to adherence, with mid-day ('during the day' = nor mornig or at night) dosings being particularly problematic.

Medication errors are among the most common medical errors, harming at least 1.5 million people every year, says a new report from the Institute of Medicine of the National Academies.

There is no "typical" medication error, and health professionals, patients, and their families are all involved.

A medication error is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer,"

Drug Naming, Labeling, and Packaging Confusion caused by similar drug names and similar colored pills accounts for up to 25% of all errors. In addition, labeling and packaging issues were cited as the cause of 33% of errors, including 30% of fatalities.

Examples of DRUG NAME CONFUSION (reported to the FDA): |Pill ID Identification |

- Serzone (nefazodone) for depression and Seroquel (quetiapine) for schizophrenia.

- Lamictal (lamotrigine) for epilepsy, Lamisil (terbinafine) for nail infections,Ludiomil (maprotiline) for depression, and Lomotil (diphenoxylate) for diarrhea.

- Taxotere (docetaxel) and Taxol (paclitaxel), both for chemotherapy.

- Zantac (ranitidine) for heartburn, Zyrtec (cetirizine) for allergies, and Zyprexa (olanzapine) for mental conditions.

- Celebrex (celecoxib) for arthritis and Celexa (citalopram) for depression.

MEDICATION ADHERENCE Devices: Compare e-pill and other manufacturers Medication Adherence systems and devices:

Currently the vast majority of home medication dispensers (pill boxes) are passive day/time organizers.

Automatic Dispenser / Log File / Reporter: There are many practical designs for electronic dispensers featuring computerized delivery and alerting systems. Examples are e-pill Med-Time XL, e-pill MedSmart, e-pill Compumed. Cost for these devices is $300-$900.

Existing devices: Many “smart” Medication Adherence systems for the home have been accepted in the marketplace. Automatic telephone calls may follow a missed dose. Premature (Early Dose) taking of abusable medicines is not detected by most devices, but we do offer the tamper proof e-pill CompuMed Automatic Pill Dispener when the patient has a history of wanting to get to meds before it is time.

Blister-Packs (Unit Dose) Self reporting blister-pack - These require specialized packaging by the pharmaceutical manufacturer or pharmacy and are not reusable. It adds about $25 per medication /per month/ per patient to medical costs independent of a monitoring system. Cost for this intervention for a typical patient can be greater than $1500 per year.

Weight Sensing Canister: These devices detect usage of medication through weight change in a loaded canister for each medication. They are useful in research on adherence with a single medication where weight of a tablet is known and the device is calibrated. However, the system is costly and nearly impossible to apply correctly to a galaxy of drugs where no manufacturer guarantees pills of identical weight. Research units for a single medication cost in excess of $1500. Alternative MDI Inhaler Patient Compliance device: PuffMinder DOSER

Care Taker Visit: Specialized Chronic Disease Management companies typically oversee adherence by telephone calls to patients, or costly nurses visits to the patient’s home. This is clearly an expensive approach but may be the only method to achieve better patient compliance / medication adherence that the patient will accept.

Listing of ALL e-pill Medication Reminders

Impact of medication packaging on adherence and treatment outcomes in older ambulatory patients

Philip J. Schneider, John E. Murphy, and Craig A. Pedersen

Abstract

Objective: To evaluate medication adherence and treatment outcomes in elderly outpatients using daily-dose blister packaging (Pill Calendar) compared with medications packaged in bottles of loose tablets.

Design: Randomized controlled trial.

Setting: Ambulatory care clinics at Ohio State University Medical Center, Columbus; University of Arizona Health Science Center, Tucson; and Riverside Methodist Hospital Family Medicine Clinic, Columbus, Ohio, from July 1, 2002, to December 31, 2004.

Patients: 85 individuals 65 years of age or older being treated with lisinopril for hypertension.

Intervention: Patients were randomly assigned to receive lisinopril in either daily-dose blister packaging (Pill Calendar) or traditional bottles of loose tablets.

Main outcome measures: Adherence was assessed by prescription refill regularity and medication possession ratio (MPR). Treatment outcome and use of medical services were assessed by medical record review of blood pressure and morbidity associated with poorly controlled hypertension.

Results: Patients receiving lisinopril in the daily-dose blister packaging (Pill Calendar) refilled their prescriptions on time more often ($P = 0.01$), had higher MPRs ($P = 0.04$), and had lower diastolic blood pressure ($P = 0.01$) than patients who had their medications packaged in traditional bottles of loose tablets.

Conclusion: Providing medications in a package that identifies the day each dose is intended to be taken and provides information on proper self-administration can improve treatment regimen adherence and treatment outcomes in elderly patients.

Keywords: Medication packaging, adherence, blood pressure.

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Previous presentation: Sixth Scientific Forum on Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke, American Heart Association, Washington, D.C., May 14–16, 2005.

Improving treatment outcomes requires more than good medications and a sound plan of pharmacotherapy; plan implementation is also necessary. Treatment failure and adverse outcomes can result if a sound plan is not implemented. This principle was recognized more than 40 years ago with the medication error studies of Barker et al.,[1] which led to better medication-use systems in hospital settings, including unit–dose drug distribution and intravenous admixture systems. These systems increased the likelihood of implementing treatment plans and reduced medication errors by as much as 10-fold. Similar systems based on improved packaging and distribution of medications in long-term care facilities have reduced medication errors to the extent that the Centers for Medicare & Medicaid Services requires no significant medication errors and an overall medication error rate of 5% or less as a condition for participation in the Medicare program.[2] Considerably more medications are administered in the outpatient setting, with ample evidence of nonadherence and errors, yet similar systems approaches using improved packaging and distribution have not been rigorously studied or widely adopted.

At a Glance

Synopsis: This study of older patients (n = 85; age, 65 years of age or older) with hypertension shows that those who received lisinopril in adherence-aiding daily-dose blister packaging were statistically significantly more likely to refill their prescriptions on time and to have a higher medication possession ratio and lower diastolic blood pressures, compared with patients receiving lisinopril in traditional bottles of loose tablets. The blister packaging, marketed as Pill Calendar and containing 28 days of therapy arranged in weekly rows, was labeled with medication-specific instructions and the day of the week on which the dose was to be taken. Unlike packaging used in some older studies, the Pill Calendar is a single card that does not allow separation of individual doses, and it therefore provides an ongoing visual record of doses taken or missed.

Analysis: *Previous research has shown special blister packaging to have either a positive effect on adherence (particularly combined with counseling) or no benefit because of patient difficulty opening the packaging. The current study used streamlined packaging that increased not only ease of handling for the pharmacist but also ease of use for the patient. As a result, better treatment outcomes (i.e., improved blood pressure values) were demonstrated. The blister package used here identified the day on which each dose was to be taken and effectively ensured proper self-administration in an elderly patient population.*

Adherence packaging has been used with oral contraceptives, corticosteroids, and antibiotics but is not widely used for medications to treat chronic diseases. Adherence-aiding packaging has also been used for short-term therapy but not necessarily for older patients, who are most likely to need help remembering to take their medications. With the implementation of the Medicare prescription drug benefit, even more patients will be treated for chronic diseases with medications. Getting the full benefit from an investment in drug therapy will be enhanced by a system of medication use that improves the likelihood of implementing the treatment plan as intended. Improved packaging is one method for accomplishing this on a widespread basis.

Objective

The purpose of this study was to examine the impact on adherence and clinical outcomes of an adherence medication package, the Pill Calendar.

Methods

Population and setting

Patients 65 years of age or older with a diagnosis of essential hypertension from three centers in Ohio and Arizona were eligible for enrollment in the study, which was conducted from July 1, 2002, to December 31, 2004.

Design

This was a randomized controlled trial of an antihypertensive medication (lisinopril) packaged in a daily-dose adherence package (Pill Calendar, Philadelphia; Figure 1) in patients aged 65 years or older with hypertension. Patients were eligible if they were taking lisinopril for hypertension or starting on lisinopril as part of study enrollment. Lisinopril doses could be changed during the study period, and other antihypertensive agents could be added or discontinued. Patients were not enrolled if, according to the assessment of their physician, they exhibited cognitive impairment (e.g., psychoses or Alzheimer's disease), had visual impairment or severe arthritis, or had terminal illness that might result in death or impairment during the study. Because packaging was the dependent variable, patients were dropped from the study and lost to follow-up if they did not have prescriptions filled after signing informed consent or if they had fewer than six prescriptions filled during the study period. Approval for this study was obtained from the human subjects committee at each center, and written informed consent was obtained from each patient before enrollment.

Patients were randomly assigned by the dispensing pharmacist at each site to a study group that received an antihypertensive medication (lisinopril) in a daily-dose adherence package or a control group that received their antihypertensive medications in traditional bottles of loose tablets. Four tablet strengths available for lisinopril were used: 5, 10, 20, and 40 mg. The dosage of lisinopril was determined by the prescribing physician, and the proper package or combination of packages was dis-

Figure 1. Daily-dose adherence package (Pill Calendar)

pensed by the pharmacist. A patient randomization assignment log was developed for the three participating pharmacies (two in Ohio and one in Arizona). Pharmacist investigators assigned patients to the study or control groups using randomization logs provided by the Department of Biostatistics at the Ohio State University and therefore were not blinded to the study assignment. Physicians who provided care to the patients were not provided information on study assignment by the investigators, and patients were instructed not to discuss their study group assignment with their physician or physician's staff (e.g., nurses working in physician's office).

Intervention

The daily-dose adherence package was blister packaged with four rows of seven tablets, allowing patients to see if the dose had been taken each day. The packaging also provided more space for patient information, including what to do if a dose is missed. The potential impact of this daily-dose adherence package was assessed by evaluating patient adherence and treatment outcome. After a baseline assessment, patients were scheduled to visit the study pharmacist and obtain refills every 28 days during the 12 months that each patient was enrolled in the study. At each visit, the pharmacist investigators recorded the time between prescription refills for the hypertension medication and recorded any study-related problems among study patients. At enrollment and 6 and 12 months after enrollment, the patients visited their physician for blood pressure measurement; the occurrence of morbidity in the prior 6 months, including angina, myocardial infarction (MI), and stroke; and any medical services required in the prior 6 months, including hospitalizations and emergency department visits. Medical charts were reviewed by two pharmacists to collect this information.

Description of the outcome variables

The following comparisons were made to assess patient adherence: percentage of times that patients had their prescriptions refilled on time, which was defined as being within 5 days before or after the due date, and medication possession ratio (MPR), which was defined as the sum of the day's supply for all prescriptions received during the study (except for the last refilling of the prescription) divided by the number of days between the dates of the first and last prescription dispensing.[3,4]

The following comparisons were made to assess treatment outcome: blood pressure at baseline, 6 months, and 12 months; number of patients who experienced morbidity during the study period; and number of hospitalizations and emergency department visits during the study period.

Description of the covariates

The continuous covariates were age, blood pressure, and serum creatinine (SCr). The categorical covariates were gender, prior MI, and stroke.

Statistical analysis

Baseline demographic characteristics were examined to determine whether the study and control groups were comparable. For the continuous covariates, summary measures of the group distributions were calculated and two-sample t tests or nonparametric Wilcoxon rank-sum tests were applied. For the categorical covariates, χ^2 tests or Fisher's exact tests were used.

To assess adherence, the percentage of refills on time and MPR in the two groups were compared using nonparametric Wilcoxon rank–sum tests. Analysis of covariance was then applied to assess the percentage of refills on time and MPR for both the study and control groups.

Mean systolic blood pressure (SBP), diastolic blood pressure (DBP), and SCr for each group were calculated at the 6- and 12-month physician visits. Simple group comparisons at baseline and each of the two follow-up visits were performed using Wilcoxon rank–sum tests. Longitudinal models were then applied to the data to assess the change in blood pressure and SCr over time; SBP and DBP were modeled separately. Baseline (initial) blood pressure value, visit month, and group (i.e., control or study) were included as covariates in the model. In addition, the presence of other significant predictors of blood pressure (such as gender and age) was assessed.

All analyses were conducted using STATA version 7.0 (Stata, College Station, Tex.) and SAS version 8.0 (SAS Institute, Cary, N.C.).

Results

A total of 112 patients were evaluated for eligibility and signed informed consent in their physician's office. Of these, 19 patients did not have prescriptions filled—9 in the study group and 10 in the control group. Of those having prescriptions filled, eight (four in the study group and four in the control group) had fewer than six prescriptions filled during the 12 months that they were enrolled in the study and were excluded from data analysis. A total of 85 patients met the criteria for inclusion in the study

and data analysis. Daily-dose adherence packages (Pill Calendar) were provided to 47 study patients, and 38 control patients received their medication in a traditional bottle of loose tablets. Data from all 85 patients were used in the analyses. At baseline, no significant differences between the study and control groups were observed for any of the medical or demographic information, such as age, gender, SBP, DBP, total number of medications currently being taken, prior stroke, or emergency department visits in the previous 6 months (Table 1).

Adherence

The percentage of on-time refills was significantly higher for the study group than the control group (Table 2). Adjusting for age and gender (using analysis of covariance) did not alter the results; the percentage of on-time refills was 13.7% higher in the study group than the control group.

MPR was significantly higher for the study group than the control group (Table 2), though the absolute difference was small (6%). After adjusting for age and gender using a statistical model, a significant difference remained in MPR between the two groups, with the mean MPR for the study group being 6.2% higher than the control group.

Clinical outcomes

Wide variation in both DBP and SBP occurred at baseline, 6 months, and 12 months. As noted, no significant differences were observed in DBP or SPB at baseline between study and control patients (Table 1).

At 6 months, the mean (± SD) DBP was 73.2 ± 8.8 mm Hg in study patients compared with 77.7 ± 10.2 mm Hg in control patients. This difference was statistically significant (P = 0.0367). SBP at 6 months was 132.7 ± 17.3 mm Hg in study patients and 138.2 ± 22.2 mm Hg in control patients. This difference was not significant (P = 0.2143). At 12 months, DBP was 72.0 ± 11.0 mm Hg in study patients and 75.2 ± 10.1 mm Hg in control patients. SBP at 12 months was 130.9 ± 18.1 mm Hg in study patients and 136.5 ± 17.3 mm Hg in control patients. These differences were not significant. Absolute change in both SBP and DBP at 6 and 12 months is reported in Table 2. DBP was 2.6 mm Hg lower at 6 months and 5.7 mm Hg lower at 12 months in the study group, compared with the control group. These differences were not statistically significant. Differences in SBP were also not significant at 6 and 12 months.

Twelve patients (48%) in the study group had a lower DBP by the 12-month visit, compared with 4 patients (18.2%) in the control group (P = 0.0313; Table 2), despite the wide variation in DBP seen throughout the study. Adjusting for initial DBP and visit in a longitudinal model, the average decrease over time in DBP was significantly lower in the study group than in the control group (P = 0.0104). Based on the longitudinal model with initial SBP as a covariate, the estimated average SBP for the study group was consistently lower at each visit. However, this difference was not statistically significant.

No significant differences were observed between the two groups in any of the long-term outcome measures (i.e., angina, MI, renal function, emergency department visits, hospitalization) for the 6- and 12-month visits.

Several patients reported some difficulty with opening the packaging, but no one dropped out of the special-packaging group because of this difficulty. No other study-related problems were noted among the participants.

Discussion

Improved adherence to treatment plan and clinical outcomes were demonstrated in this randomized controlled trial comparing outpatient use of daily-dose blister packaging and traditional packages of loose tablets. Several other studies have investigated the impact of packaging on adherence in patients with hypertension, some of which were either not randomized controlled trials or did not evaluate the impact of packaging on

Table 1. Comparison of patient characteristics at baseline

Characteristic	Study group (adherence package) (n = 47)	Control group (traditional bottle) (n = 38)	*P* value
Mean age (± SD)	71.6 ± 5.9	72.3 ± 5.2	0.21
Mean no. medications (± SD)	5.0 ± 2.8	5.3 ± 3.0	0.61
Gender			0.23
Men	26	16	
Women	21	22	
Prior ED visits, last 6 months (%)	2 (4.3)	0	0.34
Prior hospitalizations, last 6 months (%)	3 (6.5)	3 (7.9)	1.00
Renal impairment (SCr > 1.2 mg/dl) (%)	3 (6.5)	1 (2.6)	0.62
Prior MI	0	1 (2.6)	0.45
Prior stroke	0	0	—
SBP (mm Hg) (± SD)	137.8 ± 19.7	141.4 ± 19.2	0.40
DBP (mm Hg) (± SD)	74.2 ± 11.6	76.3 ± 11.1	0.41
SCr (mg/dL) (± SD)	1.1 ± 0.3	1.1 ± 0.3	0.45

Abbreviations used: ED, emergency department; MI, myocardial infarction; SCr, serum creatinine; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Impact of daily-dose adherence package

Outcome	Study group (adherence package) (n = 47)	Control group (traditional bottle) (n = 38)	*P* value
Adherence	Mean (± SD)	Mean (± SD)	
% Patients who had prescriptions refilled on time	80.4 (± 21.2)	66.1 (± 28.0)	0.012
MPR	0.93 (± 11.4)	0.87 (± 14.2)	0.039
Blood pressure			
Patients with reduced blood pressure	No. patients (%)	No. patients (%)	
DBP at 6 months	21 (46.7)	13 (37.1)	0.393
DBP at 12 months	12 (48.0)	4 (18.2)	0.031
SBP at 6 months	22 (48.9)	22 (62.9)	0.213
SBP at 12 months	14 (46.0)	9 (40.9)	0.312
Absolute change in blood pressure	Mean (± SD)	Mean (± SD)	
DBP at 6 months	−0.8 (± 12.4)	1.8 (± 9.1)	0.287
DBP at 12 months	−3.0 (± 11.6)	2.7 (± 10.7)	0.125
SBP at 6 months	−4.2 (± 21.5)	−4.2 (± 20.9)	0.992
SBP at 12 months	−2.7 (± 16.5)	−1.3 (± 17.8)	0.669

Abbreviations used: MPR, medication possession ratio; DBP, diastolic blood pressure; SBP, systolic blood pressure.

treatment outcome. Eshelman and Fitzloff[5] examined the impact of providing chlorthalidone in a "Compliance PAK," compared with traditional prescription vials. While the study package was not described in the publication, it was designed to "help them remember to take their medication." Using a urinalysis to assess adherence, patients who received their antihypertensive medication in the adherence packages were significantly more adherent than control patients. However, in contrast to the present study, the effect on blood pressure control was not measured. Our study was also designed to evaluate adherence and treatment outcome, both of which were positively affected.

Rehder et al.[6] studied the impact of patient counseling and use of "special medication containers" on adherence among 100 patients with hypertension. Patients were divided into four groups: control, counseling only, medication container only, and medication container with counseling. The special medication container was a 7 × 4 box with 28 sections for doses to be placed by day of the week, up to 4 times per day. The pharmacist loaded four of these containers per patient for each 28-day refill cycle. The group receiving counseling kept more appointments than the control group or the group receiving medications in special medication containers. When adherence to medications was compared, counseling and the special medication container had an additive effect. Patients receiving medications in the special medication container experienced a statistically significant decrease in DBP. The authors concluded that a special medication container that was loaded by the pharmacist helped patients follow prescribed regimens more closely, particularly if patients were counseled by a pharmacist. Our study evaluated a package given to patients without additional counseling that unlike the special container studied by Rehder could be made commercially available and not require extra work by a pharmacist to fill.

In contrast, Becker et al.[7] conducted a randomized trial of "special packaging" of antihypertensive medications to test the effect on adherence and blood pressure control. The special packaging allowed all doses that were to be taken at the same time to be placed in a single package. The special packaging of the medications was done at the hospital pharmacy using a commercially available system. All tablets and capsules that were to be taken together were enclosed in a single plastic blister sealed with a foil backing on which was printed the day of the week and time of day the doses were to be taken. Each medication package contained 28 foil-backed blisters representing 28 consecutive doses of medication. The packets were perforated, allowing patients to separate one or more doses from the larger packet. No significant improvements in blood pressure control or adherence were found between the special packaging group and the group receiving medications in regular prescription vials. Patients in this study found that the "special package" was more difficult and less convenient to use than regular packaging. The authors suggested that "future studies might compare different forms of the more streamlined packages now becoming available."[6] Our study was designed to evaluate a different type of package that was easier for pharmacists to dispense and patients to use.

The daily-dose blister packaging (Pill Calendar) used in our study was different from the package studied by Becker et al. in that it contained a single medication in a single 6.25 × 5-inch card labeled with medication-specific instructions and the day of the week on which the dose was to be taken. It could not be separated by the patient; therefore, the package provided an ongoing visual record of doses taken or omitted (Figure 1). Thus, the design of the package may have influenced the effectiveness of this strategy to improve adherence. Although some studies have only examined and demonstrated the impact of special packaging on a single drug, blister packaging has been

shown to improve adherence with more complex treatment regimens (e.g., for sexually transmitted diseases).[8]

This single-blind, randomized, controlled study was designed to measure the impact of a single intervention: packaging. Finding significant differences in blood pressure can be difficult in a population of patients because of the wide variation typical in hypertension. Of note, in addition to showing improved adherence to medication regimens, the current work demonstrated significant differences in DBP between the study and control groups. This simple strategy of improving the packaging of prescription medications could help large numbers of patients, including elderly patients and those with memory deficits, take their medications more reliably with better treatment outcomes. Furthermore, Sokol et al.[9] demonstrated that improving medication adherence in patients with chronic disease substantially decreases other health care costs, such as hospital care. While this is not the only way to address problems with adherence, other more individualized and time-consuming strategies for improving adherence, such as patient counseling and self-monitoring, can be built upon this foundation.

