RESEARCH

Descriptive Analysis of Mail Interventions with Physicians and Patients to Improve Adherence with Antihypertensive and Antidiabetic Medications in a Mixed-Model Managed Care Organization of Commercial and Medicare Members

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ABSTRACT

BACKGROUND: Medication nonadherence is a major concern for many health care stakeholders. Improving medication adherence in health plan members who have both hypertension and diabetes is essential for the successful management of these chronic diseases, with anticipated outcomes in decreased health care utilization, all-cause mortality and cost.

OBJECTIVE: To (a) identify patients who are potentially nonadherent to antidiabetic or antihypertensive agents within 1 managed care organization and (b) determine the relationship of rates of medication nonadherence with 2 mail intervention programs that involved quarterly medication-specific profiles of patients with potential nonadherence sent to primary care physicians (PCPs) and general medication adherence letters sent to patients with potential nonadherence.

METHODS: The study sample consisted of commercial members, Medicare Advantage-Prescription Drug Plan (MA-PD) members and Medicare Prescription Drug Plan (PDP) members who filled prescriptions for antihypertensive and antidiabetic medications and utilized their managed care pharmacy benefit during each measurement quarter (3 months) in the 2-year study period. Nonadherence was defined as a medication possession ratio (MPR) less than 77.0% for 1 or more antihypertensives and/or antidiabetic medications for each standalone calendar quarter. The first intervention, letters to PCPs with patient-specific medication profiles for 2008 Q2, began 6-8 weeks after 2008 Q2 and continued for each standalone calendar quarter through the end of the study period in 2010 Q1 (January 1, 2010, through March 31, 2010). We assumed that patient care was managed by PCPs for hypertension and diabetes treatment. The medication profile also included antihyperlipidemic medication claims information, but there was no adherence analysis performed for antihyperlipidemic medications. The second intervention, letters sent to potentially nonadherent patients, began 6-8 weeks after 2009 Q1 for patients with MPR less than 77% for 1 or more antidiabetic or antihypertensive medications in 2009 Q1 and continued for each standalone calendar quarter through the end of the study period in 2010 Q1.

RESULTS: Because there were 2 different interventions, 2 baseline adherence rates were calculated, for 2008 Q2 for the PCP mailing and for 2009 Q1 for the patient mailing. Compared with the baseline nonadherence rate in 2008 Q2 (35.6%), a small increase in nonadherence was observed in 2008 Q3 (36.4%), following by 6 calendar quarters of lower rates of nonadherence with a 27.7% nonadherence rate in the last measurement period in 2010 Q1. Compared with the nonadherence rate of 30.8% in baseline 2 (2009 Q1), the patient mailings were associated with small increases in nonadherence to 31.4% in 2009 Q2 and 31.1% in 2009 Q3, respectively, followed by lower nonadherence rates in 2009 Q4 (29.2%) and 2010 Q1 (27.7%).

CONCLUSIONS: A 2-part intervention that involved mailings to PCPs for patients with both diabetic and antihypertensive medications who were potentially nonadherent to at least 1 medication, followed 9 months later by a general mailing sent to these potentially nonadherent patients regarding medication adherence, was associated with apparent improvement. However, the effect of the 2-part intervention on medication nonadherence could not be isolated because of coincident disease management interventions in diabetes and hypertension during the 2-year study period.

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What is already known about this subject

- There are many barriers to medication adherence especially in members with chronic disease(s) such as diabetes, hypertension, and hyperlipidemia. Many different interventions have been used to improve medication adherence including educational strategies. Effects of educational strategies alone have produced inconsistent results, and multifaceted or multidisciplinary interventions are generally more effective.
- A real-time fax intervention with prescribers of antidepressant medications for patients with delayed refills (more than 10 days) did not improve adherence; average antidepressant nonadherence rates among patients with delayed refills were approximately 75% (Baumbauer et al., 2006). The combination of monthly mailed personalized letters to patients nonadherent to antidepressants and lists of nonadherent patients sent to prescribers was associated with a small difference in adherence rates (MPR of 67% or more) at 90 days (66.9% intervention vs. 65.5% control, $P<0.001$) and at 180 days (52.3% intervention vs. 50.2% control, $P<0.001$; Hoffman et al., 2003).
- Roumie et al. (2006) in a multifaceted intervention that included letters sent to patients combined with provider education (e-mail with Web-based link with hypertension treatment guidelines) and computerized alerts to providers found significantly better mean blood pressure after 6 months of follow-up compared with provider education alone or provider alerts plus provider education, and more patients in the combination intervention with patient letters attained systolic blood pressure control (140 millimeters mercury [mm Hg]), 60% versus 42% for provider education only and 41% for provider education plus alert ($P=0.012$).

What is already known about this subject *(continued)*

- Márquez Contreras et al. (2005) in a prospective controlled multicenter clinical trial of hypertensives newly diagnosed or with uncontrolled hypertension found that telephone intervention (3 calls made by nurses over 15 weeks) and mail intervention (3 letters over 16 weeks) were associated with a higher proportions of patients who were compliant with antihypertensive therapy (96% and 91%, respectively, vs. 69% in usual care) and blood pressure control (63% and 61%, respectively, vs. 47% in usual care).

What this study adds

- An intervention program composed of mailing medication profiles quarterly to primary care physicians (PCPs) for patients who were treated with both antihypertensive and antidiabetic medications and who were potentially nonadherent with at least 1 drug in either class was associated with a decrease in the proportion of patients deemed potentially nonadherent within 6 months of initiation of the intervention, from a baseline rate of 35.6% to rates of 30.8% and 27.7% at 6 and 18 months following the intervention start date, respectively .
- The proportion of patients deemed potentially nonadherent continued to decrease after addition of quarterly mailings to potentially nonadherent patients. However, coincident disease management interventions in this managed care organization prevented isolation of the effects of the mailings to PCPs and patients.