Improvements in adherence and treatment outcome in elderly patients with a chronic disease such as hypertension are desirable. Achievement of treatment goals has been shown to reduce the morbidity and mortality resulting from untreated and poorly treated hypertension.[10] Developing a simple way to improve blood pressure in patients with hypertension is therefore desirable.

Limitations

This study was limited by the relatively small number of patients, the tracking of only one disease, and the short time frame relative to some of the long-term outcomes measured. The study patients may not reflect a typical Medicare population. Nevertheless, improvements were noted in both adherence measures and the intermediate outcome measure (DBP).

Conclusion

Providing medications in a package that identifies the day each dose is intended to be taken and provides information about proper self-administration can improve adherence to treatment regimen and treatment outcomes in elderly patients being treated for hypertension. Incorporation of this durable strategy could also lead to improvements in medication-related outcomes in elderly patients with other chronic diseases. Considering the potential effect of the new Medicare prescription benefit on the U.S. health care system, further research into the benefits of durable strategies in various patient groups on health and economic outcomes is important. Because benefits have already been demonstrated with adherence-aiding packaging, such packaging should be made increasingly available for long-term medications. Better packaging may be used for medications as a way to create an improved system of care that results in better adherence to treatment regimens and enhanced treatment outcomes.

References

1. Barker KN, Heller WM, Brennen JJ, et al. The development of a centralized unit dose dispensing system, part VI: the pilot study: medication errors and drug losses. Am J Hosp Pharm. 1964;21:609–25.
2. Centers for Medicare & Medicaid Services. CFR 483.25 (m). Accessed at http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/cfr_2002/octqtr/pdf/42cfr483.25.pdf, July 25, 2007.
3. Fairman K, Motheral B. Evaluating medication adherence: which measure is right for your program? J Manag Care Pharm. 2000;6:499–506.
4. Sclar DA, Skaer TL, Chin A, et al. Utility of a transdermal delivery system for antihypertensive therapy: part II. Am J Med. 1991(suppl 1A):57S–60S.
5. Eshelman FN, Fitzloff J. Effect of packaging on patient compliance with antihypertensive medication. Curr Ther Res Clin Exp. 1976;20:215–9.
6. Rehder TL, McCoy LK, Blackwell B, et al. Improving medication compliance by counseling and special prescription container. Am J Hosp Pharm. 1980;37:379–85.
7. Becker LA, Glanz K, Sobel E, et al. A randomized trial of special packaging of antihypertensive medications. J Fam Pract. 1986;22:357–61.
8. Wright JM, Htun Y, Leong MG, et al. Evaluation of the use of calendar blister packaging on patient compliance with STD syndromic treatment regimens. Sex Transm Dis. 1999;26:556–63.
9. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care. 2005;43:521–30.
10. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda, Md.: National Institutes of Health; 2004.

HEALTHCARE COMPLIANCE PACKAGING COUNCIL
IMPROVING PATIENT ADHERENCE AND OUTCOMES THROUGH PACKAGING

Two-Plus Decades of Research Studies Support Improved Patient Adherence With Calendarized, Compliance-Prompting Packaging

Executive Summary

The US Healthcare System is heading for a dramatic overhaul. Projects targeting improvement of care and cost reduction are well underway. Data suggests that poor medication adherence has a detrimental effect on the healthcare, contributing to the increasing problem of poor outcomes. Improving medication adherence is critical and many organizations are looking for adherence solutions. Unfortunately, pharmaceutical prescription packaging is not often targeted in these activities and has been largely untouched for more than 55 years. Over two decades of research studies, however, support the use of modern packaging solutions, including patient prompting, also known as compliance-prompting, packaging, as a successful option for improving patient adherence.

Over two decades of research studies, support the use of modern packaging solutions.

It is the intention of the Healthcare Compliance Packaging Council to highlight the improvements in patient adherence obtained through the use of compliance-prompting packaging. By sharing the results of these nine cumulative studies, beginning with the 1984 Modulus Hormone Replacement Study, then citing the well-known Ohio State study, followed by current peer-reviewed research from a major mass merchandise pharmacy retailer, as well as results from a newly published adherence study from a major pharmaceutical supplier, the HCPC and its member companies, aspire to have compliance-prompting packaging recognized as a key tool to improving patient adherence and outcomes.

The Healthcare Compliance Packaging Council is a not-for-profit trade association whose mission is to promote the greater use of compliance-prompting packaging to improve patient adherence and patient outcomes. For more information on HCPC, please visit our website, www.hcpconline.org. To contact the HCPC, please email vickiwelch@hcpconline.org, cal 804-338-5778, or write the HCPC at 2711 Buford Road, #268 Bon Air, VA 23235 USA

It should be noted that none of the data cited in this report were influenced in any way by the HCPC. The HCPC did not fund, suggest, participate in research or otherwise contribute to any of the quoted data or studies in this document.

HEALTHCARE COMPLIANCE PACKAGING COUNCIL
IMPROVING PATIENT ADHERENCE AND OUTCOMES THROUGH PACKAGING

Two-Plus Decades of Research Studies Support Improved Patient Adherence With Calendarized, Compliance-Prompting Packaging

A compilation of peer and non-peer reviewed compliance-prompting packaging studies.

The US Healthcare System is heading for a dramatic overhaul due to gross inefficiencies in current practices. Not only are we overspending for care (based on international statistics) but the quality of care we receive is not up to developed western nation standards. The World Health Organization (WHO), in 2000, ranked the U.S. healthcare system as the highest in cost, first in responsiveness, 37th in overall performance, and 72nd by overall level of health (among 191 member nations included in the study) [1][2] The Commonwealth Fund ranked the United States last in the quality of healthcare among similar countries,[3] and notes U.S. care costs the most.[4]

One of the major but often overlooked problems in US Healthcare is the severe lack of medication adherence, a topic that is finally gaining nationwide attention as our government focuses on healthcare costs and improving outcomes. The estimated annual cost the US incurs as a result of poor medication adherence approaches $300 billion[5], as recently noted in the New England Healthcare Institute paper "Thinking Outside the Pillbox", 2010. Data points to poor adherence in America as being the primary cause for 125,000 deaths annually (342 people every day) and an estimated 10% - 25% of hospital and nursing home admissions.[6] While insurance companies and managed care organizations bear the greatest economic burden from poor medication adherence, including the largest payer, Center for Medicare and Medicaid Services (CMS), everyone pays a share for the inefficiency in the form of higher taxes, grossly higher premiums, and lost productivity.

Estimated annual cost the US incurs as a result of poor medication adherence approaches $300 billion.

There are many reasons for patients' non-adherence with their medication regimen, including forgetfulness, lack of understanding for the drug or the disease, or simply not filling the prescription. Many of these issues are beyond the control of the pharmaceutical and packaging industry but there is one aspect of US prescription dispensing which has gone virtually unchanged for 55 years that is well within our reach to improve - the pharmacy-filled amber vial. While other nations have moved away from pharmacy repackaging of prescription medications, the US has clung to this antiquated method that is fraught with opportunity for medication and dispensing errors and leaves the consumer with an outdated

package that offers no support for medication adherence.

The practice of pharmacy packaging started in a time when compounding pharmacists were the norm. It was the correct place to package pharmaceuticals. Today, however; pharmaceutical manufacturing takes place in multi-million dollar pharmaceutical manufacturing facilities and not in the backroom of pharmacies. These pharmaceutical companies design and test packages according to FDA and ICH guidelines to protect the product until it reaches the consumer and yet, our system discards that package in pharmacy and opts for the plain amber vial that has not been tested for the particular chemical makeup of the individual drug. Worse yet, we have a system that has ignored the successful performance demonstrated again and again by unit dose packaging with compliance-enhancing formats. Packaging that reminds people whether they have taken their medications. Birth control pills, certain antibiotics, hormone replacement therapies, and steroids are already being dispensed in compliance-prompting, unit dose packaging that has proven highly effective in helping people manage their pharmaceutical regimens. There is a wealth of data to support the idea that if more products were packaged in a these formats, patient adherence would be greatly increased and the associated improvement in health outcomes would greatly reduce healthcare costs that exist today. That is why the HCPC's goal is to inform and educate consumers, health professionals and policy makers about the role that compliance-prompting packaging can play in improving pharmaceutical adherence.

> Calendarized blister packaging can have a positive impact.

> There is a wealth of data to support that patient adherence would be greatly increased.

The best examples of significant patient adherence achieved through compliance-prompting packaging are birth control pill packages used in various calendarized forms since 1960. While some may object to this reference, citing that the high compliance with birth control pills is associated with known risk, data from National Council on Patient Information and Education (NCPIE) does not support that conclusion. According to NCPIE, birth control pills have a compliance rate of 92 percent (some list it as high as 95%) while organ rejection drugs (with a “known risk” of death) have an average compliance rate of 82 percent. The unprecedented 95% adherence rate experienced with birth control pills can be correlated with the calendarized blister that reminds the patient if she has taken her daily dose and not with the associated risk. Given the high rate of adherence, one can only wonder why this form of compliance-prompting packaging has not been introduced in other areas of drug therapy, particularly those dealing with chronic conditions where non-adherence can result in increased hospital admissions and poor health outcomes.

The HCPC has been tracking and informing the industry of compliance packaging research conducted over the years. Contained herein is an overview of both peer-reviewed and non-peer reviewed studies that have successfully demonstrated that compliance-prompting packaging can improve patient

adherence and outcomes. As you will see, those focusing on the issue of **medication adherence,** which is defined as the "extent to which patients follow provider recommendations about day-to-day treatment with respect to the timing, dosage, and frequency,"[7] are realizing that calendarized blister packaging can have a positive impact. And, as recent data has shown, **medication persistence**, or the duration of medication-taking from initiation to discontinuation[8], can also be assisted by calendarized packaging by influencing the rate at which a patient will refill their prescription.

It should be noted that none of the data cited in this report were influenced in any way by the HCPC. The HCPC did not fund, suggest, participate in research or otherwise contribute to any of the quoted data or studies in this document.

Modulus, Inc. Hormone Replacement Therapy

Leonard W.G., Leonard D.: Calendar oriented compliance. Maturitas, the international journal for the study of the climacteric. Sept. 1984, MATURITAS

A study conducted over 20 years ago, six years prior to the formation of the HCPC, still provides confirmation that calendarized blister packaging can increase patient compliance. In a study conducted by Walter Leonard, MD, and Dawn Leonard, RN, BSN, the researchers found that a "calendar-oriented, structured dosage package" increased patient compliance with estrogen-replacement therapy as compared with a two-drug regimen administered from bottles. In the article the authors describe how two groups of 50 women are each given two prescriptions of hormone therapy, one is for estrogen and the other for progesterone. The women in the control group receive their prescriptions in amber vials, one for each prescription. The other group of women, known as the research group, is provided with a compliance-prompting blister card housing both medications. The data from this research highlights that those women who received their prescription in amber vials were only 30% compliant, while those 50 women with the calendarized blister cards were 82% compliant.

> Women with the calendarized blister cards were 82% compliant.

Unit Dose Packaging and Elderly Patient Compliance

In a highly recognized study presented at the Unit-of-Use – Contemporary Issues Open Conference, Baltimore, Maryland, December 13-15, 1992, and also published in the New Zealand Medical Journal in 1991, it was revealed that in a study of 84 elderly patients, those using unit-dose calendar packaging were more likely to comply with their regimens than those using bottles or other noncalendarized packs. The 45 seniors using compliance-prompting calendar-packs led in compliance rates throughout the study.

> Patients using unit-dose calendar packaging were more likely to comply with their regimens.

Those using the compliance-prompting packs, exhibited an 86.7% compliance rate compared to the 39 seniors using amber vials, who had a 66.7% compliance rate at the start of the program. After the patients were discharged the seniors using calendarized packaging continued to lead in compliance, 68.8% versus the control group's 41.0% after 10 days, then, 64.4% to 38.5% after one month, and 48.9 to 23.1% after three months.

A Project to Increase Medication Compliance and Reduce Costs in Domiciliaries

Also in 1992, the results of the U.S. Department of Health and Human Services Grant Award 90-AM-0433, Jefferson County Office of Senior Citizens Activities, Birmingham, Alabama, were published in February of that year. In this study, bulk medications were put up in compliance-prompting formats for assisted living facilities in Alabama. The conclusion drawn at the end of this study was that "results indicated significant improvements in average compliance" . . . with "overall average compliance improved from 85 percent to 95 percent."

"Results indicated significant improvements in average compliance"

"Effect of Value-Added Utilities in Promoting Prescription Refill Compliance Among Patients with Hypertension"

The following year, Current Therapeutic Research, Vol. 53, No. 3, March, 1993, published the results of a study that focused on the adherence of 128 hypertensive patients. These patients were monitored for one entire year. The control group received no intervention in compliance and their compliance rate was only 0.64, those with a reminder card maintained a 0.71 compliance rate, those with a compliance-prompting package demonstrated a compliance rate of 0.75. Those who received their medications in compliance-prompting packaging coupled with a reminder card achieved the highest level of compliance at 0.87, demonstrating that compliance-prompting packaging can be a advantageous portion of a multi-faceted compliance enhancing program.

Compliance-prompting packaging can be an advantageous portion of a multi-faceted compliance enhancing program.

"Use of Blister Packaging to Improve Patient Medication Compliance in the Treatment of Depression"

In 1996, SmithKline Beecham, Inc. conducted research of 150 patients diagnosed with depression among 43 different sites throughout Canada. These patients were monitored for 12 weeks. The control group was provided their prescription in typical amber vials. The research group was provided

with compliance-prompting blisters. Prior to the distribution of the differing packaging, the Baseline Beck Depression Index (BID) for both groups was 27.5. At 24 weeks, the Mean BID for control group measured 13.1, while the mean BID for the research group was 11.0 and it was concluded "Patients randomized to the blister pack preferred the blister packaging scheme over traditional bottle formats."

"Patients preferred the blister packaging scheme over traditional bottle formats."

"Impact of Innovative Packaging on Adherence and Treatment Outcome in Elderly Patients with Hypertension"

(Journal of the American Pharmacists Association, Jan/Feb 2008, 48:1 pp. 58-63)

A more recent study conducted by Ohio State University compares compliance rates of an anti-hypertensive drug administered to some elderly patients in a bottle and others in a blister. The results of this study continue to prove the point that calendarized blister packaging can provide increases in patient adherence. In the OSU research, 88 adults, all 65+ years of age, were included in the study. All had blood pressure readings of at least 140/90. Forty-eight participants received Prinivil in blister packs with compliance-prompting features. These partipants constituted the study group. Forty received Prinivil in traditional pharmacy vials and composed the control group. The patients were tracked for 12 months.

Over these months, the percent of on-time refills of the control group was only 66.1%, while the study group's percent of on-time refills was 80.4%. Dramatic improvements in blood pressure were also measured in the study group. The change in DBP of the control group was -17% and SBP was -40%. For the study group , DBP was -50% and SBP was – 57%.

The conclusions drawn by the researchers: "Patients in the study group had better adherence as measured by: 1) Significantly more likely to refill prescriptions on time; and 2) Medication possession ratios significantly higher for study group (MRP = "proportion of days a patient has medication available to be taken") and "At 12 months, a significantly greater proportion of patients in the study group had lower diastolic blood pressure (compared to baseline) than patients in the control group."

Patients in the study group had better adherence

New Catalent/SDI Study Shows Adherence Packaging Solutions Drive Substantial Gains in Patient Persistency – April 2011

Since the highly-noted OSU study, pharmaceutical packaging suppliers have had third party research conducted in the past several months. In April 2011, Catalent Pharma Solutions, a drug delivery technology and packaging provider, announced the results of an independent study in which unit-dose patient adherence packaging was associated with a 17-point increase in patient persistency to a drug over 12 months, as compared to conventional 30-count bottle packaging. The study utilized patient data from SDI, a provider of anonymous patient-based prescription data for US retail pharmacies.

The adherence study looked at patient persistency rates over a 12-month period by analyzing a cohort of ~200,000 qualified patients from SDI who filled their prescriptions in either a traditional bottle or a patient adherence package. Persistency rates were defined as the percentage of patients who remained compliant or restarted therapy over the 12-month tracking cycle. This new study again suggests that appropriately tailored packaging can provide customers with compliance solutions that positively impact patient adherence and treatment outcomes.

Appropriately tailored packaging can provide customers with compliance solutions that positively impact patient adherence and treatment outcomes.

"A Pharmacoepidemiologic Analysis of the Impact of Calendar Packaging on Adherence to Self-Administered Medications for Long-Term Use."

(Clinical Therapeutics, May 2011, Vol. 33, Number 5)

Shortly after the Catalent results were revealed, MWV, a packaging manufacturer, shared their compliance-prompting packaging research results. The MWV study was conducted to assess the effect of new MWV calendar packaging technology on prescription refill adherence and persistence for daily, self-administered, long-term medication use. The study group involved 76,321 new users and 249,040 current users, aged 18 – 75 years, who filled prescriptions for oral lisinopril or enalapril (control group) at a mass merchandise study pharmacy during 1 year prior and after the switch of lisinopril packaging from vials to calendarized blister packaging.

Within the study, the use of MWV's Shellpak®, a proprietary calendarized 30-day, unit-of-use medication package, demonstrated improvement in the adjusted estimates of refill persistence and adherence as measured by length of therapy (LOT) and proportion of days covered (PDC) with medication.

Results revealed the Shellpak refill persistence benefit was especially pronounced among certain subgroups. New medication users had an average length of therapy increase of 9 days over a year.

Ongoing medication users had an average length of therapy increase of 4 days over a year. Persons taking fixed-dose combination formulations, or 2 medications in a single tablet experienced an average 17-day increase in length of therapy for new users and 12 days for ongoing medication users. In addition, the study revealed that Shellpak users overall were more likely to reach "full refill adherence" – at least 80% of days covered with medication in a year – than vial users, with the greatest effect observed in new medication users.

A 30 day calendarized unit-of-use package demonstrated improvement in the adjusted estimates of refill persistence.

The conclusion reached by the researchers: "Calendarized Blister Packaging of medication prescribed for daily, self-administered, long-term use was associated with modest improvement in prescription refill adherence and persistence. And adherence strategy of even small effect size that is broadly implemented on a population level could significantly leverage therapeutic effect and provide substantial cumulative public health benefit."

"Real-world impact of reminder packaging on antihypertensive treatment adherence and persistence."

(Patient Preference and Adherence 2012: 6 499-507, Dovepress Open Access to Scientific and Medical Research)

As cited in the publication of this real-world study on the introduction of a reminder package for a Novartis hypertensive tablet, "Adherence-oriented blister packaging may improve treatment of adherence and reduce compliance barriers in community and outpatient settings. However, improved packaging has not been used widely and has rarely been studied for medications used to treat chronic and long-term illnesses." The HCPC has always been puzzled by this lack of interest in reminder packaging for the treatment of long-term chronic illnesses, and heralds the release of recent results from the open access research from Novartis and Xcenda for the DiovanHCT blister package.

In this study, Novartis Pharmaceuticals, through Walmart pharmacies, began to distribute a single-pill combination of valsartan-hydrochlorothiazide in reminder packaging. The DiovanHCT package introduced to hypertensive patients at Walmart pharmacies consists of 30 tablets in a push-thru calendarized blister in three rows of ten. To facilitate compliance with the medication regimen, tablets are laid out with color coded days and weeks, including reminders for refilling the prescription. Diovan HCT® is offered in four strength combinations with each strength combination using a unique color

(Brown, Blue, Purple, Red) and a photograph of the unique tablet design for each strength to ensure correct dosing. This plus additional important labeling information is clearly provided on the exterior of the child-resistant MWV Shellpak™ which houses the calendarized blister. The back label provides the designated area for the patient's prescription label as well as an adhered prescription insert. The front of the pack features an extended content booklet label and the photograph of the pill. Multiple pages within the front label provide patients assistance with dosing instructions and guides to joining the BP Success Zone Program, including both the website and toll-free number, and additional regulatory information.

When 4,633 Walmart patients obtained refills of the single-pill combination in this new reminder packaging, their adherence rates were studied over 11 months by measuring the following: medication possession ratio, time to refill, proportion of days covered, and time to discontinuation. An additional 4,633 patients from the SourceLx (Wolters Kluwer) database who did not receive their single-pill combination of valsartan-hydrochlorothiazide in reminder packaging were also included in the study for the 11month period.

At the end of the study period, those who received the DiovanHCT reminder package, exhibited a medication possession ratio of 80%, while those patients not utilizing the reminder package demonstrated a lesser ratio of 73%. Proportion of days covered for the Walmart pharmacy customers was 76% versus the 63% for the non reminder package group. Those patients with the reminder package also refilled their prescriptions four days earlier, on average, than the other patients. Finally, those patients with the Diovan HCT reminder package were also more likely to continue their therapy in the long term.

Reminder packaging has a positive effect on medication possession ratio, proportion of days covered and refill rates.

It should be noted that the Novartis DiovanHCT reminder package was awarded the HCPC's highest honor in 2010 as the Compliance Package of the Year, prior to the study results being published. Even then, the independent industry panel of judges, including pharmaceutical manufacturing engineers and pharmaceutical packaging media representatives, recognized that the DiovanHCT reminder package was a well developed design that focused on the patients' adherence in order to improve their disease states. And, the results provided in this very recent study support the broad adaptation of compliance-prompting, reminder packaging throughout the industry.

The nine studies cited all draw a similar conclusion, as reiterated by the Institutes of Medicine in the National Academy of Sciences article *Preventing Medication Errors*, ***"The strategy of using calendar blister packs could help large numbers of patients (including seniors, children, and those challenged by cognitive, physical, or functional impairment) take their medication more reliably***

and safely, and enhance their treatment outcomes."[9] The WHO identifies two categories of nonadherence. The first is ***preventable*** nonadherence where the patient forgets, or misunderstands. The second category is *nonpreventable* where the medication may have life-threatening adverse effects. The WHO recommends targeting tailored treatment interventions for *preventable* nonadherence[10] and now, due to the most recent studies cited the industry's attention has refocused to relatively simple approaches, such as "reminder" packaging, that can be widely implemented for once-daily medications take for chronic diseases.[11]

The WHO recommends targeting tailored treatment interventions for *preventable* nonadherence.

As previously mentioned, those focusing on the issue of medication adherence, or the "extent to which patients follow provider recommendations about day-to-day treatment with respect to the timing, dosage, and frequency, **are realizing that calendarized blister packaging can have a positive impact** and medication persistence, i.e., a patient's duration of medication-taking from initiation to discontinuation, **can also be assisted by calendarized packaging by influencing the rate at which a patient will refill their prescription**.

A large segment of the healthcare industry regularly uses calendarized blisters on a daily basis, the "bingo card" containing 28-30 doses is found in a large percentage of Long Term Care institutions where tracking patients daily (and often multiple) meds is critical to maintaining the health of patients in their care. It is curious that this segment of professional caregivers sees the benefit of calendarized packaging for managing daily medication regimen in a professional setting but the industry neglects to offer that same benefit to the broader home based population where similar gains in health outcomes could be realized.

Building on Technology

The referenced studies provide a great beginning, but there is much more that can be achieved through enhanced packaging developments and creative thinking. If we separate package improvements into three categories we can gauge their potential benefit. The categories are:

Passive features

Active features

Interactive features

The goals of incorporating these features are basic: communicate, remind, engage and, verify.

Passive features can take the form of simple educational graphics on the package. They are put in the path of the consumer and we hope they do some good.

Active features include the calendarized blister pack. It qualifies as an active solution since its use leaves evidence of dispensing that can provide feedback to the patient and caregiver. Also included in this category are lights, buzzers or other components that will gain patient attention with similar goals as

the passive solutions. Integrated electronics from companies such as Cypak and IMC that can record dispense events and create a real time record of adherence performance also fall into this category.

Interactive features go beyond the simple package. Certain packages with imbedded electronics provide feedback and elicit response from the patient. Some, like Vitality's Glow Caps, incorporate internet based or cellular feedback features to provide professional caregivers real time data on patient adherence. This link is critical since it provides the opportunity to intervene if a non-compliant patient is putting themselves in a dangerous situation. Call centers are another example of interactive solutions. Human to human interaction can be quite effective in prompting adherence but, unless we intend to have one half the world call the other half of the world, they are an impractical solution long term. In addition, call centers have developed due to poor primary packaging that does little to communicate or promote adherence.

The goal at the end of the day is verifiable use. Family members, caregivers and health professionals need some way to know that a drug was taken by the patient. Only with verifiable use can we prevent Adverse Drug Events (ADE's) that are responsible for as much as 28% of Emergency Room visits, 10% of hospitalizations, and 25% of Nursing Home admissions.

As well, we have a growing number of Pay-for-Performance insurance models that will pressure caregivers to improve medical outcomes for patients in their care with this performance linked to financial compensation. Programs such as Care Transitions and Patient Centered Medical Homes need improvements in medication adherence in order to meet their goals. Smarter packaging can help them reach their goals and improve the welfare of patients at the same time.

The HCPC believes all this work is leading toward broader adoption of compliance-prompting packaging for the benefit of the patient, and the healthcare industry, overall. Industry efforts to incorporate reminders and positive reinforcement cues have been introduced and tested in the form of calendarized blister packaging. By utilizing today's amazing technology additional functions such as real-time data feedback are possible,. This type of compliance-prompting packaging, when used in combination with education and other reminders, has been shown to improve patient medication adherence. We, as part of the US Healthcare industry, need to put these options in the hands of the patient. Consumers need to have a choice how their prescriptions are packaged: either the standard cap and vial format that does nothing to help them manage their medications, or a compliance-style, unit dose package that will help ensure that they actually take the medication as it has been prescribed. We believe, like the World Health Organization, that "Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the [world] population than any improvement in medical treatment."[12]

> The HCPC is working towards the day that calendarized blister packaging will be more widespread for the benefit of patients.

1. World Health Organization assesses the world's health system. Press Release WHO/44 21 June 2000.

2. Health system attainment and performance in all Member States, ranked by eight measures, estimates for 1997

3.Roehr, Bob (2008). "Health care in US ranks lowest among developed countries". *BMJ* 337 (jul21 1): a889. doi:10.1136/bmj.a889. PMID 18644774.

4. Davis, Karen, Schoen, Cathy, and Stremikis, Kristof (June 2010). "Mirror, Mirror on the Wall: How the Performance of the U.S. Health Care System Compares Internationally, 2010 Update". The Commonwealth Fund. http://www.commonwealthfund.org/Content/Publications/Fund-Reports/2010/Jun/Mirror-Mirror-Update.aspx?page=all. Retrieved June 23, 2010.

[5]http://www.thecollaborativeforum.com/91/thevaluequadrantofhealthcarerefo/

[6]Journal of Managed Care Pharmacy, Supplement, July 2008, Vol. 14, No. 6-b, Continuing Education Activity

[7]American Heart Journal 2011;162: Medication adherence: A call for action. pp. 412-24.

[8]American Heart Journal 2011;162: Medication adherence: A call for action. pp. 412-24.

[9]Institutes of Medicine (IoM), National Academy of Sciences, August, 2006, Page 250.

[10]Apaotiocpoats-amfc.

[11]American Heart Journal 2011;162: Medication adherence: A call for action. pp. 412-24.

[12]RB Haynes, as quoted in *Adherence to Long-Term Therapies: Evidence for Action*, World Health Organization, 2003.

RESEARCH

Medication Therapy Management: 10 Years of Experience in a Large Integrated Health Care System

Djenane Ramalho de Oliveira, PhD; Amanda R. Brummel, PharmD; and David B. Miller, RPh

ABSTRACT

BACKGROUND: Medication therapy management (MTM) was officially recognized by the federal government in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, which requires Medicare Part D plans that offer prescription drug coverage to establish MTM programs (MTMPs) for eligible beneficiaries. Even though the term "MTM" was first used in 2003, pharmacists have provided similar services since the term "pharmaceutical care" was introduced in 1990. Fairview Health Services, a large integrated health care system, implemented a standardized pharmaceutical care service system in 1998, naming it a pharmaceutical care-based MTM practice in 2006.

OBJECTIVE: To present the clinical, economic, and humanistic outcomes of 10 years of delivering MTM services to patients in a health care delivery system.

METHODS: Data from MTM services provided to 9,068 patients and documented in electronic therapeutic records were retrospectively analyzed over the 10-year period from September 1998 to September 2008 in 1 health system with 48 primary care clinics. Patients eligible for MTM services were aged 21 years or older and either paid for MTM out of pocket or met their health care payer's criteria for MTM reimbursement; the criteria varied for Medicaid, Medicare, and commercially insured enrollees. All MTM was delivered face to face. Health data extracted from the electronic therapeutic record by the present study's investigators included patient demographics, medication list, medical conditions, drug therapy problems identified and addressed, change in clinical status, and pharmacist-estimated cost savings. The clinical status assessment was a comparison of the first and most recent MTM visit to measure whether the patient achieved the goals of therapy for each medical condition (e.g., the blood pressure of a patient with diabetes and hypertension will be less than 130/80 millimeters mercury [mmHg] in 1 month; the patient with allergic rhinitis will be relieved of his complaints of nasal congestion, runny nose, and eye itching within 5 days). Goals were set according to evidence-based literature and patient-specific targets determined cooperatively by pharmacists, patients, and physicians. Cost-savings calculations represented MTM pharmacists' estimates of medical services (e.g., office visits, laboratory services, urgent care visits, emergency room visits) and lost work time avoided by the intervention. All short-term (3-month) estimated health care savings that resulted from addressing drug therapy problems were analyzed. The expenses of these avoided services were calculated using the health system's contracted rates for services provided in the last quarter of 2008. The return on investment (ROI) was calculated by dividing the pharmacist-estimated savings by the cost of MTM services in 2008 (number of MTM encounters times the average cost of an MTM visit). The humanistic impact of MTM services was assessed using the results from the second patient satisfaction survey administered in 2008 (new patients seen from January through December 2008) for the health system's MTM program.

RESULTS: A total of 9,068 patient records were in the documentation system as of September 30, 2008. During the 10-year period, there were 33,706 documented encounters (mean 3.7 encounters per patient). Of 38,631 drug therapy problems identified and addressed by MTM pharmacists, the most frequent were a need for additional drug therapy (n = 10,870, 28.1%) and subtherapeutic dosage (n = 10,100, 26.1%). In the clinical status assessment of the 12,851 medical conditions in 4,849 patients who were not at goal when they enrolled in the program, 7,068 conditions (55.0%) improved, 2,956 (23.0%) were unchanged, and 2,827 (22.0%) worsened during the course of MTM services. Pharmacist-estimated cost savings to the health system over the 10-year period were $2,913,850 ($86 per encounter) and the total cost of MTM was $2,258,302 ($67 per encounter), for an estimated ROI of $1.29 per $1 in MTM administrative costs. In the patient satisfaction survey, 95.3% of respondents agreed or strongly agreed that their overall health and well-being had improved because of MTM.

CONCLUSION: Pharmacist estimates of the impact of an MTM program in a large integrated health care system suggest that the program was associated with improved clinical outcomes and cost savings. Patient satisfaction with the program was high.

J Manag Care Pharm. 2010;16(3):185-95

What is already known about this subject

- The pharmacy profession has been moving from a product-focused to a patient-focused practice. The recognition of medication therapy management (MTM) by the federal government in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 provides pharmacists with the opportunity to expand and to be reimbursed for direct patient care services.
- Types of MTM programs vary from drug utilization reviews to comprehensive face-to-face pharmaceutical care services.
- Studies have demonstrated the effectiveness of MTM programs in improving the control of several disease states such as hypertension. In one randomized controlled trial (RCT) of community pharmacy-based MTM in patients with diabetes and hypertension, the percentage of patients at goal blood pressure increased from 16.0% to 48.0% in patients who received MTM and decreased from 20.0% to 6.67% in the control group. In another RCT of physician/pharmacist collaboration in patients with hypertension, mean blood pressure decreased from baseline to 6-month follow-up by 6.8/4.5 millimeters mercury (mmHg) in the control group and by 20.7/9.7 mmHg in the group that received collaborative care.

What this study adds

- In an MTM program implemented in a large integrated health care system, pharmacists found that 85% of patients had at least 1 drug therapy problem, and 29% of patients had 5 or more drug therapy problems.
- The results suggest that the major drug therapy problem in this population is the underutilization of effective medications. Of 38,631 drug therapy problems identified and addressed by MTM pharmacists, the most frequent were a need for additional drug therapy (n=10,870, 28.1%) and subtherapeutic dosage (n=10,100, 26.1%).
- Pharmacist-estimated cost savings to the health system over the 10-year period were $2,913,850 ($86 per encounter), and the total cost of MTM was $2,258,302 ($67 per encounter), for an estimated return on investment of $1.29 per $1 in MTM costs.

Medication therapy management (MTM) was officially recognized by the federal government in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA 2003).[1] The Centers for Medicare and Medicaid Services (CMS), through the MMA 2003, requires each Medicare Part D plan to establish MTM programs (MTMPs) for eligible beneficiaries as part of their benefits. MTMPs must be designed to "optimize therapeutic outcomes through improved medication use" and "reduce the risk of adverse events, including adverse drug reactions."[2] Pharmacists were the only health care provider specifically mentioned as potential MTM providers; however, "other qualified providers" can also deliver these services.[2] Additionally, the MMA 2003 did not include a specific list of services that should be provided to Medicare beneficiaries.[3] The draft Medicare Prescription Drug Benefit Manual released by CMS in December 2006 stated that "CMS believes that existing standards and performance measures are insufficient to support further specification for MTMP services and service level requirements, and therefore plans need the discretion to decide on which methods and which providers are best for providing MTMP services available under their specific MTMP."[4]

Even though the term "MTM" was introduced with the MMA 2003, pharmacists have previously developed and implemented similar programs called "pharmaceutical care."[3] Whereas MTM in the MMA 2003 is specific to Part D enrollees, pharmaceutical care can be provided to anyone. Pharmaceutical care is a practice in which the pharmacist works directly with a patient and other health care providers using interventions designed to enhance the results obtained from medication therapies.[5,6] MTM provided to Part D patients is a logical extension of the provision of pharmaceutical care services to diverse groups of patients, which has been performed by pharmacists for many years. Programs of this kind represent the pharmacy profession's shift from a product-focused to patient-centered practice.[7-14]

Several studies have shown the effectiveness of pharmaceutical care in patients with diabetes,[15,16] in patients with heart failure,[17,18] and in high-risk Medicare beneficiaries.[19] Other studies also demonstrate the positive effect of various pharmacist interventions on patients' outcomes.[20-22] Planas et al. (2009) found in a randomized controlled trial (RCT) that a community pharmacy-based MTM program was effective in improving blood pressure control of managed care enrollees with diabetes and hypertension; the percentage of patients at blood pressure goal increased from 16.0% to 48.0% in patients who received MTM and decreased from 20.0% to 6.67% in the control group.[15] In another RCT, Doucette et al. (2009) evaluated the effect of a diabetes care service provided by community pharmacists on primary clinical outcomes and on patients' reported self-care activities.[16] These authors found that compared with the control group, patients who received pharmacists' interventions significantly increased the number of days per week that they engaged in a set of diet and diabetes self-care activities, although changes in hemoglobin A1c, low-density lipoprotein cholesterol (LDL-C), and blood pressure were not significantly different between the 2 study groups.

Welch et al. (2009) assessed the impact of an MTMP on mortality, health care utilization, and prescription medication costs. They found that Medicare Part D beneficiaries who opted into the MTMP were less likely to die compared with beneficiaries who opted out (adjusted odds ratio [OR] = 0.5, 95% confidence interval [CI] = 0.3-0.9) but were more likely to be hospitalized (OR = 1.4, 95% CI = 1.1-2.0) and to have increased medication costs (OR = 1.4, 95% CI = 1.1-1.9) during follow-up.[19] Moreover, Carter el al. (2009) found in an RCT that patients treated with collaborative intervention between pharmacist and physician achieved significantly better mean blood pressure and overall blood pressure control rates compared with a control group, with mean blood pressure declining from baseline to 6-month follow-up by 20.7/9.7 millimeters mercury (mmHg) in the intervention group and by 6.8/4.5 mmHg in the control group.[22] However, in another RCT, Nietert et al. (2009) found no significant differences between time to refill of prescriptions for common chronic conditions, comparing patients contacted by pharmacists via telephone or fax with patients in usual care.[23]

The pharmacy profession has developed and reached consensus on an MTM definition.[24-29] Although this definition has not been officially recognized by CMS or most other nonpharmacy entities, in 2005 the American Medical Association established Current Procedural Terminology (CPT) codes for reimbursement of MTM services provided by a pharmacist.[29]

In 2005, the Minnesota state legislature authorized coverage of MTM services provided by pharmacists to medical assistance and general assistance medical care recipients.[30] Medical assistance is the largest of Minnesota's 3 publicly funded health care programs, providing coverage for low-income senior citizens, children and families, and people with disabilities. MTM is defined in Minnesota statute as the provision of pharmaceutical care services by a licensed pharmacist to "optimize the therapeutic outcomes of the patient's medications."[30] Coverage of MTM services is provided for medical assistance recipients "taking four or more prescriptions to treat or prevent two or more chronic medical conditions, or when prior authorized by the commissioner for a recipient with a drug therapy problem that is identified and has resulted, or is likely to result, in significant nondrug program costs."[30] The Minnesota statute promulgated requirements for the types of services encompassed by MTM (Figure 1). This legislation also specified the requirements for pharmacists' enrollment as providers and the space and privacy requirements for the consultation area where the patient receives MTM services. In 2007, the results of a nonpeer-reviewed report evaluating the effectiveness of the first year of the Minnesota MTM care program showed significant improvement in patients' clinical outcomes but no significant differences in health care expenditures in a preliminary analysis.[31] A significant body of evidence has been produced in Minnesota related to MTM from the time that pharmaceutical care theory was put into practice until more recently when investigations of MTM outcomes began.[9,31-35]

FIGURE 1 *Minnesota Legislative Requirements for Pharmacists' Provision of Medication Therapy Management Services for Medical Assistance and General Assistance Medical Care Recipients*[a]

Medication therapy management means the provision of the following services:

1. Performing or obtaining necessary assessments of the patient's health status
2. Formulating a medication treatment plan
3. Monitoring and evaluating the patient's response to therapy, including safety and effectiveness
4. Performing a comprehensive medication review to identify, resolve, and prevent medication-related problems, including adverse drug events
5. Documenting the care delivered and communicating essential information to the patient's other primary care providers
6. Providing verbal education and training designed to enhance patient understanding and appropriate use of the patient's medications
7. Providing information, support services, and resources designed to enhance patient adherence with the patient's therapeutic regimens
8. Coordinating and integrating medication therapy management services within the broader health care management services being provided to the patient

[a]*Minnesota legislative requirements are consistent with nationally accepted consensus statements on the content of an effective medication therapy management program.*[25,30]

Description of the Fairview MTM Program

The MTM program assessed in the present study is a service of Fairview Pharmacy Services, which is a subsidiary of Fairview Health Services, a Minnesota nonprofit corporation and one of the largest health care provider organizations in the state. Fairview Health Services, in partnership with the University of Minnesota, is a network of 7 hospitals, 48 primary care clinics, 55 specialty clinics, and 28 retail pharmacies that serves Minneapolis-St. Paul, as well as communities throughout greater Minnesota and the Upper Midwest. More than 2.7 million patients are seen in 1.1 million Fairview clinic visits annually. From 1997-1998, Fairview Pharmacy Services established pharmaceutical care practices, initially in Fairview retail pharmacies and then in primary care clinics, where pharmacists were not associated with dispensing activities and could more easily become part of the health care team. All MTM pharmacists within the system use the same standardized patient care process and are overseen by the MTM management team to promote consistency.

Fairview Pharmacy Services provides MTM to the following groups: (a) Medicaid beneficiaries taking 4 or more prescriptions to treat or prevent 2 or more chronic medical conditions; (b) patients enrolled with contracted Medicare Part D plan sponsors; (c) beneficiaries of contracted self-funded employers; (d) all Fairview employees regardless of the number of diseases or medications; and (e) private-pay patients. The eligibility criteria for MTM services vary among Medicare Part D plan sponsors and contracted employers. Some employers target participants based on the number of chronic medications used, whereas others target specific disease states.

The MTM program enrollment process is "opt-in." Eligible patients are recruited directly by the program using mailed letters. In order to participate, patients must complete and return an enrollment form. The patient is then contacted to set up an appointment with the MTM pharmacist. To stay enrolled in the program, the patient must come to all appointments with the pharmacist, as agreed upon by the patient and the pharmacist at the first visit. Sponsors pay per visit to the pharmacist for patients enrolled in the program. The cost of the MTM visit depends upon the complexity of each patient's case as determined by the patient's number of current medications, number of medical conditions, and number of drug therapy problems identified by the pharmacist.

MTM is provided to patients through face-to-face consultations. Initial appointments are scheduled for 60 minutes, and follow-up visits are scheduled for 30 minutes. MTM is provided in a private space, usually a consultation/exam room at a clinic. As required by Minnesota law, the space is private and entirely devoted to patient care.

MTM pharmacists follow the philosophy and the patient care process of pharmaceutical care.[6,7,14] Each MTM encounter follows a systematic review process designed to identify and resolve drug therapy problems and promote optimal patient outcomes (Figure 2). MTM pharmacists' responsibilities include the following: (a) focus on the "whole" patient (i.e., the pharmacist assesses all of the patient's diseases and medications); (b) identification of a patient's drug-related needs; (c) promotion of appropriate indications, safety, and compliance for all drug therapies by identification, resolution, and prevention of drug-related problems; (d) achievement and documentation of therapy outcomes; and (e) collaboration with all members of a patient's care team.

MTM pharmacists document therapeutic outcomes at every patient encounter using a pharmaceutical care software documentation program. Therapeutic goals are established for each of a patient's medical conditions during the initial stage of care plan development. The patient, prescriber, and pharmacist communicate to discuss patient expectations and goals of therapy. For some medical conditions, such as diabetes, there are collaborative practice agreements in place under which the MTM pharmacist can initiate, modify, or discontinue drug therapy as well as order laboratory tests related to diabetes, hypertension, and hyperlipidemia, according to the terms of the collaborative agreements.