Successful management of diabetes and hypertension is directly associated with patient adherence to prescribed drugs. A wide array of medications is used to manage these conditions, yet their clinical impact is limited by poor adherence rates.[1] By receiving preventive care and by controlling blood glucose, hypertension, and hyperlipidemia through diet, exercise, and medication adherence, patients with diabetes can potentially avoid complications including (but not limited to) heart disease, stroke, blindness, and renal failure.[2] Studies have shown that rates of refilling prescriptions are an accurate measure of overall adherence in a closed pharmacy system, provided that refills are measured at several points in time.[3-5]

Medication nonadherence is a recognized public health concern, and nonadherence rates vary considerably among studies. For example, nonadherence for diabetic patients receiving oral antidiabetic agents ranged from 36% to 93% in 1 systematic review by Cramer (2004).[7] Most studies of nonadherence use medication possession ratios (MPR), but other measures of adherence include proportion of days covered or the proportion of doses taken as prescribed.[5-7] Investigators have found that improving medication adherence is associated with decreases in adverse drug events, hospitalizations, health care costs and utilization, and all-cause mortality.[6,8,9] Due to the adverse consequences of uncontrolled diabetes and hypertension, medication adherence is important to improve treatment benefits and prognosis.[10]

Numerous articles in the medical literature have described barriers to medication adherence.[1,6,11-15] Interventions that have been associated with improved medication adherence include combined behavioral and educational approaches, such as (a) patient medication plan followed by patient visits and medication plan revisions, or telephone assessment of follow-up medication use; (b) pharmacist-tailored counseling session on medication adherence and knowledge; (c) pharmacist identification of potential drug-related problems (DRPs) or actual DRPs with specifically developed interventions; (d) patient-centered, educational-behavioral interventions, such as pharmacist tailored education programs and counseling sessions or patient education on self-monitoring of blood pressure/blood glucose; and (e) tablet counts and customized telephonic counseling and custom packaging of medications.[16,17]

For patients receiving medications for chronic diseases, improvements in health outcomes and adherence are most often realized when multiple interventions have been utilized, such as information/education, counseling, reminders, psychological therapy, mailed communications, reinforcement, family therapy, manual telephone follow-up, involving patients in their own care through self-monitoring, and others.[10] The Cochrane systematic review by Haynes et al. (2008) found that 4 of 10 interventions for short-term treatments reported in 9 randomized controlled trials (RCTs) had significant effects on both medication adherence and clinical outcome, and 1 intervention in 1 RCT improved patient adherence but not clinical outcome.[17] Of 81 interventions for long-term treatments reported in 69 RCTs, 36 (44%) improved medication adherence, but only 25 (31%) improved at least 1 clinical outcome; almost all of the effective long-term interventions were complex (e.g., combinations of reminders, psychological therapy, telephone calls). Additionally, even effective interventions produced only modest results.[17]

Kripalani et al. (2007) also found that most educational interventions to help patients understand their conditions and become empowered to adhere to treatment do not improve health outcomes or adherence rates.[18] However, one of the studies reported by Haynes et al., by Márquez Contreras et al. (2005), did show significant improvement in antihypertensive medication adherence and blood pressure control when educational messages provided either by nurse telephone calls (separate calls at 15 days, 7 weeks, and 15 weeks to encourage compliance) or a patient letter (information about the importance of compliance mailed at 15 days, 2 months, and 4 months) were added to usual care.[19] Rates of compliance and blood pressure control, respectively, were 96% and 63% for telephone calls, 91% and 61% for mail, and 69% and 47% for

usual care. Therefore, a multidisciplinary team approach and/or a multifaceted approach may increase medication adherence and improve patient outcomes.

Hoffman et al. (2003) conducted an RCT in which patients newly prescribed antidepressant medication were assigned either to a control group or to an educational intervention consisting of personalized letters to patients describing the importance of medication adherence and letters to physicians that included lists of nonadherent patients, with both sent 20-25 days after the end of each month.[20] Outcomes were followed for 6 months using a pharmacy claims database and included (a) MPR indicating less than 10 gap days per 30-day period (i.e., 67% or more) and (b) the 2 principal Healthcare Effectiveness Data and Information Set (HEDIS) scores in depression pharmacotherapy, the percentages of patients who take the medication with no more than 30 gap days for the initial 12-week (84 days) acute phase and continue taking the medication with no more than 51 gap days for at least 6 months (180 days). In intention-to-treat analysis, the intervention group (n = 4,899 patients and 3,474 prescribers) displayed slightly greater adherence compared with the control group (n = 4,665 patients and 3,547 prescribers) at both 90 days (66.9% vs. 65.5%, respectively) and 180 days (52.3% vs. 50.2%, respectively, $P < 0.01$). After adjusting for covariates, the intervention showed a significant impact on adherence ($P < 0.01$).

Bambauer et al. (2006) used an interrupted time series analysis to evaluate the effects of real-time faxed alerts to physicians for potentially nonadherent adult, antidepressant therapy-naive patients (n = 13,128) in a large nonprofit managed care organization (MCO).[21] Potential nonadherence was defined as a gap of more than 10 days from the prior medication fill (or refill) during the first 6 months of medication therapy. Nonadherence rates among patients with delayed refills remained constant at approximately 75% ($P = 0.22$) over the 2-year study period (2002-2004). Adherence rates decreased over time, with patients not having antidepressants available for approximately 40% of the days of treatment. The authors suggested that a multifaceted approach including multiple mailings, patient phone calls, or patient visits, or a multidisciplinary approach using pharmacists, nurses, or specific case managers might be more likely to improve adherence.

Roumie et al. (2006) evaluated the effects of provider and patient interventions on blood pressure control in a 6-month, cluster RCT in a hospital- and community-based Veterans Affairs (VA) population in Tennessee, using a sample of 1,341 veterans (n = 182 providers) who filled prescriptions at the VA, had 2 uncontrolled systolic blood pressure (SBP) values (greater than 140 millimeters mercury [mm Hg]) in the prior 6 months, and were taking 1 antihypertensive agent.[22] Providers were randomly assigned to (a) provider education only, including an e-mail with a Web-link to the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) Guidelines; (b) provider education plus a computerized patient-specific electronic notification/alert; or (c) provider education, alert, and patient education, which consisted of a personalized patient letter containing educational information on hypertension, medication adherence, lifestyle modification, conversations with providers, and where to go to get more information. The primary outcome, the proportion of patients with an SBP less than 140 mm Hg at 6–month follow-up, was significantly better for the combination of provider education, alert, and patient education (60%) than for either provider education plus alert (41%) or provider education only (42%; $P = 0.012$). In a separate analysis under the conservative assumption that no patient lost to follow-up (27% of study patients) achieved SBP control, control rates for the 3 groups were 45%, 27%, and 33%, respectively ($P = 0.013$). Mean follow-up blood pressures were 138/75 mm Hg in the 3-intervention combination group, compared with 146/76 mm Hg for provider education plus alert and 145/78 mm Hg for provider education only.