Ten pharmacists (6.1 full-time equivalents [FTEs]) provide MTM services in 17 of the 48 clinics in the Fairview system. All MTM pharmacists have been certified in the practice of

FIGURE 2 Description of Drug Therapy Problem Categories and Assumed Medical Services Avoided

Drug-Related Needs	Categories of Drug Therapy Problems	Examples	Assumed Medical Services Avoided[a]
Indication	1. The drug therapy is unnecessary because the patient does not have a clinical indication at this time.	Patient is taking 2 ACE inhibitors to treat hypertension.	1 office visit
		Patient is taking 2 different proton pump inhibitors to treat symptoms of reflux.	1 office visit
	2. Additional drug therapy is required to treat or prevent a medical condition in the patient.	Patient with diabetes requires low-dose aspirin to prevent heart attacks and/or strokes.	1 office visit
		Patient requires a second medication to control his or her blood pressure.	1 office visit
Effectiveness	3. The drug product is not effective at producing the desired response in the patient.	Patient with otitis media is not responding to amoxicillin after 7 days of therapy.	1 urgent care visit[b]
		Patient is taking an antidepressant, which is not controlling his or her depression; a new medication is recommended.	None[c]
	4. The dosage is too low to produce the desired response in the patient.	Patient is taking an antihypertensive medication and is not responding to the dose; an increase in dose is recommended.	1 office visit
		Patient is on a controller inhaler, which is not effectively controlling asthma; a dose increase is recommended.	1 ER visit[d]
Safety	5. The drug is causing an adverse drug reaction in the patient.	Patient has developed persistent cough caused by enalapril.	1 office visit
		Patient has increased anxiety while being treated for depression with buproprion.	1 office visit
	6. The dosage is too high, resulting in undesirable effects experienced by the patient.	Patient developed bradycardia resulting from digoxin 0.5 mg per day. The dose was too high because of his age (72 years).	1 office visit
		Patient is having hypoglycemia because basal insulin dose is too high.	1 office visit
Compliance	7. The patient is not able or willing to take the drug therapy as intended.	Patient cannot afford the medication.	None
		Patient did not understand the instructions for a medication, resulting in incorrect administration.	None

[a]*Represents pharmacists' estimates of the reasonable and foreseeable cost savings resulting from the MTM intervention. MTM pharmacists assumed they saved office visits because: (a) Fairview MTM pharmacists work under collaborative practice agreements for medical conditions such as diabetes, and consequently they are able to initiate, modify, and interrupt medications used to treat hypertension, hypercholesterolemia, and diabetes; and (b) MTM pharmacists work at clinics with physicians, and as a result they are able to make recommendations to the provider at the time of an MTM visit, avoiding an additional office visit.*

[b]*The MTM pharmacist saved an urgent care visit because patients with otitis media nonresponsive to the first course of antibiotics likely have an urgent care visit.*

[c]*When the patient does not respond to an antidepressant, MTM pharmacists typically refer the patient back to the primary care physician for additional clinical assessment.*

[d]*The pharmacist saved an ER visit because patients with uncontrolled asthma normally have an ER visit.*

ACE = angiotensin-converting enzyme; ER = emergency room; mg = milligrams; MTM = medication therapy management.

pharmaceutical care by the Peters Institute of Pharmaceutical Care at the University of Minnesota and credentialed by Fairview Pharmacy Services. A practice management team comprising a pharmacy director, a product manager, an operations manager, and a business specialist supports the MTM program. Moreover, MTM pharmacists are preceptors for pharmacy students during 10-week rotations in their last year of pharmacy school. The Fairview MTM program also offers a 1-year residency in pharmaceutical care. Practitioners and the management team of the MTM program are involved in education at the University of Minnesota, College of Pharmacy, by teaching pharmacy students and graduate students how the principles of MTM are put into practice.

Quality assurance is a key component of the MTM program to promote consistency in the care provided to each patient. One important initiative is the biannual evaluation of practitioners' documentation. A random sample of patients from all MTM practitioners is evaluated by the MTM operations manager for full documentation in accordance with the MTM program's policies and procedures. Another quality improvement initiative is the monthly practitioners' meeting, when MTM pharmacists present patients' cases and discuss their practices.

The objective of the present study's analysis was to describe the clinical, economic, and humanistic outcomes of services provided by the MTM program since September 1998.

FIGURE 3 Description of the Goals of Therapy for the Most Common Medical Conditions in the MTM Program

Most Common Medical Conditions	Goals of Therapy[a]
Hypertension	Resting pulse between 50 and 100 beats per minute; blood pressure goal <140/90 mmHg unless comorbidities require a new goal.
Hyperlipidemia	Total cholesterol <200 mg per dL; triglycerides <150 mg per dL; HDL-C >40 mg per dL; LDL-C based on patient-specific goal.
Diabetes	A1c <7%, unless other goal is determined; blood pressure <130/80 mmHg; LDL-C <100 mg per dL.
Osteoporosis	Prevent, reduce, or eliminate signs and symptoms associated with osteoporosis.
Depression	Reduce or eliminate depressed mood, fatigue, insomnia, loss of appetite or interest, guilt, or other signs or symptoms associated with this depressive disorder. Work, school, or activities are not missed. Constipation, dry mouth, waking hour drowsiness, and orthostatic hypotension are not a problem. Patient understands the length of time on therapy that is necessary to see improvement.
Esophagitis	Eliminate discomfort associated with esophageal problem.
Allergic rhinitis	Congestion, sneezing, runny nose, irritated eyes/nasal passages, or other symptoms of allergic rhinitis should clear up within 5 days of adequate therapy.
Hypothyroidism	Prevent, reduce, or eliminate signs and symptoms associated with hypothyroidism.
Menopause	Reduce or eliminate menopausal symptoms.
Insomnia	The goal of therapy is to reduce or eliminate insomnia in the short term. Other methods should be evaluated for long-term problem.

[a]*The described goals of therapy are general goals, which might change slightly according to the needs of a specific patient.*

A1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; mg per dL = milligrams per deciliter; mmHg = millimeters mercury; MTM = medication therapy management.

Methods

A retrospective analysis of the 9,068 patients seen in the Fairview MTM program from September 1, 1998, through September 30, 2008, was conducted. All patients who were aged 21 years or older and who either met their health care payer's reimbursement criteria for MTM or paid for MTM out of pocket were included in the analysis. Data were abstracted from the MTM documentation system (Assurance System) that stored all the documented data from all patients enrolled in the MTM program during the 10-year period. Data abstracted by the first author of this article included the following fields: patients' demographics, number of MTM consultations, number of medications taken, number and types of medical conditions, types of drug therapy problems identified and addressed, types of interventions implemented to resolve drug therapy problems, change in patients' clinical status, and pharmacist-estimated health care savings.

The number of medications taken by patients included all active over-the-counter (OTC) medications, supplements, herbal products, medications used to treat acute conditions or used for a limited time period (e.g., antibiotics, analgesics), and medications prescribed for chronic conditions (e.g., antihypertensive medications, antidepressant agents). The presence of medical conditions was determined using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes documented first in the patient's electronic medical record and then in the Assurance System by the MTM pharmacist.

Drug Therapy Problems

Drug therapy problems were classified into 4 major categories—indication, effectiveness, safety, and compliance—and 7 subcategories (Figure 2). The classification of drug therapy problems was carried out using a systematic process of problem solving referred to as Pharmacotherapy Workup.[6,36] The workup algorithm asks if the medication is appropriate for that specific patient; if the medication is the most effective and the right dose to help the patient to achieve his or her clinical goals; if the medication is the safest for that patient; and if the patient is able and willing to adhere to the drug regimen. Nonadherence is defined in the pharmaceutical care practice model as the patient's inability or unwillingness to take a drug regimen that the practitioner has clinically judged to be appropriately indicated, adequately efficacious, and able to produce the desired outcomes.[6] In this decision-making process, before evaluating patients' medication-taking behaviors (following or not following the instructions), practitioners attempt to certify that patients are taking all the medications and only the medications that they need and that all of the medications they are taking are effective and safe. The documentation of drug therapy problems also includes the medications involved, the medical conditions affected, the causes of the problem, and the interventions implemented to attempt resolution of the problem. For nonadherence, the MTM pharmacist documents the main reason the patient is nonadherent, which will determine the intervention used to address this drug therapy problem.

Clinical Status Assessment

For each patient, change in clinical status was evaluated and documented by the MTM pharmacist at each MTM consultation.[6] A clinical outcome status was documented as "resolved," "stable," "improved," or "partially improved" when the patient was considered to be achieving the goal of therapy for a specific medical condition, and the following terms were used when the patient was not achieving the goal of therapy:

"unimproved," "worsened," or "failure."

The pharmacist, patient, and physician cooperatively determined goals of therapy that served as the agreed-upon targets for care plan actions and interventions. For each drug therapy indication, goals included clinical parameters described in the literature and patient-specific goals. Drug therapy goals were intended to be measurable, observable, realistic, and achievable within a specified time frame (Figure 3).

For the present study's analysis, we evaluated the patients' clinical status at the first and at the most recent MTM consultation. Specifically, for patients not at goal at the first MTM visit, the number of patients not at therapy goal (including clinical status unimproved, worsened, and failure) and the number with improved clinical status (resolved, stable, improved, or partially improved) in the last visit were documented. This approach was deemed reliable and valid based on the results of a quality assessment analysis conducted by Isetts et al. (2003), in which a 12-member panel of physicians and pharmacists reviewed clinical determinations made by Fairview MTM pharmacists from January 1999 through March 2002 for 300 randomly selected patient records.[32] For each patient, 4 types of determinations were assessed, including identification of the drug therapy problem, actions taken to resolve the problem, assessment of clinical status including goal achievement, and estimate of costs avoided by the intervention. Panel members concurred with 94.2% of determinations, disagreed with 2.2%, and expressed neutrality on 3.6%. Intraclass correlation coefficients ranged from 0.73 to 0.85.[32]

To assess clinical status outcomes in more detail, a subset of data for employees of a self-funded employer was analyzed. This analysis focused on the clinical outcomes of 110 patients with diabetes who were followed by MTM pharmacists from August 2007 to December 2008. Even though the MTM pharmacist assesses all of a patient's conditions and medications, for the purposes of this analysis only the clinical outcomes associated with diabetes care were described. Five measures ("the D5") that assess optimal diabetes care, as it is suggested by the State of Minnesota, were used to determine the clinical outcomes of this group of patients.[37] The D5 is a set of 5 treatment goals that when achieved together represent the gold standard for managing diabetes. Reaching all 5 goals greatly reduces a patient's risk for the cardiovascular problems associated with diabetes. The D5 goals include the following: (a) A1c less than 7%; (b) blood pressure less than 130/80 mmHg; (c) LDL-C less than 100 milligrams per deciliter (mg per dL); (d) daily aspirin use (for patients aged 41 to 75 years), and (e) documented tobacco-free status. The percentage of MTM patients reaching all 5 goals in December 2008 was compared with the percentage of patients reaching all goals in the first MTM visits that occurred in August 2007.

Economic Outcomes

To estimate the economic impact of MTM, all health care savings documented by MTM pharmacists in the Assurance System were reviewed. MTM pharmacists projected the short-term (3-month) cost savings resulting from their interventions to resolve drug therapy problems (Figure 2). Direct savings included medical services avoided as a result of the intervention, including office visits, emergency room (ER) visits, urgent care visits, long-term care stays, and hospitalizations. Avoidance of lost work time was also estimated. Only those savings considered reasonable and foreseeable by the MTM pharmacist and the MTM management team, based on clinical judgment, quality control procedures, and those changes allowed per the program's collaborative agreements, were included in the documentation system. This process was standardized, meaning that a particular problem was almost always associated with the same avoided medical service. Additionally, the estimates included only short-term (3-month) savings that might be realized as a direct result of an MTM encounter, not any longer-term savings that might have occurred as a result of implementing preventive drug therapies, such as aspirin to prevent myocardial infarction and stroke, calcium supplementation to prevent osteoporosis and fractures, or immunizations to prevent influenza or pneumonia.

As a quality control procedure, the cost savings claims were adjudicated by an independent clinical pharmacist, external to the Fairview system, who could disallow or downgrade the cost-savings estimate if evidence documented by the practitioner was insufficient. Each time an MTM pharmacist determined that a hospital admission, ER visit, or nursing home admission was avoided as a result of MTM, additional documentation of agreement by the patient and the patient's primary physician was required. This method of estimating health care cost savings was included in the Isetts et al. study that assessed the validity of determinations made by Fairview MTM pharmacists.[32]

To estimate total cost avoidance, the expenses of the avoided health care services were linked to the average costs of services provided and charged by Fairview Health Services in the last quarter of 2008. Specifically, for each medical service, total avoided expense was calculated by multiplying the number of avoided services by the average cost per service. The value of avoiding lost work time was estimated by multiplying $30.00 (average hourly wage in Fairview) by 8 (daily working hours), then multiplying that result by the number of workdays gained by the intervention, as determined by the pharmacist. For a calculation of the return on investment (ROI) for the program, the cost of providing MTM services was determined by multiplying the average cost of an MTM visit in the last quarter of 2008 by the number of MTM consultations during the 10-year period. The ROI was calculated by dividing the pharmacist-estimated total health care savings by the cost of MTM visits in 2008.

Patient Satisfaction

Since 2001, patient satisfaction surveys have been administered biannually to all patients enrolled in the MTM program in that year. The survey consists of a 7-item questionnaire using a Likert-type scale with 5 options (i.e., agree, strongly agree, neither agree nor disagree, disagree, strongly disagree) that measures patients' satisfaction with MTM services. Respondents are asked to evaluate the following statements: (1) The pharmacist provided me with education that will help me achieve my goals of therapy;

(2) The pharmacist helped me to understand the intended use (purpose) of my medication(s); (3) The pharmacist helped me to understand the intended results (goals of therapy) of my medication(s); (4) The pharmacist helped me understand how to take my medication(s) safely and correctly; (5) I feel that my overall health and well-being improved because of my MTM visit; (6) Health care benefits should include MTM services; and (7) I would recommend this MTM service to my family and friends. Beneath the 7 statements, there is room for respondents to write comments and suggestions about the MTM program.

In 2008, only patients newly enrolled in the MTM program were surveyed after 2 visits with the MTM pharmacist. Patients received the surveys in the mail along with a pre-addressed postage-paid envelope. For the purposes of the present study, the results of the surveys administered from July to December 2008 were analyzed.

Results

From 1998 to 2008, there were 33,706 documented encounters in a cohort of 9,068 patients, yielding an average of 3.72 visits per patient. The patients ranged in age from 21 to 102 years with 55.5% of patients younger than age 65 years (Table 1). Females constituted 75.9% of the patients.

Medical Conditions and Drug Therapies Used

The average number of medical conditions being treated or prevented per patient through September 2008 was 6.8; 72.4% of patients had 5 or more conditions, and 23.0% had more than 10 conditions. The most frequent indications for drug therapy were hypertension (8.4%), hyperlipidemia (7.9%), nutritional/vitamin supplements (7.3%), diabetes (6.5%), osteoporosis (4.1%), depression (3.7%), and esophagitis (3.5%; data not shown).

The number of medications per patient ranged from 1 to 52. The mean (SD) number of medications per patient encounter was 12.4 (5.9). Forty-five percent of the patients (n = 4,081) were taking 59,427 different OTC medications, and 633 patients (7.0%) were also using 1,783 different sample products.

Drug Therapy Problems Identified and Addressed

The number of drug therapy problems identified and addressed by MTM pharmacists from 1998 to 2008 was 38,631. At the first MTM visit, 7,708 (85.0%) of patients had 1 or more drug therapy problems, and 2,630 (29.0%) had 5 or more drug therapy problems. The most frequent drug therapy problem was the need for additional drug therapy (28.1% of all drug therapy problems; Table 2). The majority of these problems involved patients who required preventive aspirin, oral calcium supplements, oral hypoglycemics, statins, or insulin. The second most common drug therapy problem category was subtherapeutic dosage (26.1% of all drug therapy problems). The top 5 categories of medications that were most commonly used in subtherapeutic dosages included oral hypoglycemics, insulin, calcium, statins, and angiotensin-converting enzyme (ACE) inhibitors. Only 16.5% of drug therapy problems were attributed to nonadherence. In the pharmacist's assessment of the single main cause for nonadherence, the most frequent cause of patients being unable or unwilling to take medications as intended was that the patient could not afford to purchase the medication or could not afford the copayment required to obtain the prescription (36.2% of 6,379 nonadherent patients; Table 3). The next most frequent reason identified for nonadherence was that the patient did not understand the instructions (24.8% of nonadherent patients). The top 5 categories of medications associated with nonadherence were

TABLE 1 Patient Population Receiving Medication Therapy Management

Patient Characteristics	Number of Patients (%)[a] N = 9,068
Gender	
Male	2,184 (24.1)
Female	6,884 (75.9)
Age (years)	
21-50	2,018 (22.3)
51-64	3,019 (33.3)
65 or more	4,031 (44.5)
Number of medications at baseline[b]	
0	35 (0.4)
1-2	130 (1.4)
3-4	248 (2.7)
5-6	444 (4.9)
7-8	716 (7.9)
9-10	844 (9.3)
More than 10	6,651 (73.3)
Number of medical conditions[c]	
0	217 (2.4)
1-2	1,015 (11.2)
3-4	1,269 (14.0)
5-6	1,741 (19.2)
7-8	1,605 (17.7)
9-10	1,135 (12.5)
More than 10	2,086 (23.0)
Number of drug therapy problems	
0	1,360 (15.0)
1	1,405 (15.5)
2	1,469 (16.2)
3	1,451 (16.0)
4	753 (8.3)
5 or more	2,630 (29.0)
Payer	
Fairview enrollees	6,196 (68.3)
Private pay	1,233 (13.6)
Medicare Part D	1,137 (12.5)
Medicaid	502 (5.5)

[a]Reflects patients who chose participation after receiving a mailed invitation from the MTM program. Columns may not sum to 100% due to rounding.
[b]Total medication count includes chronic and acute prescription drugs, over-the-counter drugs, supplements, and herbal products.
[c]Count of medical conditions was based on the number of different International Classification of Diseases, Ninth Revision, Clinical Modification codes contained in the patient's electronic medical record.
MTM = medication therapy management.

TABLE 2 Drug Therapy Problems Identified and Addressed by MTM Pharmacists[a]

	Categories of Drug Therapy Problems	Number of Drug Therapy Problems (%)
Indication	1. Unnecessary drug therapy	2,196 (5.7)
	2. Needs additional drug therapy	10,870 (28.1)
Effectiveness	3. Ineffective drug	3,387 (8.8)
	4. Dosage too low	10,100 (26.1)
Safety	5. Adverse drug reaction	3,197 (8.3)
	6. Dosage too high	2,502 (6.5)
Compliance	7. Nonadherence	6,379 (16.5)
	Total	38,631

[a]*Reflects services provided from September 1998 through September 2008 to 9,068 patients.*
MTM = medication therapy management.

TABLE 3 Drug Therapy Adherence Problems Addressed by MTM Pharmacists[a]

Drug Therapy Problem	Count (%)
Cannot afford drug product	2,311 (36.2)
Patient does not understand instructions	1,585 (24.8)
Patient prefers not to take	1,014 (15.9)
Patient forgets to take	806 (12.6)
Drug product not available	546 (8.6)
Cannot swallow/administer	117 (1.8)

[a]*Reflects MTM services provided from September 1998 through September 2008 to 9,068 patients with a total of 6,379 adherence problems. Table shows the problem that, in the opinion of the pharmacist, was the main reason that the patient was nonadherent. For patients with more than 1 reason, only the main reason is shown.*
MTM = medication therapy management.

statins, insulin, oral hypoglycemics, proton pump inhibitors, and ACE inhibitors.

Eighty percent of drug therapy problems identified in Fairview's MTM program were resolved without the direct involvement of patients' physician(s), perhaps because the MTM program has collaborative practice agreements signed with physicians in Fairview Health Services. The most common resolutions of drug therapy problems with patients were education (35.8%), elimination of a barrier to access a medication (26.8%), initiation of a new drug therapy (11.8%), and change in dose (10.5%). The most frequent resolutions of drug therapy problems with physicians were initiation of a new drug therapy (32.4%), change in drug dosage (25.2%), change in drug product (14.7%), and discontinuation of a drug therapy (12.1%).

Clinical Outcomes

In the clinical status assessment of the 12,851 medical conditions in 4,849 patients who were not at goal when they enrolled in the MTM program, 7,068 conditions (55.0%) improved, 2,956 (23.0%) were unchanged, and 2,827 (22.0%) worsened during the course of MTM services. Of the 31,858 medical conditions evaluated on at least 2 occasions in 5,054 patients, 17,203 (54.0%) conditions were unchanged, 10,513 (33.0%) improved, and 4,141 (13.0%) declined in clinical status during MTM therapy.

In the subset of patients with diabetes (110 employees of a self-funded employer), 47 (42.7%) reached all D5 goals for diabetes (A1c less than 7%, blood pressure less than 130/80 mmHg, LDL-C less than 100 mg per dL, no tobacco use, and daily aspirin use) at the last MTM visit. At baseline, only 19 (17.3%) of these patients were reaching all goals, representing an absolute 25.4% change. By comparison, in Minnesota as a whole, only 8% and 13% of patients with diabetes who were covered by public and private payers, respectively, were reaching all these goals in 2008.[38]

Economic Outcomes

Over the 10-year study period, pharmacist-estimated direct savings to Fairview Health Services were $2,913,850 ($86.45 per encounter for 33,706 encounters; Table 4). The average cost of an MTM visit for Fairview was $67.00 in the last quarter of 2008, for a total MTM programmatic cost of $2,258,302 and an estimated ROI of $1.29 per $1 in MTM costs.

Patient Satisfaction

From July to December 2008, 317 patients responded to the patient satisfaction survey (28.0% response rate of 1,132 surveys mailed), expressing a generally high level of satisfaction with the program: 97.1% of respondents agreed or strongly agreed that the pharmacist provided them with the education that will help them to achieve their goals of therapy; 95.3% of respondents agreed or strongly agreed that their overall health and well-being had improved because of MTM; 98.1% of patients agreed or strongly agreed that they would recommend this service to their family and friends; 99.0% of respondents agreed or strongly agreed that the pharmacist helped them to understand the intended use (purpose) of their medications; 99.9% of patients agreed or strongly agreed that the pharmacists helped them to understand the intended results (goals of therapy) of their medications; 99.0% of respondents agreed or strongly agreed that the pharmacist helped them to understand how to take their medication(s) safely and correctly; and 98.1% of patients agreed or strongly agreed that health care benefits should include the MTM program. Moreover, the patients' comments about the MTM program were overwhelmingly positive, including a patient who commented that the MTM service had changed her life by permitting her to gain control of her diabetes.

Discussion

In a large integrated health care system, MTM was provided to a diverse group of 9,068 patients, using a standardized patient care process to address numerous drug therapy problems identified by pharmacists. In this population, patients rarely experienced a single medical condition, and 72% had 5 or more medical conditions. The high level of comorbidities makes patients' drug regimens complex, which can make adherence difficult and confusing for patients. Focusing on only a single disease state is unlikely

to adequately meet all of a patient's drug-related needs.

Moreover, despite extensive use of nonprescription medications (OTC, supplements, herbal medicines, etc.) by this population, those drug products are usually not recorded in standard payer claims database systems or pharmacy dispensing systems. MTM is an effective mechanism to facilitate assessment of the indications, effectiveness, and safety of OTC products, especially in patients who are using multiple prescription medications.

More than one-half (54.2%) of drug problems involved the need for a new medication or dosage increase. The medical conditions associated with these most common drug therapy problems were diabetes and hyperlipidemia. These results suggest that when pharmacist practitioners work closely and over time with patients to facilitate reaching the goals of therapy, there is usually an increase in medication use. These results are consistent with those of previous research that assessed the clinical outcomes of pharmaceutical care services.[19,31,39,40] For example, Welch et al. found that Medicare Part D beneficiaries who opted in to receive MTM were more likely to incur an increase in medication costs than were those who opted out of MTM.[19] These results also indicate that health care providers might choose nonpharmacological interventions when drug therapy is needed or use a dose that is too low to control the patient's medical condition. Other studies have shown a failure to titrate medications, such as statins, to effective doses in patients at risk of complications.[41,42] Some authors who stress the importance of using more aggressive therapy, such as higher doses or introducing combination therapy to get patients to goal, have described "clinical inertia," a failure of health care providers to initiate or intensify therapy when indicated.[43,44]

Even though most work conducted within pharmacy has focused on adverse drug effects, drug interactions, duplicate therapy, and compliance, our data suggest that the major problem related to medications can be attributed to underuse of potentially efficacious drug therapy. As stated by O'Connor et al. (2005), failure to intensify therapy in patients with chronic conditions and suboptimal biomarker readings for blood glucose, blood pressure, or serum lipids represents a type of medication error as defined by the Institute of Medicine by leading to adverse events.[44] O'Connor et al. assert that the main distinction between the adverse events caused by overuse or misuse of therapies, and adverse events caused by underuse of therapies in chronic disease care, is the time frame over which the adverse event occurs. Clinical inertia, or the underuse of efficacious drug therapy, "may take years or even decades for the consequent adverse event to declare itself."[44]

The Fairview MTM program's experience suggests that patients often have good reason for not adhering or persisting with drug treatment. As discussed by Ramalho de Oliveira and Shoemaker (2006), pharmacists should look at noncompliance from the perspective of the patients, taking into consideration their subjective experiences with their illnesses and medications.[45] In this context, it is essential to understand the patient's unique medication experience, which is connected with patients' previous experiences with medications, what they think and feel about their medications, and their concerns and beliefs about them.[46] This experience will influence the patient's decisions about whether to take the medication, to decrease or increase the dose, or to make necessary modifications to the drug regimen. In a recent review on compliance and adherence, Touchette and Shapiro (2008) suggested that because adherence is a multifaceted issue, programs designed to impact adherence should focus on identifying patient-specific adherence barriers and tailor interventions to eliminate or reduce these barriers.[47] The authors emphasize that tailoring interventions to meet each patient's needs will bring about better outcomes than offering the same blanket intervention to all patients.[47] This review corroborates the approach of using the patient's unique medication experience to assist him or her to achieve therapeutic goals.

Stebbins et al. (2005) examined pharmacists' interventions that combined drug utilization review with patient and physician education in a medical clinic for low-income elderly patients.[48] In this study, pharmacists' interventions increased the use of generic drugs, decreased out-of-pocket drug expenses by patients, and promoted use of needed treatments. Another study by Barnett et al. (2009) that analyzed 7 years of MTM claims from an MTM administrative services company suggested that from 2000 to 2006, there was a shift in the type of pharmacists' interventions from patient education involving acute medications to prescriber consultation for chronic medications.[49] Barnett et al. also found an increase in the MTM reimbursement over time, from $7.65 to $12.28 per intervention. As underscored by Benner and Kocot (2009), we are moving towards a health care system that will emphasize and reward quality and high value, and pharmacists must take the opportunity to redefine themselves as medication therapy managers who will add significant value by improving medication outcomes.[50] The

TABLE 4 Estimated Health Care Savings[a]

Health Care Savings	Number of Events	Cost Per Event	Total Savings
Clinic outpatient visit avoided	10,313	$162.00	$1,670,706
Specialty office visit avoided	1,346	$207.00	$278,622
Employee work days saved	277	$240.00	$66,480
Laboratory service avoided	240	$22.45	$5,388
Urgent care visit avoided	144	$121.24	$17,459
Emergency room visit avoided	211	$755.00	$159,305
Hospital admission avoided[b]	41	$16,983.00	$696,303
Nursing home admissions	3	$6,398.00	$19,194
Home health visit	1	$392.84	$393
Total	12,576		$2,913,850

[a]Reflects services provided to 9,068 patients in 33,706 encounters from September 1998 through September 2008. Savings were calculated as the number of events avoided by MTM, as estimated by the MTM pharmacist and validated by external review, times the average costs of services at Fairview Health Services in the second quarter of 2008.

[b]Cost per event is the average cost of a hospital admission in Fairview Health Services in the second quarter of 2008.

MTM = medication therapy management.

profession of pharmacy must focus on the unmet needs of patients and provide consistent and standardized services that can be recognized, measured, and paid for.

The economic results of this study were positive as the calculated ROI suggests that MTM services decreased the total cost of health care in Fairview Health Services. Our results are similar to those of other studies that also indicated potential cost-saving effects of MTM services.[34,49]

This study is an important step in the direction of examining the outcomes of a comprehensive, standardized, and holistic approach to MTM. As stressed by Doucette et al. (2005),[39] policy makers seeking models of MTM services for Medicare beneficiaries should consider a model as comprehensive as pharmaceutical care for patients at high risk of developing drug-related problems.

Currently, MTM pharmacists are considered an indispensable part of the health care team in Fairview Health Services because they assume responsibility for patients' drug therapy outcomes and collaborate with other providers to facilitate high-quality patient care. In 2010, Fairview's MTM program is expanding to 6 additional clinics, and 3 MTM pharmacists are providing care on-site at major employers' headquarters in the Twin Cities area.

Limitations

First, the lack of a comparison group makes this a descriptive study without the ability to attribute outcomes to the MTM interventions. Participating patients opted into the program and therefore might be especially motivated to comply with medical and drug treatments. Second, the economic outcomes described here are the result of a process of estimation and documentation by MTM pharmacists, which is based on clinical judgment instead of a thorough analysis of medical claims. Third, our programmatic cost estimates do not include additional costs associated with added medications or increased dosages. Fourth, because our survey response rate was low, the satisfaction level of survey respondents might not reflect that of the MTM population as a whole. Fifth, our results may be partly attributable to the collaborative practice agreements that permitted pharmacists to make 80% of interventions without physician involvement. A final limitation is the inability to generalize the findings outside of the health system environment where access to needed patient information is not as readily available.

Conclusion

The pharmaceutical care-based MTM services assessed in this study identified numerous drug therapy problems; 85% of patients had 1 or more drug therapy problems, and 29% had 5 or more drug therapy problems. Because the most prevalent drug therapy problems were related to the underuse of effective medications, the number of medications used by patients tends to increase with MTM services. However, MTM may save total health care costs by helping patients avoid office visits, ER visits, and hospitalizations.

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DISCLOSURES

There was no external funding for this manuscript. The 3 authors are employees of Fairview Pharmacy Services. Ramalho de Oliveira had primary responsibility for the concept and design, writing, and revision of the manuscript, with the assistance of Brummel and Miller. Ramalho de Oliveira performed the data collection, and all 3 authors shared equally in data interpretation.

REFERENCES

1. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (January 7, 2003). Available at: http://www.cms.hhs.gov/MMAUpdate/downloads/hr1.pdf. Accessed March 16, 2010.

2. Centers for Medicare and Medicaid Services. Medicare Part D medication therapy management (MTM) programs 2009 fact sheet. Updated July 21, 2009. Available at: http://www.cms.hhs.gov/PrescriptionDrugCovContra/Downloads/MTMFactSheet.pdf. Accessed March 16, 2010.

3. Hassol A, Shoemaker SJ. Exploratory research on medication therapy management: final report. July 8, 2008. Available at: http://www.cms.hhs.gov/Reports/downloads/Blackwell.pdf. Accessed March 16, 2010.

4. Center for Medicare and Medicaid Services. Medicare Prescription Drug Benefit Manual, Chapter 7–Medication Therapy Management and Quality Improvement Program. December 1, 2006. Available at: http://www.cms.hhs.gov/PrescriptionDrugCovContra/Downloads/PDBManual_Chapter7.pdf. Accessed March 16, 2010.

5. Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice.* New York: McGraw-Hill; 1998:359.

6. Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice: The Clinician's Guide.* 2nd ed. New York: McGraw-Hill; 2004:394.

7. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm.* 1990;47(3):533-43.

8. Hepler CD. The future of pharmacy: pharmaceutical care. *Am Pharm.* 1990;NS30(10):23-29.

9. Tomechko MA, Strand LM, Morley PC, Cipolle RJ. Q and A from the Pharmaceutical Care Project in Minnesota. *Am Pharm.* 1995;NS35(4):30-39.

10. Hepler CD, Strand LM, Tromp D, Sakolchai S. Critically examining pharmaceutical care. *J Am Pharm Assoc (Wash).* 2002;42(5 Suppl 1):S18-S19.

11. Ramalho de Oliveira D. Pharmaceutical care uncovered: an ethnographic study of pharmaceutical care practice. [dissertation]. Minneapolis, MN: University of Minnesota; 2003.

12. Strand LM, Cipolle RJ, Morley PC, Frakes MJ. The impact of pharmaceutical care practice on the practitioner and the patient in the ambulatory practice setting: twenty-five years of experience. *Curr Pharm Des.* 2004;10(31):3987-4001.

13. McGivney MS, Meyer SM, Duncan-Hewitt W, Hall DL, Goode JV, Smith RB. Medication therapy management: its relationship to patient counseling, disease management, and pharmaceutical care. *J Am Pharm Assoc (2003).* 2007;47(5):620-28.

14. Ramalho de Oliveira D. *The Reality of Pharmaceutical Care-Based Medication Therapy Management: Patients', Pharmacists' and Students' Perspectives*. Saarbrücken, Germany: Lambert Academic Publishing; 2010:384.

15. Planas LG, Crosby KM, Mitchell KD, Farmer KC. Evaluation of a hypertension medication therapy management program in patients with diabetes. *J Am Pharm Assoc (2003).* 2009;49(2):164-70.

16. Doucette WR, Witry MJ, Farris KB, McDonough RP. Community pharmacist-provided extended diabetes care. *Ann Pharmacother.* 2009;43(5):882-89.

17. Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med.* 2007;146(10):714-25.

18. Murray MD, Ritchey ME, Wu J, Tu W. Effect of a pharmacist on adverse drug events and medication errors in outpatients with cardiovascular disease. *Arch Intern Med.* 2009;169(8):757-63.

19. Welch EK, Delate T, Chester EA, Stubbings T. Assessment of the impact of medication therapy management delivered to home-based Medicare beneficiaries. *Ann Pharmacother.* 2009;43(4):603-10.

20. Choe HM, Bernstein SJ, Cooke D, Stutz D, Standiford C. Using a multidisciplinary team and clinical redesign to improve blood pressure control in patients with diabetes. *Qual Manag Health Care.* 2008;17(3):227-33.

21. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy.* 2008;28(4):421-36.

22. Carter BL, Ardery G, Dawson JD, et al. Physician and pharmacist collaboration to improve blood pressure control. *Arch Intern Med.* 2009;169(21):1996-2002.

23. Nietert PJ, Tilley BC, Zhao W, et al. Two pharmacy interventions to improve refill persistence for chronic disease medications: a randomized controlled trial. *Med Care.* 2009;47(1):32-40.

24. American Pharmacists Association, National Association of Chain Drug Stores Foundation. Medication therapy management in community pharmacy practice: Core elements of an MTM service (version 1.0). *J Am Pharm Assoc (2003).* 2005;45(5):573-79. Available at: http://www.nacdsfoundation.org/user-assets/Documents/PDF/MTM%20Model%20final.pdf. Accessed March 17, 2010.

25. Bluml BM. Definition of medication therapy management: development of professionwide consensus. *J Am Pharm Assoc (2003).* 2005;45(5):566-72.

26. The Lewin Group. Medication therapy management services: A critical review. *J Am Pharm Assoc (2003).* 2005;45(5):580-87. Available at: http://www.michiganpharmacists.org/resources/clinicalProjects/MTM_CriticalReview.pdf. Accessed March 16, 2010.

27. Academy of Managed Care Pharmacy. Sound medication therapy management programs, Version 2.0 with validation study. *J Manag Care Pharm.* 2008;14(1 Suppl B):S2-S44. Available at: http://www.amcp.org/data/jmcp/JMCPSuppB_Jan08.pdf.

28. American Pharmacists Association, the National Association of Chain Drug Stores Foundation. Medication therapy management in pharmacy practice: core elements of an MTM service model (version 2.0). *J Am Pharm Assoc (2003).* 2008;48(3):341-53. Available at: http://www.pharmacist.com/AM/Template.cfm?Section=Home2&CONTENTID=15496&TEMPLATE=/CM/ContentDisplay.cfm. Accessed March 16, 2010.

29. Gonzalez J, Noga M. Medication therapy management. *J Manag Care Pharm.* 2008;14(6 suppl S-c):8-11. Available at: http://www.amcp.org/data/jmcp/Aug%20suppl%20C_S8-S11.pdf.

30. Minnesota Senate. Minnesota Senate, S.F. No. 973, 1st Engrossment - 84th Legislative Session (2005-2006). Medication therapy management care. 2005. Available at: https://www.revisor.leg.state.mn.us/bin/bldbill.php?bill=S0973.1&session=ls84. Accessed March 16, 2010.

31. Isetts BJ. Evaluating effectiveness of the Minnesota Medication Therapy Management Care Program: final report. December 14, 2007. Available at: http://www.dhs.state.mn.us/main/groups/business_partners/documents/pub/dhs16_140283.pdf. Accessed March 16, 2010.

32. Isetts BJ, Brown LM, Schondelmeyer SW, Lenarz LA. Quality assessment of a collaborative approach for decreasing drug-related morbidity and achieving therapeutic goals. *Arch Int Med.* 2003;163(15):1813-20.

33. Isetts BJ, Schondelmeyer SW, Heaton AH, Wadd WB, Hardie NA, Artz MB. Effects of collaborative drug therapy management on patients' perceptions of care and health-related quality of life. *Res Social Adm Pharm.* 2006;2(1):129-42.

34. Isetts BJ, Schondelmeyer SW, Artz MB, et al. Clinical and economic outcomes of medication therapy management services: the Minnesota experience. *J Am Pharm Assoc.* 2008;48(2):203-11.

35. Thompson CA. State-paid medication therapy management services succeed. *Am J Health-Syst Pharm.* 2008;65(6):490,493,498.

36. Peters Institute of Pharmaceutical Care. Pharmacotherapy notes. Updated 2008. Available at: http://www.pharmacy.umn.edu/centers/peters/teaching/pharmacotherapynotes/home.html. Accessed February 26, 2010.

37. Minnesota Community Measurement. The D5: About the D5. 2009. Available at: http://www.thed5.org/index.php?p=about_the_d5. Accessed March 16, 2010.

38. Minnesota Community Measurement, Minnesota Department of Human Services. 2008 Health Care Disparities Report for Minnesota Health Care Programs. 2009. Available at: http://edocs.dhs.state.mn.us/lfserver/Legacy/DHS-5573A-ENG. Accessed March 17, 2010.

39. Doucette WR, McDonough RP, Klepser D, McCarthy R. Comprehensive medication therapy management: identifying and resolving drug-related issues in a community pharmacy. *Clin Ther.* 2005;27(7):1104-11.

40. Rao D, Gilbert A, Strand LM, Cipolle RJ. Drug therapy problems found in ambulatory patient populations in Minnesota and South Australia. *Pharm World Sci.* 2007;29(6):647-54.

41. Alsheikh-Ali AA, Lin JL, Abourjaily P, Ahearn D, Kuvin JT, Karas RH. Extent to which accepted serum lipid goals are achieved in a contemporary general medical population with coronary heart disease risk equivalents. *Am J Cardiol.* 2006;98(9):1231-33.

42. Ansell BJ. Not getting to goal: the clinical costs of noncompliance. *J Manag Care Pharm.* 2008;14(6 Suppl B):S9-S15. Available at: http://www.amcp.org/data/jmcp/JMCPSuppB_S9-S15.pdf.

43. Phillips LS, Branch WT, Cook CB, Doyle, J. P. et al. Clinical inertia. *Ann Intern Med.* 2001;135(9):825-34.

44. O'Connor PJ, Sperl-Hillen JAM, Johnson PE, Rush WA, Biltz G. Clinical inertia and outpatient medical errors. *Advances in Patient Safety.* 2005;2:293-308. Available at: http://www.ahrq.gov/downloads/pub/advances/vol2/OConnor.pdf. Accessed March 16, 2010.

45. Ramalho de Oliveira D, Shoemaker SJ. Achieving patient centeredness in pharmacy practice: openness and the pharmacist's natural attitude. *J Am Pharm Assoc (2003).* 2006;46(1):56-66.

46. Shoemaker SJ, Ramalho de Oliveira D. Understanding the meaning of medications for patients: the medication experience. *Pharm World Sci.* 2008;30(1):86-91.

47. Touchette DR, Shapiro NL. Medication compliance, adherence, and persistence: current status of behavioral and educational interventions to improve outcomes. *J Manag Care Pharm.* 2008;14(6 Suppl D):S2-S10. Available at: http://www.amcp.org/data/jmcp/Aug08%20Suppl%20D_S2-S10.pdf.

48. Stebbins MR, Kaufman DJ, Lipton HL. The PRICE clinic for low-income elderly: a managed care model for implementing pharmacist-directed services. *J Manag Care Pharm.* 2005;11(4):333-341. Available at: http://www.amcp.org/data/jmcp/contemporary_333_341.pdf.

49. Barnett MJ, Frank J, Wehring Hea. Analysis of pharmacy-provided medication therapy management (MTM) services in community pharmacies over 7 years. *J Manag Care Pharm.* 2009;15(1):18-31. Available at: http://www.amcp.org/data/jmcp/018-031.pdf.

50. Benner JS, Kocot SL. Medicare Part D: good for patients and an opportunity for pharmacists. *J Manag Care Pharm.* 2009;15(1):66-70. Available at: http://www.amcp.org/data/jmcp/066-070.pdf.

Impact of a Medication Management System on Nursing Home Admission Rate in a Community-Dwelling Nursing Home–Eligible Medicaid Population

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ABSTRACT

Background: Community-dwelling frail elderly have an increased need for effective medication management to reside in their homes and delay or avoid admission to nursing homes.

Objective: The objective of this study was to examine the impact of a medication management system on nursing home admission within the community-dwelling frail elderly.

Methods: This prospective cohort study compared nursing home admission rates in intervention and control clients of a state Medicaid home and community-based waiver program. Groups were matched on age (±5 years), race, gender, and waiver program start date (±120 days). The medication management service consisted of 2 parts: 1) prescription medicines dispensed from the client's local pharmacy in a calendar card, and 2) a coordinating service by a health educator to address medication-related problems as they arose. The primary dependent variable was admission to a nursing home.

Results: A total of 273 clients agreed to participate, enrolled, and had at least 1 prescription dispensed. The matched control group was composed of 800 other clients. The client sample was 72 years of age, 73% (785/1073) non-white, 75% (804/1073) female, and enrolled in the waiver program approximately 50 months. The 2 groups were similar on all demographic variables examined. Six clients (2.2%) in the intervention group and 40 clients (5.0%) in the control group were admitted to a nursing home at least once during the study period. Logistic regression was used to test the model predicting at least 1 nursing home admission. Control group clients were 2.94 times more likely to be admitted to a nursing home than clients in the intervention group.