Although many medication adherence improvement interventions are multifaceted and complex, we sought to develop an intervention based on an automated process for reporting to physicians and patients that is feasible for MCOs to use on a routine basis. Thus, we performed a descriptive, business-case analysis to assess the association of potential medication nonadherence with an intervention that involved quarterly letters mailed to primary care physicians (PCPs) with potentially nonadherent patient-specific medication profiles. We later added a patient educational mailing component to the intervention. The primary objective of this study was to determine whether these interventions would be associated with reduction in nonadherence rates for antihypertensive or antidiabetic medications in a target population of patients receiving at least 1 drug in both medication classes in standalone calendar quarters.

Methods

Study Sample and Design

EmblemHealth provides health insurance through its companies Group Health Incorporated (GHI) and HIP Health Plan of New York (HIP). Groups and individuals can choose a preferred provider organization, an exclusive provider organization, or a health maintenance organization (HMO). The Clinical Pharmacy Department serves as its own pharmacy benefit management (PBM) company and is integrally involved in the health plan's Pharmacy & Therapeutics (P&T) Committee, which reviews the drug formulary to ensure that it is up-to-date and reflects evidence-based practice. The P&T Committee approved the present study.

The study involved a retrospective analysis of pharmacy claims data for approximately 380,000 Medicare and commercial members who obtained their pharmacy benefits through HIP, the largest HMO in New York City based on membership.

Only paid pharmacy claims (net of removal of matched paid and reversed claims) were used in an effort to minimize mailing of false-positive letters. The analysis was conducted for all pharmacy claims including both community and mail order pharmacy; members can receive up to a 90-day supply at either a community pharmacy or from mail order.

Data assessments were made for each calendar quarter, beginning at the end of the second quarter of 2008 (2008 Q2) using the pharmacy claims data from April 1, 2008, to June 30, 2008. Eight calendar quarters were included in this analysis—2008 Q2 (April 1, 2008, through June 30, 2008) through 2010 Q1 (January 1, 2010, through March 31, 2010). Each quarterly mailing was sent out approximately 6-8 weeks after the quarter ended. All Medicare Advantage-Prescription Drug Plan (MA-PD), Medicare Prescription Drug Plan (PDP), and commercial members regardless of age who had an assigned PCP and active pharmacy coverage as of the last day of each calendar quarter in the study period were eligible for this study. For example, in order to be included in the analysis for the first measurement quarter (April 1, 2008, through June 30, 2008), the patient must have had active status in the plan's system on June 30, 2008. We did not exclude patients who joined the health plan during the analysis quarter (i.e., patients were included who may have had pharmacy benefits that commenced after the first day of the calendar quarter).

To identify the study sample at the end of each quarter, all members who had active pharmacy benefit coverage as of the last day of the previous quarter were separated into 2 groups using First DataBank GC3 codes (Table 1). Group 1 included members who had at least 1 pharmacy claim for an antidiabetic medication, and group 2 included members who had at least 1 claim for an antihypertensive medication. These 2 groups of patients were then cross-referenced to obtain our final total study sample for that particular quarter (Figure 1). Because some members move in and out of plan coverage for personal reasons (e.g., employment change, retirement), the study sample varied throughout the study period. During the study, we tried to keep the GC3 tables updated as new GC3 codes became available, were deleted, or were changed (e.g., the GC3 code for Exubera [inhaled insulin] was deleted after it was taken off the U.S. market; the GC3 code for Exforge hydrochlorothiazide [HCT] was added after it became available on the U.S. market).

TABLE 1 First DataBank GC3 Codes and Code Descriptions

Code	Description
Antihypertensives	
A4A	Antihypertensives, vasodilators
A4B	Antihypertensives, sympatholytic
A4D	Antihypertensives, ACE inhibitors
A4F	Antihypertensives, angiotensin receptor antagonist
A4K	ACE inhibitor/calcium channel blocker combination
A4Y	Antihypertensives, miscellaneous
A9A	Calcium channel blocking agents
J7A	Alpha/beta-adrenergic blocking agents
J7B	Alpha-adrenergic blocking agents
J7C	Beta-adrenergic blocking agents
R1H	Potassium sparing diuretics
R1L	Potassium sparing diuretics in combination
R1M	Loop diuretics
R1F	Thiazide and related diuretics
A4C	Antihypertensives, ganglionic blockers
Antidiabetics	
C4F	Antihyperglycemic, (DPP-4) inhibitor and biguanide combinations
C4G	Insulins
C4H	Antihyperglycemic, amylin analog-type
C4I	Antihyperglycemic, incretin mimetic (GLP-1 receptor agonist)
C4J	Antihyperglycemic, DPP-4 inhibitors
C4K	Antihyperglycemic, insulin-release stimulant type
C4L	Antihyperglycemic, biguanide type (non-sulfonylurea)
C4M	Antihyperglycemic, alpha-glucosidase inhibitor (N-S)
C4N	Antihyperglycemic, insulin-response enhancer (N-S)
C4O	Antihyperglycemic, absorption modifier, unspecified
C4P	Antihyperglycemic, unspecified mechanism
C4Q	Antihyperglycemic combinations
C4R	Antihyperglycemic, insulin-response and release combinations
C4S	Antihyperglycemic, insulin-release stimulant and biguanide combinations
C4T	Antihyperglycemic, insulin-response enhancer and biguanide combinations
C4U	Antihyperglycemic, biguanide and dietary supplement combinations
Antihyperlipidemics	
M4C	Lipotropics (continued 2)
M4D	Antihyperlipidemic—HMG-COA reductase inhibitors
M4E	Lipotropics
M4F	Lipotropics (continued 1)
M4L	Antihyperlipidemic—HMG-COA reductase inhibitor and niacin
M4M	Antihyperlipidemic—HMG-COA reuctase inhibitor and cholesterol absorption inhibitor
M4J	Antihyperlipidemic—HMG-COA and platelet inhibitor combination
D7L	Bile salt sequestrants