Conclusions: The medication management service implemented within this study was effective in reducing nursing home admissions in a group of frail community-dwelling elderly. (*Am J Geriatr Pharmacother*. 2011;9:69–79) © 2011 Published by Elsevier HS Journals, Inc.

Key words: elderly, medication adherence, medication management service, nursing home admission.

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INTRODUCTION

Patients not taking prescribed medicine as directed has been well-documented and is the subject of several excellent reviews.[1–7] The extent of this phenomenon varies greatly and has been observed across a broad range of medical conditions.[8–13] For chronic conditions, it is estimated that only 50% of patients follow medication directions over time.[14–18] This phenomenon has assumed various names, such as medication nonadherence, noncompliance, and lack of persistence. Regardless of its name, the problem can most broadly be considered one in which a patient does not take medicine as prescribed, regardless of reason.

Failure to take medicine as prescribed may result in important consequences to both patients and society. In a retrospective observational study of health care utilization and use of medicines for asthma, patients with the lowest quartile for medication adherence for leukotriene inhibitors experienced 80 emergency department visits and 34 admissions per 1000 patient-years, whereas patients in the highest quartile for adherence experienced 36 emergency department visits and 13 admissions per 1000 patient-years.[19] In another study, the personal impact of medication nonadherence was assessed in 4 chronic diseases in a historical cohort of 137,277 patients. For all 4 conditions examined, the more patients took the medicine as directed, the lower their risk of hospitalization.[20] Societal costs, as measured by productivity losses, were measured in a national cohort of employees with bipolar disease in the United States. Relative to employees who were adherent with their medicines, those assessed as nonadherent had higher indirect costs due to absenteeism, short-term disability, and worker compensation claims.[21] Total cost of nonadherence, including both lost productivity and early mortality, has been estimated at $300 billion.[22] The impact of programs designed to improve patients' medication-taking behavior can be significant. In a review of interventions to improve medication adherence, 19 of 39 interventions were associated with statistical improvements in adherence, whereas 17 were associated with statistical improvements in clinical outcomes.[23]

The frail elderly are particularly susceptible to problems with medication management and adherence. Declining cognition, increasing diagnoses, and associated prescribed medicines make them more likely to experience poor outcomes.[24] For these reasons, emphasis has been placed on improving medication management in this group. A recent review of studies examining the effectiveness of adherence interventions in older patients reported that less than half of the studies employing educational-only strategies found improvement in adherence. However, 4 of the 5 studies with memory aids or cues as part of the intervention, coupled with newer technologies, showed improvement.[25] The authors concluded that the evidence does not support any one intervention as being superior in improving medication adherence in the elderly. However, they also indicated that tailored interventions with consistent contact with health professionals seemed to be more effective than alternatives.

An outcome of particular interest for the elderly and society is nursing home placement. In 2008, approximately $138 billion was spent on nursing home services, accounting for 6% of national health care expenditure.[26] Studies designed to identify predictors of nursing home placement typically do not assess the impact of medication management.[27,28] In studies where medications are considered, however, a simple count is identified as a predictive factor.[29]

In 1 study, up to 23% of nursing home admissions were reportedly due to elderly patients' ability to self-administer medications.[30] Programs designed to assist the elderly in managing their medicines might reduce nursing home admissions and reduce the impact on society.

The purpose of this study was to examine the impact of a medication management system on nursing home admission within the community-dwelling frail elderly.

MATERIALS AND METHODS

Population

The participants of this prospective cohort study were clients in a state Medicaid home and community-based waiver program—a waiver program for persons eligible for nursing home care, but who prefer to receive their services in the community. Elderly/disabled clients who received their prescriptions from participating pharmacies were contacted by program case managers, who sought their voluntary participation and obtained signed informed consent. These clients formed the intervention group. The control group consisted of clients who did not receive the intervention, and thus received standard care that was provided in their community pharmacies. Control group clients were matched to intervention group clients on age, gender, race, and time in waiver program.

Pharmacies

Selection of participating pharmacies was done through convenience sampling. First, only independently owned community pharmacies were considered

possible participating pharmacies. Chain pharmacies were excluded from the list of potential participating pharmacies for 2 reasons: 1) the corporate organizational structure of chain pharmacies would remove decision-making from local control, and 2) participation involved purchase of a dispensing system that was considered unlikely within a chain environment. Second, the waiver program provided the names of pharmacies and the names of elderly/disabled clients who received prescriptions from the pharmacies. Pharmacies were then ranked according to the number of elderly/disabled clients they served. Pharmacies with the most elderly/disabled clients were asked to participate.

Overview of Intervention

Study clients received an intervention consisting of 2 parts: 1) a calendar card,* in which a client's medicines were dispensed instead of in prescription bottles, and 2) a coordinating service that facilitated communication among clients or caregivers, case managers, and providers to address medication adherence and management issues.

Calendar Card

Each calendar card contained multiple dosage bubbles or blister packs, which can hold up to 6 tablets or capsules for a single administration time. Calendar cards were color-coded, representing different times of the day or night. Each card, therefore, held in its dosage bubbles the medicines that a client would take during a particular time of day. Each card contained medicine for a 30-day supply. To take medicines prescribed for morning administration, for example, the client broke the morning bubble or blister pack, which contained all medicines to be taken at that time. Therefore, clients in the intervention group received their prescription medicines in calendar cards that held all medicines for each dosing time for 1 month. Clients in the control group received their prescription medicines in traditional prescription vials.

Coordinating Service

The coordinating service was designed to improve communication among clients/caregivers, pharmacists, and physicians and to identify and solve many of the practical problems that arise in medication management with this group. A more detailed description of the service is found in the section **Coordinator**.

*The calendar card used was Medicine-On-Time® (Hunt Valley, Maryland 21030).

Summary of Intervention

These 2 components, calendar card and coordinating service, were designed to assist in medication management in the home and to identify and address any medication-related problem quickly. The client's pharmacy prepared the calendar cards each month; a coordinator provided the coordinating service by frequent contact with caregivers, case managers, pharmacists, and physicians, Clients in the control group did not receive this intervention, and thus received standard care (ie, their prescriptions were dispensed in traditional prescription vials, and they did not participate in the coordinating service).

Coordinator

One individual provided the coordinating function throughout the project. The coordinator, a masters-trained health educator, communicated with pharmacists, physicians, case managers, clients, and caregivers regarding clients' prescription medicine. For example, the coordinator would be notified by a participating pharmacy if a client was late in receiving a prescription refill. In that situation, the coordinator would contact the caregiver to notify them of the situation and assist in resolving the problem. Also, the coordinator mailed or faxed a patient profile quarterly to prescribers that described the client's current drug therapy. This list was generated by software used by participating pharmacies. This service provided a written record of medication dispensed from the pharmacy, allowing prescribers to clarify discrepancies between prescribed and dispensed medicines, and gave prescribers a mechanism to communicate back to the pharmacist any adjustments to therapy that had been made. This software also generated order request forms for prescriptions with no remaining refills. Pharmacists faxed or mailed this form to prescribers to facilitate refill processing, thus avoiding interruptions in therapy.

Case Managers

As a regular part of the Medicaid waiver services provided to clients, each client has a choice of case manager who assists the client with what services and supplies are needed and available through the waiver program. In addition, the case manager assists with locating other resources in the community and in problem solving. Ongoing support is provided by calling or visiting the client monthly. The case manager operates from the community waiver office closest to the client, which is separate from the community Medicaid office. Case managers described the project to potential participants,

obtained informed consent, and were in personal or telephone contact with the client at least once a month throughout the study. This frequency of contact is standard care regardless of whether the client is participating in the study. Case managers received training from the project researchers before implementing the intervention. During the monthly contact, case managers inquired about the health status of the client and determined if the client was having any difficulties with the prescription medication or calendar pack. Case managers entered data on a standardized encounter form. Case managers also were instructed to contact the coordinator to report any medication-related problems that arose during the regularly scheduled monthly contact with clients or whenever a medication problem or issue occured.

Training and Coordination

Considerable effort was made to assure standardization of the intervention. First, all participating pharmacies were trained to use the Medicine-on-Time calendar card system by the group that developed and provided the hardware and software. Second, only 1 coordinator provided the service throughout the study. Third, all case managers were trained to follow the study protocol by the research team. In addition, the coordinator contacted all prescribers, described the study, and informed them of their patients' participation in the study.

Duration of Intervention

Each client enrolled in the program was followed for up to 12 months. Enrollment occurred on a rolling basis, beginning in September 2006 and ending March 2007. Outcomes were assessed until November 2007.

Data Source

The dependent variable, indication of admission to a skilled nursing facility that could include a short-term rehabilitation stay or a long-term placement, was based on skilled nursing home facility (excluding assisted living and community residential care facilities and personal care homes) admission data obtained from the State Office of Research and Statistics (SORS). SORS has legislatively derived authority to collect data and maintain health care databases for all state Medicaid enrollees. Utilization and cost data are sent to SORS by hospitals, state agencies, and insurers. Independent variables were obtained from both SORS and waiver databases.

Study Period

For the purposes of this study, the study period began for each client on the date of first prescription dispensed (index date) using the medication management service calendar pack and ended 30 days past the date of last refill. The "pre-period" was represented by the time from index date back to the individual's entry date into the waiver programs or January 2002, whichever was more recent. The "post-period" was represented by the time from index date forward to 30 days past the date of the last prescription dispensed. The first occurrence of nursing home admission before the index date constituted an outcome event in the pre-period. The first occurrence of nursing home admission after the index date constituted an outcome event in the post-period.

Statistical Analysis

Conditional logistic regression was used to test the hypothesis that nursing home admission was associated with the service intervention. Variables were selected for inclusion in the regression model for 1 of the following reasons: 1) significant association with nursing home admission in bivariate analysis, 2) support within the relevant literature,[31] and 3) experience of senior program managers within the state Medicaid home and community-based waiver program. As a result, the following variables comprised the full model: $\geq$3 drugs, cognitive skills, total activities of daily living, prior nursing home admission, education, residence (rural/urban), emergency disaster priority, cancer, missing limb, renal failure, seizure disorder, hypertension, emphysema, weight loss/gain, vision, not able to shop, and illness-altered diet. The final model was determined using the change-in-estimate method.[32,33] Briefly, each variable was evaluated based on its influence on the estimated group effect. When a variable was deleted, if the change in group effect was within 10% of its estimated value, the variable remained deleted from the model. However, if the deletion resulted in a change $>$10% of the estimated group effect, the variable was retained in the model. Confounding was controlled in the design (matching) and in the analytic (multivariate regression) phases. All analyses were conducted using SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

Human Subject Protection and Health Insurance Portability and Accountability Act

This study was approved by the University of South Carolina Institutional Review Board. Data were secured at the research office of the authors. Also, the coordinator was Health Insurance Portability and Accountability

Act trained, and previously served as an instructor on Health Insurance Portability and Accountability Act compliance.

RESULTS

Pharmacies

Twelve pharmacies at 15 locations participated in the study; 1 of the pharmacies operated 4 locations under the same name. Each of these locations served a different patient mix and were considered separately. Pharmacies were geographically distributed throughout the state.

Patients

Of the 283 intervention group clients who received at least 1 dispense of medication via "bubble pack," 273 were successfully matched on year of birth (±5 years), gender (exact), race (exact, white vs non-white), and the waiver program start date (±120 days). Of the 273 intervention group participants included in the analysis, 273 were matched to at least 1 control, 266 were matched to 2 controls, and 261 were matched to 3 controls, for a total of 800 controls. Mean (SD) number of days participants in the intervention group remained in the study was 270 (130); mean (SD) number of days for the control group was 244 (134).

A profile of the intervention and control groups at baseline is presented in **Table I**. Due to matching, age, gender, race, and length of time in the waiver program are similar. On most variables examined, the intervention group and control group were similar. The groups were significantly different with respect to the following variables, with the intervention group having a higher percentage than the control group: presence of hypertension (228 [84%] vs 602 [75%]; <0.01), having an illness that altered diet (157 [58%] vs 382 [48%]; $P < 0.01$), taking ≥3 drugs a day (249 [91%] vs 662 [83%]; $P < 0.01$), and not always being physically able to shop (265 [97%] vs 748 [94%]; $P = 0.03$).

Nursing Home Admission

Of the 273 intervention group participants, 6 (2.2%) were admitted to the nursing home at least once during the study period. Of the 800 control subjects, 40 (5.0%) were admitted to the nursing home at least once during the study period. Logistic regression was used to test the model predicting at least 1 admission to a nursing home (**Table II**). Group membership (intervention or control: odds ratio [OR] 0.340; 95% CI 0.119–0.968) and residence (rural or urban: OR 0.409; 95% CI 0.174–0.963) were predictive of nursing home admission. A client who had the medication management service was 66% less likely to be admitted to a nursing home than clients who did not have the service. Conversely, clients who did not have the medication management service were 2.94 times more likely to have a nursing home admission compared with clients who had the service. Location of residence (urban or rural) was also found to be independently associated with nursing home admission. Controlling for the influence of the intervention, clients who lived in rural areas were 59% less likely to have a nursing home admission during the study period. Conversely, clients living in urban areas were 2.45 times more likely to have a nursing home admission compared with clients living in rural areas.

Table III reports nursing home admission throughout the study. There were no nursing home admissions in the intervention group during the pre-period. During the post-period, the intervention group had 6 clients (2.2%) with at least 1 nursing home admission. Within the control group, there were 6 clients (0.8%) who had a nursing home admission during the pre-period. During the post-period, the control group had 40 clients (5.0%) with at least 1 nursing home admission. The difference (post – pre) in annualized rate of nursing home admission in the intervention group was 3 nursing home admissions per 100 persons. The difference (post – pre) in annualized rate of nursing home admission in the control group was 8 admissions per 100 persons. Participation in the intervention was associated with an avoidance of 5 nursing home admissions per 100 persons.

Services continued for intervention clients as long as they continued to receive their prescriptions from participating pharmacies in the calendar cards. Services, and therefore, study participation, discontinued 30 days after the last prescription was dispensed. Although services were not provided, investigators could assess nursing home activity for some time after the last refill through the SORS database. **Table IV** shows the nursing home rates for clients in both groups at 30 days past date of last prescription (6 [2.2%] vs 40 [5.0%], $P < 0.05$), and at 120 days past date of last prescription. Over the 120 days past date of last refill, during which neither group received prescriptions using the calendar card nor received the coordinating service (ie, level of service was the same), the rate of nursing home admission was similar (5.9% in both groups).

DISCUSSION

The purpose of this study was to assess the effectiveness of a medication adherence and management service in influencing nursing home admission within a Medicaid, nursing home–eligible population. The results indicate

Table I. Intervention and control groups characteristics at baseline.

Variable	Level	Intervention (n = 273)	Controls (n = 800)	P
Age, mean (SD)	N/A	71.95 (15.17)	71.95 (14.77)	0.99
Race	Non-White	199 (73%)	586 (73%)	0.91
Gender	Female	204 (75%)	600 (75%)	0.93
Education	Less than high school education	144 (53%)	378 (47%)	0.12
No. of months on waiver, mean (SD)	N/A	51 (35.15)	49.19 (33.52)	0.45
Ability to understand others	Understands	176 (64%)	527 (66%)	0.78
	Usually understands	58 (21%)	160 (20%)	
	Sometimes understands	32 (12%)	83 (10%)	
	Rarely/never understands	7 (3%)	28 (4%)	
Cognitive skills	Independent	64 (23%)	185 (23%)	0.35
	Modified independence	79 (29%)	272 (34%)	
	Moderately impaired	79 (29%)	222 (28%)	
	Severely impaired	51 (19%)	121 (15%)	
Long-term memory	Memory OK	182 (67%)	526 (66%)	0.77
	Memory problem	75 (27%)	217 (27%)	
	Unable to rate	16 (6%)	57 (7%)	
ADL–Transfer	Independent	18 (7%)	57 (7%)	0.16
	Supervision	24 (9%)	39 (5%)	
	Limited assistance	22 (8%)	78 (10%)	
	Extensive assistance	174 (64%)	506 (63%)	
	Total dependence	35 (13%)	119 (15%)	
ADL–Locomotion	Independent	6 (2%)	45 (6%)	0.07
	Supervision	4 (1%)	26 (3%)	
	Limited assistance	21 (8%)	60 (8%)	
	Extensive assistance	208 (76%)	560 (70%)	
	Total dependence	34 (12%)	109 (14%)	
ADL–Dressing	Independent	7 (3%)	18 (2%)	0.87
	Supervision	7 (3%)	16 (2%)	
	Limited assistance	33 (12%)	95 (12%)	
	Extensive assistance	187 (68%)	537 (67%)	
	Total dependence	39 (14%)	134 (17%)	
ADL–Eating	Independent	0 (0%)	9 (1%)	0.25
	Supervision	1 (0%)	9 (1%)	
	Limited assistance	16 (6%)	60 (8%)	
	Extensive assistance	230 (84%)	647 (81%)	
	Total dependence	26 (10%)	75 (9%)	
ADL–Toileting	Independent	23 (8%)	35 (4%)	0.08
	Supervision	5 (2%)	17 (2%)	
	Limited assistance	30 (11%)	71 (9%)	
	Extensive assistance	171 (63%)	530 (66%)	
	Total dependence	44 (16%)	147 (18%)	
ADL–Bathing	Independent	3 (1%)	7 (1%)	0.91
	Supervision	1 (0%)	7 (1%)	
	Limited assistance	22 (8%)	59 (7%)	
	Extensive assistance	199 (73%)	580 (73%)	
	Total dependence	48 (18%)	147 (18%)	

Table I (continued).

Variable	Level	Intervention (n = 273)	Controls (n = 800)	*P*
Bowel incontinence	Continent	155 (57%)	444 (56%)	0.35
	Usually continent	37 (14%)	84 (11%)	
	Occasionally incontinent	21 (8%)	70 (9%)	
	Frequently incontinent	25 (9%)	66 (8%)	
	Incontinent	35 (13%)	136 (17%)	
Bladder incontinence	Continent	69 (25%)	210 (26%)	0.68
	Usually continent	23 (8%)	53 (7%)	
	Occasionally incontinent	34 (12%)	98 (12%)	
	Frequently incontinent	100 (37%)	276 (35%)	
	Incontinent	47 (17%)	163 (20%)	
Emergency priority	Yes	12 (4%)	27 (3%)	0.44
Congestive heart failure	Yes	57 (21%)	177 (22%)	0.67
Hypertension	Yes	288 (84%)	602 (75%)	<0.01
Myocardial infarction	Yes	30 (11%)	82 (10%)	0.73
Peripheral vascular disease	Yes	55 (20%)	121 (15%)	0.05
Alzheimer's disease	Yes	22 (8%)	78 (10%)	0.41
Other dementias	Yes	24 (9%)	106 (13%)	0.05
Cerebrovascular accident	Yes	83 (30%)	266 (33%)	0.39
Parkinson's disease	Yes	9 (3%)	17 (2%)	0.28
Anemia	Yes	45 (16%)	128 (16%)	0.85
Arthritis	Yes	183 (67%)	512 (64%)	0.37
Cancer	Yes	30 (11%)	77 (10%)	0.52
Diabetes	Yes	128 (47%)	365 (46%)	0.72
Missing limb	Yes	19 (7%)	64 (8%)	0.58
Renal failure	Yes	24 (9%)	59 (7%)	0.45
Seizure disorder	Yes	29 (11%)	86 (11%)	0.95
Depression	Yes	45 (16%)	174 (22%)	0.06
Emphysema	Yes	60 (22%)	162 (20%)	0.54
Pneumonia	Yes	10 (4%)	35 (4%)	0.61
Diet supplement	Yes	22 (8%)	86 (11%)	0.20
25% Food uneaten at meals	Yes	8 (3%)	30 (4%)	0.53
Weight loss/gain	Yes	88 (32%)	244 (31%)	0.59
Illness-altered diet	Yes	157 (58%)	382 (48%)	<0.01
≥3 drugs	Yes	249 (91%)	662 (83%)	<0.01
Eats alone most times	Yes	73 (27%)	200 (25%)	0.57
Not able to cook	Yes	253 (93%)	729 (91%)	0.43
Not able to feed self	Yes	15 (5%)	66 (8%)	0.14
Gain weight	Yes	27 (10%)	72 (9%)	0.66
Loss weight	Yes	29 (11%)	90 (11%)	0.78
Not enough money to buy food	Yes	18 (7%)	50 (6%)	0.84
Not able to shop	Yes	265 (97%)	748 (94%)	0.03

ADL = activities of daily living.
P values derived from *t* test for continuous level data, and χ^2 for categorical data.

Table II. Odds of nursing home admission.

		Odds Ratio Estimates	
Variable	Comparison	Adjusted Odds Ratio	95% Wald CIs
Group	Intervention/control	0.340	0.119–0.968
Residence	Rural/urban	0.409	0.174–0.963
Renal failure	Yes/no	2.281	0.583–8.920
Seizure	Yes/no	2.547	0.471–13.774
Hypertension	Yes/no	0.408	0.145–1.152
Emphysema	Yes/no	0.397	0.112–1.407
Vision	Impaired/adequate	2.240	0.988–5.078
Not able to shop	Not able/able	3.448	0.994–11.960

The intervention group had lower odds of being admitted to the nursing home within 30 days after receiving their last dispense of drugs via the intervention compared with the controls. Those in the control group were 2.94 times more likely to be admitted to a nursing home. This final model had the lowest Akaike Information Criterion value, demonstrating that the model was the best fit of models tested.[34]

that clients who had the service, composed of a calendar card dosage administration system coupled with a coordinating service, experienced a significantly lower rate of nursing home admission than similar clients who did not have the service. Furthermore, when the intervention was no longer applied, the nursing home rate for the intervention group rose to a level similar to the rate in the control group.