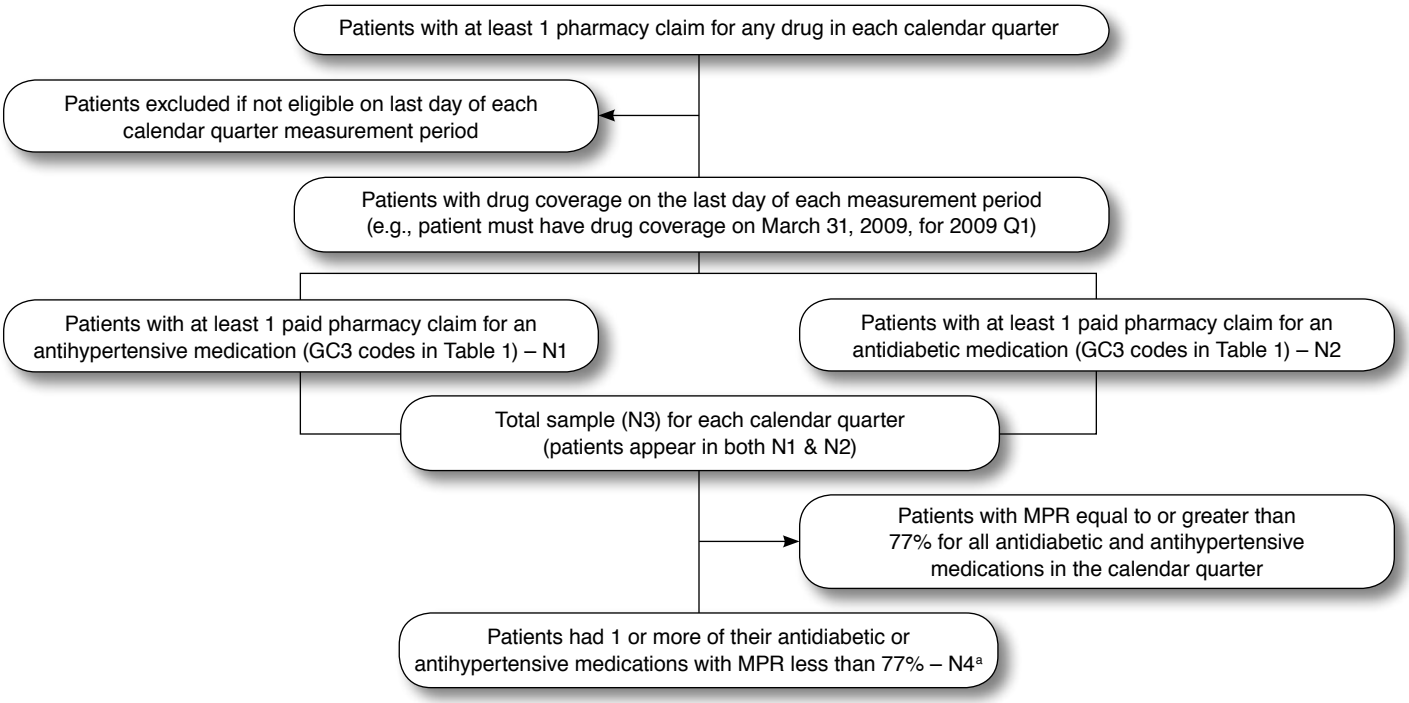
ACE = angiotensin-converting enzyme; DPP = dipeptidyl peptidase; GLP = glucagon-like peptide; HMG-COA = 3-hydroxy-3-methylglutaryl-coenzyme A.

Adherence Calculation

The MPR was the study adherence measure. Nonadherence was defined as an MPR less than 0.77 (77%), meaning that a patient missed an average of at least 7 days supply of medication within a 30-day period. Medication adherence rates were calculated at the end of each quarter as follows:

First, for each member in the sample, we calculated the MPR for each antihypertensive and antidiabetic medication using the sum of days supply during the measurement quarter divided by the total number of days in the measurement quarter (90 days for all measurement quarters). Prescriptions with the same generic composition but with different strengths were considered to be the same medication. If the calculated MPR was equal to or greater than 1.0 (100%) for any individual medication, the patient was considered to have perfect

FIGURE 1 Member Selection Flowchart for Intervention Letters



[a]N4 = the number of potentially nonadherent members. Quarterly mailings were sent to the primary care physicians containing each patient's medication profile for antihypertensive, antidiabetic, and antihyperlipidemic medications beginning 6-8 weeks after the end of 2008 Q2 (April 1, 2008 through June 30, 2008). Beginning 6-8 weeks after the end of the 2009 Q1 (January 1, 2009 through March 31, 2009), mailings were sent to members with potential nonadherence in each calendar quarter.
MPR = medication possession ratio; Q = calendar quarter.

adherence to that particular medication, and all subsequent claims for that particular medication were excluded from further analysis in that calendar quarter. However, if the patient had paid claims for other hypertension or diabetes medications in that quarter, those claims were analyzed. For example, if a patient took both lisinopril and metformin, and only the prescriptions for lisinopril had a total of 90 days supply in the measurement quarter, all claims for lisinopril were excluded after this step and the claims for metformin were analyzed. Because we analyzed claims by calendar quarter, without longitudinal analysis across quarters, false positive indications of nonadherence (i.e., MPR less than 0.77) could have occurred (see Limitations section).

Following this step, medications with an MPR less than 1.0 (100%) were separated into 2 groups for further analysis. If the MPR was less than 77% using any of the following methods, the member was considered to be nonadherent:

Medications with 1 Claim. For medications with only 1 claim during the measurement quarter, the MPR was calculated as the total days supply on the claim divided by the number of days from the claim date to the end of the quarter. For example, for a member with only 1 pharmacy claim for a 30-day supply of atenolol on October 10, 2008, the MPR was calculated using 30 days supply divided by 82 (number of days between October 10, 2008, and December 31, 2008). This example has an MPR of 0.366, and the patient was considered nonadherent to atenolol in 2008 Q4.

Medications with 2 or More Claims. For medications with 2 or more claims during the quarter, 2 calculations were performed. First, the MPR was calculated using the total days supply for all the claims (excluding the last claim's days supply) divided by the total days from the date of the first claim to the date of the last claim. For example, for a member with three 30-day supply pharmacy claims for atenolol on October 1, 2008, November 15, 2008, and December 25, 2008, the MPR was calculated using 60 (total of 90 days supply for all 3 prescriptions minus 30, which is the days supply on the last claim on December 25) divided by 84 (number of days between October 1, 2008, and December 25, 2008), which yielded an MPR of 0.714, and the patient was deemed nonadherent to atenolol in 2008 Q4. Second, the MPR was calculated by dividing the last claim's days supply by the number of days

from the date of the last claim to the end of the measurement quarter. For example, for a member with two 30-day supply pharmacy claims for atenolol on October 1, 2008, and November 1, 2008, the MPR was calculated using 30 (the days supply for the last claim on November 1, 2008) divided by 60 (the number of days between November 1, 2008, and December 31, 2008), which yielded an MPR of 0.50, and the patient was deemed nonadherent to atenolol in 2008 Q4.

Approximately 6 to 8 weeks after identifying potentially nonadherent patients at the end of each quarter, we mailed a cover letter and patient medication profiles to PCPs who had at least 1 nonadherent patient. Each PCP received a cover letter explaining the initiative (Appendix 1) and a patient-specific medication profile for each nonadherent patient (i.e., some PCPs received as little as 1 patient medication profile and other PCPs received multiple patient medication profiles). The medication profile included information about medication names, dosage, dispensing date(s), quantity dispensed, days supply, and name of the prescriber(s). If patients were also taking antihyperlipidemic medications based on the GC3 codes in Table 1, they were also included in the report; however MPRs were not calculated for these antihyperlipidemic medications.

In an effort to further improve medication adherence and potentially enhance clinical outcomes related to diabetes and hypertension treatment, we added a second quarterly intervention beginning after the analysis for 2009 Q1 (January 1, 2009, through March 31, 2009). This intervention, mailings to patients, provided general educational materials related to hypertension and diabetes medication adherence (i.e., specific medication use history derived from pharmacy claims was not part of the intervention), as well as information about the importance of taking medication as prescribed. The mailings also included a "tip sheet" with likely situations that members may encounter as obstacles to adherence to their medication regimens and a list of possible solutions to overcome these obstacles (Appendix 2). All members identified as potentially nonadherent each quarter (i.e., MPR of less than 77% for any antihypertensive or antidiabetic medication) received this general patient mailing approximately 6-8 weeks after the end of each calendar quarter beginning on approximately May 15, 2009, through May 31, 2009.

Measurement and Analysis

Because 2 types of interventions were implemented at different times, 2 baseline nonadherence rates were calculated. The first baseline (baseline 1) was the percentage of potentially nonadherent patients for claims with dates of service in 2008 Q2 (i.e., from April 1, 2008, through June 30, 2008). The second baseline (baseline 2) was the percentage of potentially nonadherent patients calculated for claims with dates of service in 2009 Q1 (i.e., from January 1, 2009, through March 31, 2009). In keeping with the descriptive, business-case nature of the analysis, rates of potentially nonadherent patients in each quarter were compared with one or both baseline rate(s) using a 2x2 Pearson chi-square test when applicable. For example, the rate of potentially nonadherent patients from October 1, 2008, through December 31, 2008 (2008 Q4) was compared with baseline 1 rate (2008 Q2) to assess the physician letter intervention; and the rate of potentially nonadherent patients from October 1, 2009, through December 31, 2009 (2009 Q4) was compared with both the baseline 1 rate (2008 Q2) and the baseline 2 rate (2009 Q1) to assess both the physician and patient interventions. Statistical analyses were performed using Minitab version 15 (Minitab Inc., State College, PA) and an a priori alpha level of 0.025.

Results

In the first baseline measurement period (2008 Q2), 30,132 total members were included in the sample, of whom 10,722 (35.6%) had an MPR less than 77% for 1 or more antihypertensive or antidiabetic drugs (Table 2). The number of members identified with pharmacy claims for antihypertensive and antidiabetic medications differed each quarter, ranging from 29,051 (2008 Q3) to 32,833 (2010 Q1). The number of potentially nonadherent members varied from 9,086 (2010 Q1) to 10,722 (2008 Q2).

The percentage of nonadherent members increased slightly in 2008 Q3 during the quarter in which the first mailings to PCPs occurred and then decreased to 34.0% in 2008 Q4 and 30.8% in 2009 Q1 (Table 2, Figure 2). Following the addition of the member intervention, the medication nonadherence rate decreased further to 27.7% in 2010 Q1, the last measurement quarter in this study.

Discussion

Numerous types of interventions have been utilized in various disease states and patient populations to improve medication adherence.[9,23,24] A small number of other researchers have utilized combined mailed (or e-mailed) interventions to prescribers and patients. Examples of these interventions include patient education, reinforcement, and reminding; simplification of the drug regimen (e.g., once-daily versus multiple-daily dosing, insulin pens versus vials); and allied health care professional consulting. Because most MCOs are required to supply HEDIS reports for the effectiveness of antidepressant medication management, some published data are available on medication adherence and the pharmacologic management of depression using mailed interventions. Bambauer et al. performed a physician-only faxed letter intervention and found that adherence rates did not improve but remained unchanged at approximately 75% among patients who were late with refills.[21] However, in the study by Hoffman et al., the combination of a personalized prescriber letter and patient letter slightly improved antidepressant adherence compared

TABLE 2 Member Adherence Rates for Antihypertensive or Antidiabetic Drug Therapy and Counts of Interventions by Calendar Quarter

	2008 Q2 Baseline 1[a]	2008 Q3	2008 Q4	2009 Q1 Baseline 2[b]	2009 Q2	2009 Q3	2009 Q4	2010 Q1
Total patients with antihypertensive and antidiabetic drug therapy – n	30,132	29,051	29,149	31,510	32,371	32,361	32,762	32,833
Commercially insured patients – n (%)	9,560 (31.7%)	9,115 (31.4%)	9,162 (31.4%)	8,903 (28.3%)	8,867 (27.4%)	8,576 (26.5%)	8,470 (25.9%)	8,199 (25.0%)
Total potentially nonadherent patients – n (%)[c]	10,722 (35.6%)	10,570 (36.4%)	9,905 (34.0%)	9,701 (30.8%)	10,175 (31.4%)	10,059 (31.1%)	9,581 (29.2%)	9,086 (27.7%)
Potentially nonadherent commercial patients – n (%)	3,569 (37.3%)	3,372 (37.0%)	3,170 (34.6%)	3,008 (33.8%)	3,075 (34.7%)	2,944 (34.3%)	2,757 (32.6%)	2,611 (31.8%)
Number of PCPs[d]	2,504	2,510	2,278	2,278	2,328	2,308	2,266	2,199
Number of patient letters[b]				9,701	10,175	10,059	9,581	9,086
P value compared with Baseline 1[e]	–	0.008	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
P value compared with Baseline 2[e]	–	–	–	–	0.078	0.417	<0.001	<0.001

[a]Baseline 1 is 2008 Q2, the pre-intervention period for quarterly mailing of member-specific nonadherence profiles that began 6-8 weeks after June 30, 2008 (i.e., the first mailing to PCPs was sent between August 15, 2008, and August 30, 2008).