A study that examined predictors of nursing home admission used number of prescriptions as a measure of general morbidity.[29] The authors reported that number of prescriptions was a predictor of nursing home admission. Although the number of prescriptions has been used as a proxy for this broader measure, an alternative interpretation is possible. In the referenced study, participants with more prescriptions perhaps had more difficulty managing their medication than those with fewer prescriptions. This interpretation can be seen as consistent with our findings, in which the intervention was designed specifically to assist in medication management. The intervention group received assistance in the form of a calendar card and coordinating service. Those who received this assistance had a lower rate of institutionalization in nursing homes than those who did not receive this assistance.

Much of the focus of intervention studies designed to reduce nursing home admission has been on the caregiver of frail or medically compromised patients. A meta-analysis was conducted assessing the effectiveness of home visitation in preventing or delaying admission to a nursing home.[35] The authors reported that the reduction in admission rate was modest and nonsignificant. However, subgroup analysis indicated

Table III. Standardized nursing home utilization.

	Intervention (n = 273)		Control (n = 800)	
	Pre	Post	Pre	Post
Nursing Home				
No. people with at least 1 utilization (%)	0 (0.0)	6 (2.2)	6 (0.75)	40 (5.0)
Total visits	0	6	6	40
Days observed	1186	270	1168	244
Total visits Annualized*	0	8	2	60
Annualized rate†	0	0.029	0.002	0.075
Rate per 100‡	0	3	0	8
Difference§		3/100 person		8/100 person
Impact of service‖		5/100 avoided		

*Total visits annualized = (total visits/days observed) × 365.
†Annualized rate = total visits annualized/N.
‡Rate per 100 = (annualized rate) × 100.
§Difference = (post rate per 100) – (pre rate per 100).
‖Impact of service = (intervention difference) – (control difference).

Table IV. Nursing home admission at different end points.

	Intervention (N = 273) N (%)	Control (N = 800) N (%)
30 d past last prescription	6 (2.2)*	40 (5.0)
120 d past last prescription	16 (5.9)	47 (5.9)

*$P < 0.05$ vs control.

that interventions were successful only if based on multidimensional assessment, included multiple in-home visits, and targeted those at low risk of death, and if participants were relatively young. Our study elaborated upon these results in several ways. Though age was not an independent factor associated with nursing home placement, the effect of the intervention was greatest in clients <80 years of age. This was consistent with the observation that dementia and incontinence exert greater influence on nursing home placement at advancing ages. Also, the intervention did not increase the number of home visits provided to clients. Where our study differed was in the type and intensity of intervention. The present study introduced a simple intervention in the form of a calendar card to address a frequently identified problem for community-based elderly, namely, medication management. The coordinator provided a service in which she had contact with multiple personnel involved in the provision of care, but managed the contact entirely through telephone, fax, and mail. This difference in targeted versus broad-based intervention might explain the difference in conclusion regarding the effectiveness in reducing nursing home admissions. Future work might elaborate on the discussion of targeted versus broad-based interventions, intensity of intervention, and value of a coordinated medication management systems for the frail elderly.

The nature of the intervention prevented an assessment that could separate the effect of the calendar card from the coordinating service. The purpose of the study, agreed to by the funding agency and academic researchers, was to assess the effectiveness of the intervention as a whole, not its component parts. Further, each client, regardless of group, received the services of the case manager as part of the regular benefit provided to all community long-term care waiver clients. In this way, the case manager was not considered part of the intervention unique to only one group.

The study has several limitations. Sampling of both participants and pharmacies was not random, and randomization of the service intervention was not feasible. Consequently, results may be attributable to factors other than the intervention. Research comparing randomized versus nonrandomized studies has shown that the use of matching in nonrandomized studies, as done in this study, can produce study groups with similar distributions of baseline covariates, a strength of traditional randomized studies.[36,37] Clients were not randomly selected within pharmacies because of the clear danger of contamination between clients. Pharmacies were not randomly selected for practical reasons. Participation required the purchase and use of equipment to dispense medicines in the calendar card. Pharmacies needed a sufficient number of waiver clients already in their patient mix to make the project economically feasible. Only pharmacies with sufficient numbers of clients could participate. Chain pharmacies were not included. Corporate approval would have been unlikely for only selected pharmacies within a region. In addition, local control within independently owned pharmacies implied a greater likelihood for accurate and consistent application of the intervention within each pharmacy. The exclusion of chain pharmacies decreases the generalizability of the study. However, the accurate and consistent application of the intervention increased the study's internal validity. Finally, Medicare Part D was implemented during the study, which prevented an accurate assessment of medication adherence within the control group. Although this prevented assessing association between medication adherence and nursing home admission, it did not prevent an assessment of the overall medication management service and nursing home admission.

CONCLUSIONS

This study found that the pharmacy-based calendar card dispensing system and coordinating service, which was designed to facilitate medication adherence, can reduce medication management issues, address problems as they arise, and reduce nursing home admissions of community dwelling, nursing home–eligible patients.

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REFERENCES

1. Julius RJ, Novitsky MA Jr, Dublin WR. Medication adherence: A review of the literature and implications for clinical practice. *J Psychiatr Pract*. 2009;15:34–44.
2. Ruppar TM, Conn VS, Russell CL. Medication adherence interventions for older adults: Literature review. *Res Theory Nurs Pract*. 2008;22:114–147.
3. Haynes RB, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008;2:CD000011.
4. Banning M. Older people and adherence with medication: A review of the literature. *Int J Nurs Stud*. 2008;45:1550–1561.
5. Krueger KP, Berger BA, Felkey B. Medication adherence and persistence: A comprehensive review. *Adv Therap*. 2005;22:313–356.
6. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487–497.
7. Vik SA, Maxwell CJ, Hogan DB. Measurement, correlates, and health outcomes of medication adherence among seniors. *Ann Pharmacother*. 2004;38:303–312.
8. Schedlbauer A, Davies P, Fahey T. Interventions to improve adherence to lipid lowering medication. *Cochrane Database Syst Rev*. 2010;3:CD004371.
9. Maddox TM, Ho PM. Medication adherence and the patient with coronary artery disease: Challenges for the practitioner. *Curr Opin Cardiol*. 2009;24:468–472.
10. Gardner EM, Burman WJ, Steiner JF, et al. Antiretroviral medication adherence and the development of class-specific antiretroviral resistance. *AIDS*. 2009;23:1035–1046.
11. Restrepo RD, Alvarez MT, et al. Medication adherence issues in patients treated for COPD. *Int J Chron Obstruct Pulmon Dis*. 2008;3:371–384.
12. Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: A systematic review of the literature. *Semin Arthritis Rheumatol*. 2009;38:396–402.
13. Tsai JC. Medication adherence in glaucoma: Approaches for optimizing patient compliance. *Curr Opin Ophthalmol*. 2006;17:190–195.
14. Schwartz GF, Quigley HA. Adherence and persistence with glaucoma therapy. *Surv Ophthamol*. 2008; 53(Suppl 1):S57–68.
15. Devabhaktuni M, Bangalore S. Fixed combination of amlodipine and atorvastatin in cardiovascular risk management: Patient perspectives. *Vasc Health Risk Manag*. 2009;5:377–387.
16. Kane SV, Brixner D, Rubin DT, Sewitch MJ. The challenge of compliance and persistence: Focus on ulcerative colitis. *J Manag Care Pharm*. 2008;14(Suppl A):S2–S12.
17. Kothwala P,Badamgarav E, Ryu S, et al. Systematic review and meta-analysis of real-world adherence to drug therapy for osteoporosis. *Mayo Clinic Proc*. 2007;82:1493–1501.
18. Dunbar-Jacob J, Erlen JA, Schlenk EA, et al. Adherence in chronic disease. In: Fitzpatrick JJ, Goeppinger J, eds. *Annual Review of Nursing Research*. New York: Springer 2000;18:48–90.
19. Mattke S, Martorell F, Hong SY, et al. Anti-inflammatory medication adherence and cost and utilization of asthma care in a commercially insured population. *J Asthma*. 2010;47:323–329.
20. Sokol MC, McGuigan KA, Verbugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43:521–530.
21. Bagalman E, Yu-Isenberg KS, Durden E, et al. Indirect costs associated with nonadherence to treatment for bipolar disorder. *J Occupl Environ Med*. 2010;52:478–485.
22. DiMatteo MR. Variations in patients' adherence to medical recommendations: A quantitative review of 50 years of research. *Med Care*. 2004;42:200–209.
23. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: Scientific review. *JAMA* 2002;288:2868–2879.
24. Owens NJ, Larrat EP, Fretwell MD. Improving compliance in the older patient. In Cramer JA, Spilker B, eds. *Patient Compliance in Medical Practice and Clinical Trials*. New York: Raven Press, 1991;107–199.
25. Schlenk EA, Bernardo LM, Organist LA, et al. Optimizing medication adherence in older patients: A systematic review. *J Clin Outcomes Manag*. 2008;15:595–606.
26. Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Groups, National Health Care Expenditure Data, January 2010.
27. Ahmed A, Allman RM, DeLong JF. Predictors of nursing home admission for older adults hospitalized with heart failure. *Arch Gerontol Geriatr*. 2003;36:117–126.
28. Buhr GT, Kuchibhatla M, Clipp EC. Caregivers' reasons for nursing home placement: Clues for improving discussions with families prior to the transition. *Gerontologist* 2006;46:52–61.
29. Bharucha AJ, Pandav R, Shen C, et al. Predictors of nursing facility admission: A 12-year epidemiological study in the United States. *J Am Geriatr Soc*. 2004;52:434–439.
30. Strandberg LR. Drugs as a reason for nursing home admissions. *J Am Health Care Assoc*. 1984;10:20–23.
31. Gaugler JE, Duval S, Anderson KA, Kane RL. Predicting nursing home admission in the US. A meta-analysis. *BMC Geriatr*. 2007;7:13.
32. Greenland S. Invited commentary: Variable selection versus shrinkage in the control of multiple confounders. *Am J Epidemiol*. 2008;167:523–529.
33. Greenland S. Modeling and variable selection in epidemiologic analysis. *Am J Public Health*. 1989;79:340–349.

34. Akaike H. A new look at the statistical model identification. *IEEE Trans Automatic Control*. 1974;19:716–723.
35. Stuck AE, Egger M, Hammer A, Monder CE, Beck JC. Home visits to prevent nursing home admission and functional decline in elderly people: Systematic review and meta-regression analysis. *JAMA*. 2002;287:1022–1028.
36. Makuch RW, Zhang Z, Charpentier PA, Inouye SK. Prospective individual matching: Covariate balance and power in a comparative study. *Stat Med*. 1998;17:1517–1526.
37. Raaijmakers M, Koffijberg H, Posthumus J, et al. Assessing performance of a randomized versus non-randomized study design. *Contemp Clin Trials*. 2008;29:293–303.

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Congressional Budget Office

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Offsetting Effects of Prescription Drug Use on Medicare's Spending for Medical Services

Summary

Prescription drugs affect people's health and their need for medical services.[1] Therefore, policy changes that influence Medicare beneficiaries' use of prescription drugs, such as those altering the cost-sharing structure of the Part D prescription drug benefit, probably affect federal spending on their medical services.[2] After reviewing recent research, the Congressional Budget Office (CBO) estimates that a 1 percent increase in the number of prescriptions filled by beneficiaries would cause Medicare's spending on medical services to fall by roughly one-fifth of 1 percent. That estimate, which applies only to policies that directly affect the quantity of prescriptions filled, represents a change in the agency's estimating methodology, which until now has not incorporated such an effect.

Previously, when estimating the budgetary effects of legislation regarding prescription drugs, CBO found insufficient evidence of an "offsetting" effect of prescription drug use on spending for medical services. But recently, more analysis has been published that demonstrates a link between changes in prescription drug use and changes in the use of and spending for medical services. This report provides background information about that relationship; reviews the literature on the size of the offset for the Medicare population; and describes how CBO synthesized the recent research. The report also provides an example of how CBO's change in methodology will affect the agency's cost estimates for proposals that would change prescription drug use by Medicare beneficiaries.

Background

In the first two years of Medicare's Part D program —which was created in 2003 with the passage of the Medicare Prescription Drug, Improvement, and Modernization Act and implemented in 2006—the number of prescriptions filled by Medicare beneficiaries increased by more than 10 percent, according to one estimate.[3] More recently, the Part D benefit was expanded by the Affordable Care Act—which, between 2011 and 2020, is gradually closing the gap in coverage in which beneficiaries were responsible for all of the costs for their prescription drugs.[4] That change is expected to further boost the use of prescription drugs. The design of Medicare's prescription drug benefit continues to be debated, as evidenced by recent proposals to change the cost-sharing rules for low-income beneficiaries and to repeal the gradual closure of the coverage gap.

A substantial body of evidence indicates that people respond to changes in cost sharing by changing their consumption of prescription drugs. From beneficiaries' perspective, the price of a prescription drug is the portion of the prescription's cost that they bear. The use of

1. For the purposes of this publication, "medical services" refers to medical and surgical services other than self-administered prescription drugs.

2. For a full description of the prescription drug benefit provided by Medicare's Part D program, see Congressional Budget Office, *Spending Patterns for Prescription Drugs Under Medicare Part D* (December 2011).

3. Becky A. Briesacher and others, "Medicare Part D and Changes in Prescription Drug Use and Cost Burden," *Medical Care*, vol. 49, no. 9 (2011), pp. 834–841.

4. That coverage gap (sometimes referred to as the doughnut hole) existed between Medicare's initial coverage limit and its out-of-pocket threshold. See Congressional Budget Office, *Spending Patterns for Prescription Drugs Under Medicare Part D*.

prescription drugs—or number of prescriptions filled—increases in response to price reductions and falls in response to price increases. That response is widespread, found within both the elderly population and the nonelderly population, and among both enrollees in public health care plans and people with private health insurance. Numerous studies have demonstrated the effect of price changes on the use of prescription drugs overall, and several others have found that lower prices for drugs used to treat chronic conditions improve the likelihood that patients take their medication as prescribed.[5]

Changes in the use of prescription drugs have the potential to affect the use of medical services. For example, overuse or inappropriate use of prescription drugs may raise the risk of adverse reactions, triggering a need for medical treatment. But most often, pharmaceuticals have the effect of improving or maintaining an individual's health. Taking an antibiotic may prevent a more severe infection, and adhering to a drug regimen for a chronic condition such as diabetes or high blood pressure may prevent complications. In either of those circumstances, taking the medication may also avert hospital admissions and thus reduce the use of medical services.

Previously, CBO did not include any offsetting effect on medical services in its estimates involving changes to prescription drug policies. Most notably, the agency's estimate for the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (which established Medicare's Part D prescription drug benefit) did not include an offset. At the time, there was little evidence of a relationship between prescription drug use and spending for medical services.[6] Likewise, CBO did not include an offset in its estimates of the cost of the Affordable Care Act (which includes the provisions closing the Part D coverage gap). However, a body of research has since developed that demonstrates a connection between prescription drug use and the use of medical services.

5. For a review of the literature, see Dana P. Goldman, Geoffrey F. Joyce, and Yuhui Zheng, "Prescription Drug Cost Sharing: Associations with Medication and Medical Utilizations and Spending and Health," *Journal of the American Medical Association*, vol. 298, no. 1 (2007), pp. 61–69.

6. See Congressional Budget Office, *Issues in Designing a Prescription Drug Benefit for Medicare* (October 2002).

CBO's Review of Recent Research

CBO recently reviewed dozens of newer studies to determine whether and how to include an offsetting effect on medical services in estimates for proposals to change prescription drug policies. CBO considered studies to be particularly relevant if the population examined was similar to the general Medicare population, the policy changes analyzed were similar to recent or recently discussed ones, and effects on medical spending were estimated.

In addition to studies examining broad populations, a large body of literature also exists on the effects of changes in cost sharing within classes of drugs that treat particular health problems or for people with specific conditions. That literature generally finds a larger offsetting effect of changes in prescription drug policies than do studies based on the broader population—probably because people with certain diseases are more sensitive to changes in prescription drug use than is the general population. However, CBO did not incorporate the results of such studies of cost sharing in its analysis because robust findings for each therapeutic class or chronic condition do not exist, so generalizing to a broader population is difficult. In addition, most proposed policies to date would apply to broad populations of Medicare beneficiaries.

As a result, CBO's analysis relied on a selected set of studies that fell into three categories:

- Estimates of the impact of pharmaceutical policies on a broad population outside of Medicare,
- Estimates of the impact of pharmaceutical policies on Medicare beneficiaries before Medicare Part D was implemented, and
- Comparisons of medical expenditures by Medicare beneficiaries before the Medicare Part D benefit was implemented with medical expenditures after the benefit was implemented.

Despite their similarities, the studies used different methodologies and examined different populations (as described in this section), so CBO needed to synthesize the results to put them on a comparable basis (as described in the following section).

CBO found one study in the first category. It analyzed the effect of differences in cost sharing for prescription drugs on their use and the use of medical services by people in employment-based insurance plans.[7] That population was younger and healthier than the Medicare population but included a larger-than-average share of nearly elderly people and people with chronic conditions (relative to the broader population covered by employment-based insurance). The authors found that a substantial fraction of the reduction in spending on prescription drugs stemming from increases in employees' cost sharing was offset by increases in spending on medical services. The offset stemmed primarily from changes in the use of outpatient medical services rather than changes in hospitalizations, unlike the results of several of the other studies CBO examined.

CBO identified four studies in the second category; all used varying prescription drug coverage among Medicare beneficiaries before the implementation of Part D to study the effect of prescription drug use on the use of medical services. Two of the studies used the Medicare Current Beneficiary Survey to analyze the effect of varying levels of supplemental coverage.[8,9] A third study focused on beneficiaries enrolled in a Medicare HMO (health maintenance organization); some beneficiaries had a cap on their prescription drug benefits of $1,000, and others did not.[10] All of these studies found that lower spending on prescription drugs among those with less generous coverage was partially offset by higher costs for their medical services.

The fourth study in this category was particularly relevant because it examined a large group of Medicare beneficiaries, considered changes in cost sharing similar to those included in the original Part D legislation and proposed amendments to it, and rigorously compared beneficiaries before and after changes in their cost sharing to an unaffected control group.[11] The study analyzed the effect of an increase in cost sharing for prescription drugs among groups of Medicare beneficiaries with supplemental coverage from the California Public Employees Retirement System. One of the groups also experienced an increase in cost sharing for office visits, but the methodology controlled for that difference and other related issues. Like the other three studies in this category, this one found that decreased use of prescription drugs (before Part D existed) was associated with increased use of medical services.

CBO identified three studies in the third category, which took advantage of the implementation of the Medicare Part D benefit to examine the effect that changes in cost sharing for prescription drugs had on spending for medical services. One of these studies compared changes in hospitalizations among people over age 65 to changes in hospitalizations among people who were between 60 and 64 years old.[12] That approach—comparing changes in hospitalizations among a group of individuals affected by Part D to changes among a group of individuals not affected by Part D—enabled the authors to control for ongoing trends in hospitalizations. The other two studies compared changes in spending for medical services among beneficiaries who had limited or no prescription drug coverage before Part D and beneficiaries who had generous prescription drug coverage before Part D.[13,14] That approach similarly enabled the authors to control for trends in spending for medical services.

One of these studies found that people with the most generous coverage before Part D existed used medical

7. Martin Gaynor, Jian Li, and William B. Vogt, "Substitution, Spending Offsets, and Prescription Drug Benefit Design," *Forum for Health Economics and Policy*, vol. 10, no. 2 (2007), pp. 1–31.

8. Baoping Shang and Dana P. Goldman, *Prescription Drug Coverage and Elderly Medicare Spending*, Working Paper No. w13358 (Cambridge, Mass.: National Bureau of Economic Research, September 2007).

9. Bruce C. Stuart, Jalpa A. Doshi, and Joseph V. Terza, "Assessing the Impact of Drug Use on Hospital Costs," *Health Services Research*, vol. 44, no. 1 (2009), pp. 128–144.

10. John Hsu and others, "Unintended Consequences of Caps on Medicare Drug Benefits," *New England Journal of Medicine*, vol. 354, no. 22 (2006), pp. 2349–2359.

11. Amitabh Chandra, Jonathan Gruber, and Robin McKnight, "Patient Cost Sharing and Hospitalization Offsets in the Elderly," *American Economic Review*, vol. 100, no. 1 (2010), pp. 193–213.

12. Christopher C. Afendulis and others, "The Impact of Medicare Part D on Hospitalization Rates," *Health Services Research*, vol. 46, no. 4 (2011). pp. 1022–1038.

13. J. Michael McWilliams, Alan M. Zaslavsky, and Haiden A. Huskamp, "Implementation of Medicare Part D and Nondrug Medical Spending for Elderly Adults with Limited Prior Drug Coverage," *Journal of the American Medical Association*, vol. 306, no. 4 (2011), pp. 402–409.

14. Yuting Zhang and others, "The Effect of Medicare Part D on Drug and Medical Spending," *New England Journal of Medicine*, vol. 361, no. 1 (2009). pp. 52–61.

services more after its implementation.[15] Overall, however, the results from these studies suggest that people who received more generous prescription drug coverage through the implementation of Part D had fewer hospitalizations and used fewer medical services as a result.