[b]Baseline 2 is 2009 Q1, the pre-intervention period for the quarterly mailing to the potentially nonadherent members that began about 6-8 weeks after March 31, 2009 (i.e., the first mailings were sent to potentially nonadherent members between May 15, 2009, and May 31, 2009).

[c]Nonadherence was defined as MPR less than 77% in each (standalone) calendar quarter.

[d]The count of PCPs is equal to the count of letters (i.e., each PCP received 1 or more profiles for all PCP-assigned members found potentially nonadherent to 1 or more antihypertensive or antidiabetic agent).

[e]P value calculated by Pearson chi-square; a priori critical alpha value was 0.025.

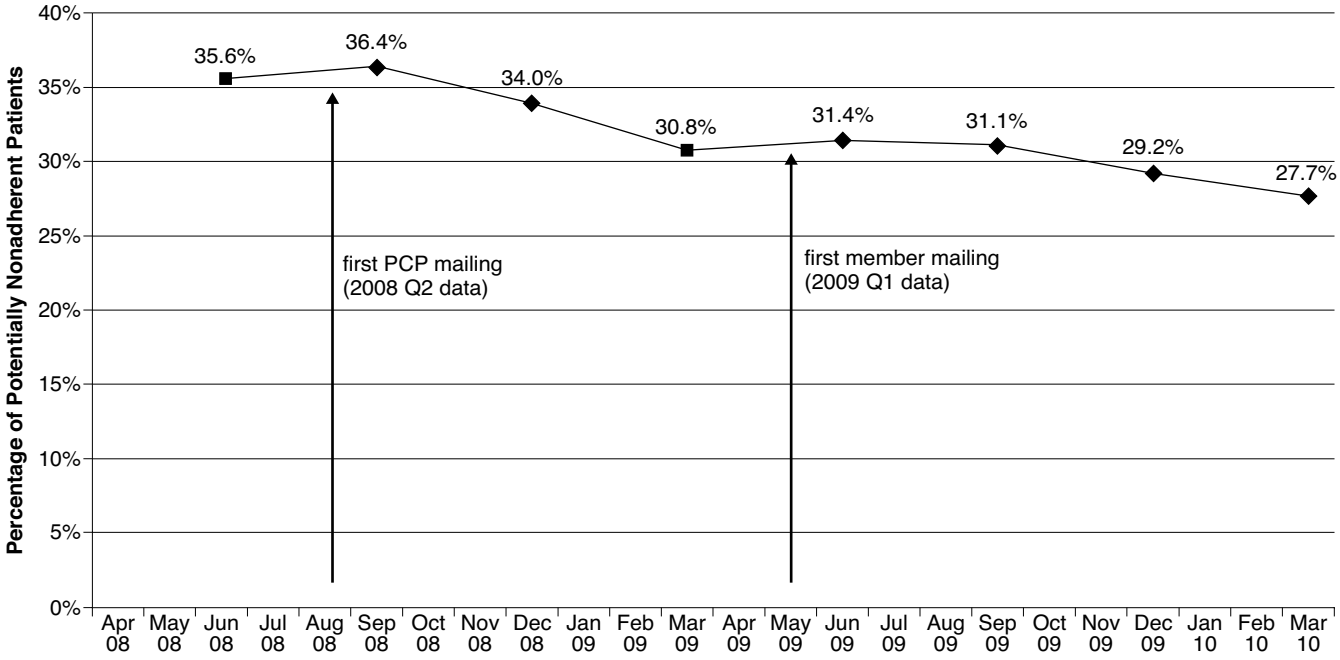
MPR = medication possession ratio; PCP = primary care physician; Q = calendar quarter.

with usual care.[20] Although the present study did not have a control or comparison group, we found that adherence was enhanced, as it was in the study by Hoffman et al., when a second intervention (the member letter) was added to the initial intervention (the PCP letter). This finding suggests that the standalone physician intervention may not have been sufficient to enhance medication adherence. Two additional studies conducted in samples of patients with hypertension have shown that interventions aimed at health care providers and/or nonadherent patients can enhance medication adherence.[19,22] These include the study by Roumie et al., which found better SBP control for a combination of provider education, alerting, and patient education compared with provider-only interventions, and by Márquez Contreras et al., which found better medication adherence and blood pressure control for either mailed or telephonic patient education compared with usual care.[19,22] The interventions in the present study were similar to those of Roumie et al., in that the PCP received both a personalized letter with a list of nonadherent patients and guideline information, and patients received a general letter describing issues related to medication adherence and education about hypertension and diabetes. Similar to the findings of the study by Roumie et al., when the mailed interventions were intensified in the present study, a better response was obtained.

The goal of the PCP mailing was to improve physician awareness of nonadherence with antihypertensive and antidiabetic agents. We hoped that PCPs would use the information to initiate personalized discussions with their patients about the importance of medication adherence. Copher et al. (2010) reported on a study of providers' awareness of patient adherence to treatments for postmenopausal osteoporosis.[25] Physicians who responded to a written questionnaire estimated that the patient adherence rate (defined as an MPR of at least 80%) would be approximately 69%. However, the actual adherence rate based on a retrospective analysis of pharmacy claims data was only 48.7%. Additionally, in a study by Lapane et al. (2007) using a convenience sample, 83% of patients reported they would never tell their physician that they were planning not to fill their prescriptions or that they did not want certain medications, and physicians did not seem to know that this lack of communication existed.[26] These interesting data suggest that physicians may not be aware of medications that their patients are taking (or are not taking). By having a copy of each patient's medication profile, PCPs have the "evidence" of potential patient nonadherence that they can use to discuss with patients during patient encounters.

We sent the patient medication adherence report to PCPs ("gatekeepers") even if they were not the prescriber so they could discuss the report with the patient and assist in coordinating the patient's care with other members of the multidisciplinary team (e.g., endocrinologist, cardiologist, ophthalmologist, nurse, case manager, nurse practitioner, diabetes educator, nutritionist, pharmacist) to "close the loop." Additionally, the mailed patient interventions informed members about how to be more medication adherent. If these members realized that they were being closely monitored, which we were unable to

FIGURE 2 Percentage of Patients Potentially Nonadherent with At Least 1 Antihypertensive or Antidiabetic Drug—by Calendar Quarter



PCP = primary care physician; Q = calendar quarter.

observe in the present study, they may have been more adherent, which would produce additional benefits to the member and to the health plan.

In the present study, antihyperlipidemic medication claims information was also provided to PCPs for their information; however, there was no adherence analysis performed for antihyperlipidemic agents. Including antihyperlipidemic agents in the patient medication profile to PCPs was meant to provide a more comprehensive list of the most common types of medications used to manage the metabolic syndrome.[27]

Another issue raised by the present study is the optimal adherence measure for an MCO. Adherence measurements are typically expressed as a percentage of the total number of doses taken, such as a pill count (if measured prospectively), or the number of days supply of the prescription received (if measured retrospectively) over a specified time period.[28] Currently, there is no uniform agreement as to what percentage is the best measure of adherence. Pharmacy refill claims have been widely used to assess medication adherence, and this approach is considered a credible and objective way to evaluate medication adherence in large population-based studies.[3,28-30]

The type of mailing used to motivate potentially nonadherent patients is also of importance to MCOs. In the present study, a general educational mailing, rather than a mailing containing patient-specific data, was used because we felt that (a) a specific mailing targeting nonadherent patients might engender negative perceptions of the health plan; (b) patients could be falsely identified as nonadherent due to study limitations; and (c) a general educational mailing did not require as much time and resources as an individually targeted intervention would have. Informational interventions, such as the member mailing used in the present study, are cognitive strategies that have been used to improve adherence to chronic therapies and are designed to educate and motivate patients.[31] This type of intervention assumes that patients who have an understanding of their medical conditions and how these conditions are best treated will be better informed, more engaged in their own care, and more likely to adhere to treatment. Our member mailing can also be thought of as a behavioral intervention because it acted as a "reminder" to the patients of their hypertension and diabetes and the importance of taking their medications.

Finally, the present study has potential implications for the use of multifaceted (combination) versus single-focus interventions in MCOs. According to Williams et al. (2008) and McDonald et al. (2002), studies that combined cognitive, behavioral, and educational components were more effective than single-focus interventions.[10,16] The present study intervention included a combination of behavioral and

educational components and was associated with positive results; however, if we were able to include more components, we might have been able to more significantly improve medication adherence.

This pharmacy quality initiative served as the baseline for establishing a model for future programs in the study health plan. A continuous evaluation of the literature will be done to make enhancements to this initiative. The program will be potentially modified in the near future to include an analysis of antihyperlipidemic medications and to increase the percentage of adherent patients. Additionally, a proactive approach of reminding patients to refill their prescriptions at the pharmacy may further improve adherence.

Limitations

First, the study sample was identified solely from pharmacy claims data. Therefore, some patients may have been mistakenly identified as nonadherent if the patient had another insurance carrier and used it for some of his or her prescriptions, participated in a community pharmacy generic drug discount program to obtain some medication, or the patient's treatment was changed for any reason during the calendar quarter. Without access to medical records or comparison with medical claims data, we could not restrict the intervention to patients with diagnoses of diabetes and hypertension. Therefore, some members may have been incorrectly identified as nonadherent if they were taking antihypertensive and antidiabetic medications for other purposes (e.g., migraine prophylaxis, polycystic ovarian syndrome, or situational anxiety) that may not require daily use.

Second, we initially assumed that the decreased medication nonadherence rates observed in this targeted sample were a result of our interventions. However, when the results of this initiative were shared with the Care Management Department, we learned that other quality improvement initiatives, disease management programs targeting a similar patient population, were ongoing at EmblemHealth and may have contributed to the reduction in nonadherence rates observed in our study. The disease management programs each targeted one disease state, and each program included more than one intervention. All of these programs had been in place for many years; however, the specific interventions changed from year to year. For example, for members with diabetes, the outreach included but was not limited to a health plan member and provider newsletter article, health coaching, and a mailing to PCPs reporting nonadherence to schedules such as hemoglobin A1c and eye exams. For members with hypertension, the major initiative focused on both blood pressure control and stroke prevention using the health plan member and provider newsletters, educational hotline for members, electronic messaging via emails to members, annual birthday card reminder to members for preventive screening, and others.

Third, the analysis was performed quarterly, and there was no longitudinal analysis (i.e., across calendar quarters). Therefore, if a member had received more than 90 days supply of a medication in 1 quarter (e.g., 2 fills of 90 days supply in a given calendar quarter), the member could have been deemed nonadherent if there were no fills in the subsequent calendar quarter. This situation would cause a false-positive nonadherence record for this member for this medication for the succeeding quarter. A member could also be deemed nonadherent in the following example: a member who had claims for HCT 30-day supply on January 1, January 30, February 28, March 30, April 30, May 30, and July 2 would have an MPR of 1.0 (100%) in Q1 and 0.67 (67%) in Q2 and would therefore be deemed nonadherent in Q2.

Fourth, our study was based on the assumption that if a prescription was filled at the pharmacy, then the member received the medication and took it, which may not have been the case. Fifth, although MPR is considered to have high predictive validity for medication nonadherence, it does not provide adequate information on the consistency of medication refill patterns.[32]

Sixth, several study-specific barriers included incorrect/outdated provider and member mail addresses in the study MCO's system that may have affected the successful delivery of information to the targeted PCPs and/or members. Additionally, some members had incorrectly listed PCPs; and although the study MCO uses the PCP-gatekeeper model, some members may not visit their PCPs regularly but instead visit specialists for their antihypertensive or antidiabetic medications.

Seventh, the objective of this study was to decrease the rate of medication nonadherence in the targeted population, and we did not measure the clinical or economic outcomes associated with nonadherence. Eighth, we did not compare the adherence rates for different classes of medications, although other studies have shown that adherence rates vary among different drug classes both in the same or different therapeutic areas.[20,33]

Finally, we did not calculate the administrative costs of conducting these interventions. However, after the initial setup, there was only 1 clinical pharmacist and 1 communication specialist working on this project, 4 times per year. We estimate that the average cost including both the labor costs (salary) and mailing costs was approximately $4,500 per quarter in the initial phase of the study for the PCP mailings and approximately $9,000 per quarter in the second phase of the interventions that involved both PCP and member mailings.