CBO's Methodology for Synthesizing the Evidence

CBO's estimates are designed to represent the middle of the distribution of possible outcomes. To estimate that midpoint, several steps were necessary to create a consistent measure of the offsetting effect of prescription drug use on medical spending across the studies that CBO reviewed. For instance, CBO needed to adjust the reported findings to apply them to the Medicare population and the prices that Medicare pays for medical services. For the studies that reported changes in hospitalizations, CBO adjusted the findings to reflect the changes as a share of overall medical spending. For the studies that analyzed people who were somewhat sicker or somewhat healthier than people enrolled in Medicare, CBO adjusted the results on the basis of the health of the study population relative to the health of the Medicare population. Finally, the agency scaled all changes in medical spending to make them consistent with a 1 percent change in prescription drug use, measured in terms of the number of prescriptions filled. Choosing that measure, rather than spending on prescription drugs, allowed CBO to isolate changes in the use of prescription drugs from shifts between different types of drugs with different prices (a shift from a brand-name drug to its generic equivalent, for instance) that do not affect overall use.

In response to a 1 percent increase in the number of prescriptions filled, the change in spending for medical services (measured consistently across the studies) ranged from a decrease of two-thirds of a percent to an increase of one-third of a percent. With the highest and lowest estimates excluded, the results from the remaining six studies ranged from a decrease in medical spending of one-tenth of a percent to a decrease of four-tenths of a percent.

The eight studies encompass a wide variety of policy changes, both in terms of the type of change and the magnitude. CBO considered whether a larger policy change, such as the implementation of the Medicare Part D program, might have a larger proportional impact on the use of prescription drugs and, therefore, on spending for medical services, than a smaller policy change, such as an adjustment to cost sharing. However, the relationship between changes in prescription drug use and medical spending appeared relatively consistent for policy changes of different magnitudes; the same was true for policy changes in different directions, that is, ones increasing benefits as well as ones reducing them.[16]

CBO pooled the adjusted results to calculate an average offset, giving greater weight to studies examining populations more closely resembling the Medicare population and changes in prescription drug policies more like ones currently discussed. With those adjustments, CBO concludes that a 1 percent increase in prescription drug use would cause spending for medical services to fall by roughly one-fifth of 1 percent; likewise, a 1 percent decrease in prescription drug use would cause medical spending to increase by roughly one-fifth of 1 percent. Because the studies found that changes in spending for medical services occurred fairly close in time to the changes in prescription drug use, CBO assumes that the change in spending on medical services would begin in the same year as the change in prescription drug use.

Approach to Future Cost Estimates

In estimating the budgetary impact of future legislation or proposals that would directly affect prescription drug use in the Medicare program, CBO will include an offsetting effect on medical spending. The agency will first estimate a proposal's direct effect on prescription drug costs; then, the agency will estimate the effect on the number of prescriptions filled and any resulting offsetting effect on spending for medical services.

For example, a policy that increased prescription drug copayments for certain Medicare beneficiaries might save $4 billion in federal drug costs in a given year but reduce the number of prescriptions filled that year by 1 percent. That reduction in use would result in a one-fifth of

15. Zhang and others, "The Effect of Medicare Part D."

16. In the studies CBO examined, the range of effects on prescription drug use suggests that the offset the agency has calculated will apply for most policy changes that might be proposed. However, proposals that would produce more extreme changes in the number of prescriptions filled might cause CBO to revise its estimate of the offset.

1 percent increase in the affected population's total spending for medical services. If that total spending would otherwise be $250 billion in that year, then those costs would increase by $0.5 billion. The net effect of the policy, combining the savings on drug costs and the costs of increased use of medical services, would be a savings for the federal government of $3.5 billion in that year.

If the policy in question targeted a particular population and the prescription drug use by and medical spending for that population could be identified, the offset would be calculated for that specific population. For example, if a policy targeted people receiving the low-income subsidy (LIS) in Medicare Part D, the change in prescription drug use would be estimated as a percentage of total prescription drug use by the LIS population. Likewise, the offset would be applied to Medicare's spending on medical services for that population.[17]

CBO will apply the offset only for policies that would change the quantity of prescriptions filled. It will not apply the offset to policies that would not affect the demand for and, therefore, the consumption of prescription drugs. For example, policies that change manufacturers' rebates to the federal government are unlikely to have a notable effect on the number of prescriptions that Medicare beneficiaries fill.

Finally, the offset described in this report applies only to the Medicare program. Further research would be needed to determine if such an offset was appropriate for changes affecting programs serving different populations—such as Medicaid beneficiaries or veterans—and what the magnitude of that offset might be.

As an illustration, CBO has applied its revised methodology to its estimate of the budgetary impact of closing the Part D coverage gap. Over the next eight years, Medicare beneficiaries' cost sharing will continue to be reduced gradually as that gap closes. That process involves two components. First, manufacturers of brand-name drugs are now responsible for 50 percent of the costs of prescriptions that are dispensed when spending is within the coverage gap, effectively lowering the price for brand-name prescriptions relative to that under prior law. Second, the generosity of the basic Part D benefit is gradually increasing so that, by the time the coverage gap is closed in 2020, Part D plans will be required to pay for 25 percent of the costs of brand-name prescriptions and 75 percent of the costs of prescriptions for generic drugs dispensed within the coverage gap. Those changes in the prescription drug benefit will affect only beneficiaries who do not receive the low-income subsidy, so CBO's estimates of prescription drug use and spending and the resulting offset to other Medicare spending apply to that population only.

By CBO's estimate, the changes in the Part D benefit will increase total annual consumption of prescription drugs by Medicare enrollees not receiving the low-income subsidy by about 5 percent by 2018. Therefore, by 2018, that change in consumption is now expected to result in a reduction of approximately 1 percent in Medicare's spending on medical services for that population. (Although the provisions largely affect beneficiaries who reach the coverage gap, the figures are presented as a proportion of prescription drug use and medical spending for the entire Medicare population not receiving the low-income subsidy.)

CBO estimates that the two provisions will boost federal spending for Medicare Part D by $86 billion over the 2013–2022 period relative to what would have been spent under prior law. Applying the offset, CBO estimates that those provisions will reduce federal spending for medical services under Medicare by $35 billion (out of $5.6 trillion)—resulting in a net increase in federal spending of $51 billion from 2013 to 2022.[18] Because the coverage gap is partially closed through manufacturers' discounts rather than federal subsidies, the offset generates larger savings in medical spending as a share of the increase in costs for prescription drugs than it would for proposals in which the change in prescription drug use came entirely from a change in federal subsidies.

17. Although a substantial share of the LIS population is dually eligible for Medicare and Medicaid, the offset would be applied only to Medicare's spending because there is little evidence of a relationship between prescription drug use and spending on long-term care, which constitutes the majority of Medicaid's spending on dually eligible beneficiaries.

18. The 10-year reduction in spending for medical services ($35 billion) is less than 1 percent of the 10-year total spending figure ($5.6 trillion) in part because the former figure applies to Medicare recipients enrolled in Part D who do not receive the low-income subsidy and the latter figure applies to the broader Medicare population.

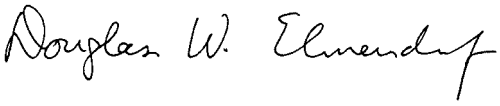
In sum, using the revised methodology, CBO estimates that the net cost of implementing the provisions closing the coverage gap will be $51 billion, rather than the $86 billion estimated prior to the revision. The estimated savings from narrowing or repealing those provisions would be similarly reduced because of the offset.[19]

CBO will continue to assess the evidence on how changes in the use of prescription drugs affect spending for medical services and will incorporate new research findings as warranted. The agency will also monitor additional channels through which changes in prescription drug use may affect federal spending. For example, increases in the number of prescriptions filled could reduce mortality in addition to reducing hospitalizations and other medical spending (and decreases in prescription drug use could raise mortality). A decrease in mortality would increase federal spending in later years through additional Social Security payments and Medicare spending. However, at present, there is insufficient evidence of a robust relationship between the number of prescriptions filled and mortality for CBO to incorporate such an effect into its estimates.

Finally, changes in the use of certain health care products or services apart from prescription drugs might also produce countervailing changes in spending on other types of health care. More generous benefits that increase the use of such products and services might result in savings elsewhere, and less generous benefits might generate costs elsewhere. CBO will continue to review evidence of such effects and incorporate that evidence into its estimates as appropriate.

19. The specifics of legislation to repeal those provisions might yield a different estimate; for example, repayments of discounts provided by manufacturers since the law went into effect would probably reduce net savings.

This Congressional Budget Office (CBO) report provides background information on the agency's estimates of the effects of prescription drug use on Medicare's spending on medical services. In keeping with CBO's mandate to provide objective, impartial analysis, the report makes no policy recommendations. Tamara Hayford and Melinda Buntin of CBO's Health, Retirement, and Long-Term Analysis Division wrote the report under the general supervision of Linda Bilheimer. Rebecca Yip and Jamease Miles of CBO's Budget Analysis Division completed the revised estimates of Medicare spending under the general supervision of Tom Bradley and Holly Harvey. Anna Cook, Alexia Diorio, Michael Levine, Andrea Noda, and Ellen Werble also contributed significantly to the report. Elizabeth Bass of CBO provided useful comments, as did Amitabh Chandra of Harvard University and Mark Miller of the Medicare Payment Advisory Commission. (The assistance of external reviewers implies no responsibility for the final product, which rests solely with CBO.) John Skeen edited the report. This report is available at the agency's Web site (www.cbo.gov).



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The $289 Billion Cost of Medication Noncompliance, and What to Do About It

By Brian Fung

New recommendations focus on relatively inexpensive fixes that could significantly reduce health-care waste.

Fillmore Photograph/Flickr

Last week, we explained how the United States spends $750 billion a year on wasted health care. Much of that comes from administrative costs and the ordering of unnecessary medical procedures.

But another major source of waste doesn't show up until after the doctor's visit. According to a meta-analysis published yesterday in the *Annals of Internal Medicine*, Americans are failing to comply with medication prescriptions for a variety of reasons -- and it's costing them anywhere between $100 billion to $289 billion a year.

In some 20 percent of cases -- and as many as 30 percent -- prescriptions for medication are never filled. Up to 50 percent of medications aren't taken as prescribed.

Medication noncompliance creates major headaches for patients and doctors alike down the road, and can sometimes be deadly. For example, someone with congestive heart failure who doesn't take their diuretics correctly, regularly, will often wind up in the hospital again and again. Failure to follow prescriptions causes some 125,000 deaths a year and up to 10 percent of all hospitalizations, the study's authors say.

As we're getting a better grasp on how individual behaviors affect the health-care system at large, we're trying to find ways to improve medication adherence. Among the recommendations in the analysis:

Switch to better packaging: At the consumer level, blister packs have been shown to boost compliance in patients with hypertension
Use case management and coordinated care more effectively: At the systemic level, appointing a pharmacist, doctor, nurse or other health professional to oversee a patient's care increased medication adherence among patients with hypertension, heart failure, depression and asthma
Invoke education and behavioral support: Phone calls, mailings, and even videoconferences may make a difference for high-cholesterol, high blood pressure, heart failure and heart attack patients
Give health professionals access to compliance data: If a doctor or pharmacist knows a patient has had trouble taking their pills regularly, they can take steps to intervene
Make drugs cheaper: Reducing out-of-pocket costs by trimming copays or expanding drug coverage led to a 14 percent decrease in the rate of heart-disease patients having their first vascular event (e.g., a stroke or heart attack), according to the meta-study. Even if they have medications in their cabinets, patients may be less likely to take them on schedule for fear of being unable to afford refills later. Improving drug affordability may therefore convince the thrifty to refill their prescriptions as needed rather than on the basis of their budgets

The fifth finding seems especially timely. It vindicates policy measures like Medicare Part D and the Affordable Care Act, the latter of which has saved seniors and the disabled some $4 billion on prescription drugs already, the Department of Health and Human Services found in July.

By saving lives and eliminating waste, increasing prescription adherence is good for the health industry and the broader economy. But as Richard Gunderman points out, health care at the individual level is still about real human beings. Even if it weren't true that better medication compliance led to reduced health-care costs -- something that otherresearch implies but which the latest meta-analysis found little evidence for -- helping people take their medications (correctly) is still the right thing to do.

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Drug non-adherence costs $290 billion year

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BALTIMORE, Nov. 3 (UPI) -- BALTIMORE, Nov. 3 (UPI) -- Nearly three out of four Americans do not always take medication as directed, adding $290 billion per year to U.S. healthcare costs, federal officials say.

Surgeon General Regina Benjamin said patient medication non-adherence is a problem that causes more than one-third of medicine-related hospitalizations, nearly 125,000 U.S. deaths each year and adds $290 billion in avoidable costs to the healthcare system annually.

In a multi-year national "Script Your Future" campaign, the surgeon general is encouraging patients with chronic conditions to speak with healthcare professionals about their medications.

The campaign brings area stakeholders in healthcare, business and government together to offer practical tools to help patients better adhere to their medication, and to help healthcare professionals better communicate with patients, Benjamin said.

"Our national challenge is to prevent poor health outcomes and to become a healthy and fit nation. One way is for the healthcare community and patients to come together to address medication non-adherence, which is a major public health problem," Benjamin said in a statement. "Doctors, nurses, pharmacists and other healthcare professionals can help prevent many serious health complications by initiating conversations with their patients about the importance of taking medication as directed. This is especially important for people with chronic health conditions such as diabetes, asthma and high blood pressure, who may have a number of medicines to take each day."

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Costs Of Patient Noncompliance

By Allan Showalter, MD

The No-Nonsense Summary
Costs Of Noncompliance

1. Characterizing the financial, physiological, and social costs patient noncompliance as catastrophic is neither hyperbole or hysteria, just fact.

2. Because the cascading effects of ongoing noncompliance can geometrically accelerate the costs of and number of people affected by a given case, prevention or, failing that, early recognition and intervention are vital.

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Direct Consequences & Costs

Inadequate implementation of treatment has devastating consequences, such as causing

- 10-25% of hospital and nursing home admissions, resulting in 340 deaths per day[1]
- 20% of unintentional pregnancies in the US at a cost of $2.6 billion[2]
- 3 times as many doctor visits and an additional $2000 of healthcare costs per year compared to patients who follow their treatment plan[3]
- 33-69% of all medication-related hospital admissions in the US at a cost of $100 billion[4]

It is especially revealing that estimates of the total annual healthcare costs in the US resulting from patient noncompliance vary from $100 billion[5] to $170 billion[6] to $300 billion[7,8] First, this range (even after adjusting for the 11 year difference between the oldest and newest figures) points to the potential risk of false precision, the dramatic influence of assumptions and methodologies in such approximations, and the difficulty of computing cost-benefit ratios of efforts to enhance compliance. Second, even the most conservative figures delineate the tremendous fiscal impact of noncompliance, fully justifying The American Heart Association's summation that "the cost of noncompliance in terms of human life and money is shocking."[9]

Complex, Cascading, Cumulative Costs

Even calculations that take into account only such basics as the likelihood that noncompliance will result in treatment failure, the pervasiveness of noncompliance, and the expense of healthcare produce terrifying results. The total damage caused by patient noncompliance, however, is too complex, multivariate, intertwined, subjective, and extensive to quantify with a straightforward algebraic formula.

My contention, in fact, is that the central tragedy of patient noncompliance results from the fact that the effects of noncompliance rarely manifest in a straightforward *If-A-Then-B* algorithm; rather, they tend to cascade. A hypothetical case may be helpful in explaining this concept and its fundamental significance.

The Case Of Routine & Tragic Patient Noncompliance

A patient with an respiratory infection does not complete the full course of the antibiotic prescribed by his physician. When symptoms persist, the patient returns to his doctor but fails to report the noncompliance. The physician consequently believes that the original medication was somehow inadequate (e.g., the pathogen was resistant to the medication or not covered within the therapeutic range of the medication) and prescribes a different agent, one that is more costly & more prone to side-effects.

Already in this scenario, noncompliance has resulted in

- One unnecessary clinic visit
- Two medications in a situation in which one might have sufficed
- An increased risk of adverse medication effects, both because the second drug causes more side-effects than the first and because the patient is exposed to two medications instead of one

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- A deviation, based on misinformation, from the initial treatment plan which, by design, should provide the optimal combination of safety, affordability, and effectiveness for that patient. At best, the new treatment plan will be similar to but somehow less advantageous than the original therapy. At worst, the noncompliance-caused treatment failure will cause the clinician to mistakenly alter the diagnosis and treatment such that the actual problem is not addressed.

This example is, admittedly, oversimplified. Some disorders improve despite noncompliance with treatment. Some clinicians might have suspected noncompliance when the patient did not improve. Some patients do confess their failure to follow the treatment plan. Nonetheless, a plethora of evidence demonstrates that noncompliance clearly increases the risk of treatment failure, that clinicians rarely recognize or even suspect noncompliance, and that patients even more rarely reveal nonadherence to treatment. This example is, in fact, statistically condensed but conceptually accurate, and countless analogous cases occur every day throughout the healthcare system.

Little imagination is required to conjure up catastrophic conclusions and mournful denouements for our noncompliance story line:

- The patient has an autoimmune reaction to the second, unneeded medication and, despite emergency interventions, dies.
- The patient experiences a number of side-effects from the second medication, resulting in his unilateral decision to discontinue treatment with that agent. The respiratory symptoms worsen, necessitating invasive testing, an eight day hospitalization, IV drugs, and treatment for a secondary fungal infection before he recovers.
- Two weeks after starting (but not completing) the first drug regimen, the patient's disorder persists, and he unknowingly infects a friend who is taking immunosuppressive agents. The patient's friend succumbs to sepsis. The patient himself returns to normal after taking the second medication.

Of course, terminal autoimmune reactions and other such dire events take place infrequently, but they are statistical realities. One can consider an episode of patient noncompliance as a ticket for a lottery that offers pain, suffering, expense, and death as the prizes. No one ticket is likely to win, but the Law Of Large Numbers is implacable, i.e., the probability of any possible event (even an unlikely one) occurring at least once in a series increases with the number of events in the series. As the lottery ads put it, "The more you play, the more you win." (Also, "Hey, You never know.")

Perhaps a more ominous alternative conclusion to this case, precisely because it invokes no rare disorders or coincidental events and therefore cannot be dismissed as an improbable long shot, depends only on a persistence of both the patient's noncompliance and his pathogen's toxicity:

- The patient's symptoms cycle, exacerbating and subsiding in rough concordance with his adherence to treatment. Over the next several months, he requires many more outpatient visits, occasional trips to the emergency department, brief hospitalizations, and repeated laboratory tests, radiological exams, and invasive diagnostic procedures. His medication schedules evolve into complex, exotic, and

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expensive regimens. Several doctors now consult on his case, and his original doctor is becoming increasingly concerned, puzzled, and frustrated. His disorder and its treatment has had a deleterious effect on his work, his marriage, and his finances. His health insurer has become more and more restrictive and intrusive. After six months, the symptom gradually subside and finally appear to dissipate totally. His treatment team never reaches a definitive diagnosis and because of their concern about a recurrence, they insist on multiple follow-up visits and tests as well as prophylactic treatment with a broad spectrum antibiotic. His final out of pocket medical bill is just over $16,000 with his company-provided insurance covering the rest. During a business downturn, he is laid off; he suspects, accurately, that he was targeted because of the huge health insurance premium increase suffered by the small firm where he had worked because of his claims. His former employer also cuts healthcare benefits for its remaining workers to protect against another such disaster.

Because of the complexity and interdependent nature of the contemporary healthcare system, the impact of patient noncompliance is rarely limited to wasting one medical treatment that would have been successful if implemented. Instead, any treatment failure caused by noncompliance is subject to an array of multipliers, some obvious and some invisible, that can easily increase the potential fiscal, physiological, and social cost exponentially and connections, both direct and indirect, that distribute a similar range of losses to others. Moreover, the extraordinarily high value western culture places on both the individual and health heightens the stakes and further drives the process.

References

[1] Zuger A. The other drug problem: forgetting to take them, *New York Times*. June 2, 1998:C1.
[2] Rosenberg M, Waugh MS, Long S. Unintended pregnancies and, misuse and discontinuation of oral contraceptives. *Journal of Reproductive Medicine* 1995; 40: 355–360.
[3] Lifeclinic.com Web site. Medication compliance aids page. Available at: http://www.lifeclinic.com/focus/blood/ supply_aids.asp. Accessed August 21, 2003.
[4] McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. *Ann Pharmacother* 2002; 36:1331-6.
[5] The Task Force for Noncompliance. *Noncompliance With Medications: An Economic Tragedy With Important Implications for Health Care Reform*. Baltimore, MD: The Task Force for Noncompliance; 1994.
[6] Dezii, C. Medication noncompliance: what is the problem? *Managed Care/Supplement*. 2000;9:7-12.
[7] DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. March 2004;42:200-209.
[8] Butler K. A spoonful of compliance helps keep costs down. WSJ CareerJournal.com (From *Employee Benefit News*). Available at: http://www.careerjournal.com/hrcenter/benefitnews/20050819-bn.html. Accessed August 19, 2005.
[9] American Heart Association, The American Hidden Health Threat Page. Available at: http://www.americanheart.org/presenter.jhtml?identifier=9206. Accessed July 19, 1999.