Conclusion

Over a nearly 2-year study period, a quality improvement initiative consisting of PCP letters with patient-specific information about nonadherence to antihypertensive and antidiabetic medications and general education letters sent to potentially nonadherent patients, was associated with decreased rates of medication nonadherence.

Authors

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DISCLOSURES

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Jing and Naliboff conceived and designed the study. The data were collected by Jing with the assistance of Naliboff, and the data were interpreted by all authors. The manuscript was written and revised primarily by Jing and Kaufman with the assistance of Choy and Naliboff.

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APPENDIX 1 Letter to Primary Care Physicians for Potentially Nonadherent Members

Date

<PCP First Name>, MD
<Address 1>
<Address 2>
<City>, <State>, <Zip Code>

Subject: 2nd Quarter 2009 Hypertensive, Diabetic and/or Antihyperlipidemic Medication Non-Adherence Report

Dear Dr. <PCP Last Name>:

The enclosed report identifies your HIP patients who had an interruption in either their antihypertensive or hyperglycemic medication during the second quarter of 2009. The interruption of treatment can be a result of a lapse in drugs or a change to an alternative product.

The data for this report is based on pharmacy claims data from the HIP Pharmacy Benefits Program as of June 30, 2009. Please note that not all HIP patients get their drugs (first fill and/or subsequent refills) through HIP. Therefore, the omission of their names from the enclosed report should not be used to validate their compliance with their medication treatment.

We ask that you discuss the importance of adhering to medication with your patients. The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) * describes the presence of multiple risk factors for coronary heart disease as "metabolic syndrome." Factors of metabolic syndrome are abdominal obesity, hyperlipidemia, hypertension and insulin resistance. Individuals who have both hypertension and diabetes, with or without hyperlipidemia, are at higher risk for cardiovascular events than individuals with only one of the conditions.

Successful treatment of hypertension and diabetes is directly associated with patient adherence to prescribed drugs. The enclosed report will help you evaluate if there is an adherence issue to medications that not only treat hypertension and diabetes, but also hyperlipidemia. We hope that this report helps you optimize patient care.

We appreciate your continued support in providing quality care to HIP members. If you have any questions, please contact Shu Jing, Clinical Pharmacy Case Manager, at **1-646-447-7284**.

Sincerely,

Chief Medical Director

Enclosure: Patient Non-Adherence Medication Report

*National Heart, Lung, and Blood Institute (May 2001). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III), executive summary (*NIH Publication No. 01-3670*). Washington, DC: U.S. Department of Health and Human Services. Available PDF: http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf.

APPENDIX 2 Member Letter Regarding Nonadherence

Date

<Member First Name> <Member Last Name>
<Address 1>
<Address 2>
<City>, <State>, <Zip Code>

Dear <Member First Name> <Member Last Name>:

HIP Health Plan of New York is dedicated to providing access to quality health care that will give you the best results. We see from our records that you recently have been seen by your doctor for high blood pressure and diabetes. We are writing to share with you how important it is to stay on top of your medications.

High blood pressure (or hypertension) has no warning signs and is often called the "silent killer." If left untreated, it can hurt arteries and even organs, like the heart and kidneys. Eventually, a person could end up with heart attacks, kidney failure and strokes. **Diabetes** is an illness in which the level of blood sugar (blood glucose) is above normal. If left uncontrolled, diabetes can raise your chances for many problems that can affect nearly every part of the body including the heart, eyes, kidneys, gums, and teeth.

Many drugs can help. They work in many different ways to lower high blood pressure and blood sugar level. No matter how they work, the most important way to make sure your treatment is successful is to take the medicines as prescribed by your doctor. Skipping doses without telling your doctor can lead to complications or even the illness getting worse. You should *never* stop taking your medication on your own before talking to your doctor.

Most of the time there is a reason for having skipped a dose. To help you stay on top of your drug schedule we have enclosed a list of possible reasons and their solutions. Also, remember to ask questions and talk to your doctor about your concerns. This is key to staying on top of your health. Only *you* know how you feel and what kind of questions you have.

At HIP, we are here to help you take care of your condition and you will be hearing from us from time to time with important information to help you have a healthy life.

Sincerely,

Chief Medical Director

Enclosure: How to Keep to Your Drug Schedule Flyer

Tips for Taking Your Medicine Regularly

Problem	Solutions
I always forget to take my medicine or order refills.	• **Set up a routine for taking your medicine.** Try mixing it in with your daily activity, such as brushing your teeth. • **Use technologies to remind you,** such as a cell phone alarm or a digital assistant alert. • **Let your pharmacy remind you.** Many pharmacies have programs that send you refills by mail or remind you to take your medicine.
My pills are too big, hard to swallow or taste bad.	• **Try cutting large pills in half.** Some pills are available at smaller sizes, so you can make up the dose with extra smaller pills. **Talk to your doctor before making any changes.** • **If you are taking generic drugs, talk to your doctor about switching to a drug from another manufacturer.** Other pills may have a different size or taste.
I have too many pills. It's too hard to keep track of them.	• **See if your medicine comes in a long-acting form, or if there is a combination medicine you can take to lower the pill count.** Talk to your doctor before making any changes. • **Use a daily or weekly pillbox** to organize your medicine.
I don't need to take my medicine because I feel fine. I feel sick when I take the pill.	• **Tell your doctor right away if you feel any discomfort or pain because of your drugs.** Your doctor can choose a different medicine for you. Don't stop taking your medicine without talking to your doctor first.
I can't read the medicine label. I don't understand the label or the directions.	• **Ask your pharmacist to explain how to take your medicine**. • **Request larger print or another language** on your medicine label.
I can't pay for my medicine.	• **Ask your doctor if your drugs come in a generic form** and if it's OK for you to switch. • **If your medicine does not have a generic form,** ask your doctor to choose a medicine for you that does come in a generic form. • **Call the pharmaceutical company.** You may be eligible for their drug assistant program. • **Try using a mail order pharmacy for some of your medicine**. This may save you money.
I don't understand why I need to take my medicine.	• **See your doctor regularly.** Form good relationships with your doctor and pharmacist. • **Don't be afraid to ask questions.** It's your doctor's job to help you understand why you need your medicine.