Pharmacotherapy After Myocardial Infarction: Disease Management Versus Usual Care

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Objective: To evaluate the effectiveness of a disease management (DM) program compared with usual care on utilization of and adherence to key evidence-based therapies (angiotensin-converting enzyme [ACE] inhibitors/angiotensin II receptor blockers [ARBs], β-blockers, and statins) after hospital discharge for patients with myocardial infarction (MI) in a managed care organization.

Study Design: Retrospective case-control cohort.

Methods: Members were included if they were 18 years of age or older and had any medical claims for hospitalization for MI, defined as *International Classification of Diseases, Ninth Revision, Clinical Modification,* codes 410.xx, from January 1, 2002, to December 31, 2002. The index date was the first date of discharge for members with an MI diagnosis. Members were categorized into the active group (automatically enrolled in the DM program) or the control group (not enrolled in the program because their employer group did not purchase the benefit). Pharmacy claims were obtained for 12 months after the index date for ACE inhibitors, ARBs, β-blockers, and statins.

Results: The study cohort included 250 members in the active group and 137 members in the control group. There were no statistical differences in utilization or time to first prescription fill of ACE inhibitors, ARBs, β-blockers, and statins between the DM and usual care groups. Adherence to each of these therapies, as measured by medication possession ratio, was not statistically different between the 2 groups.

Conclusion: Compared with usual care, participation in the DM program did not improve ACE inhibitor, ARB, statin, or β-blocker utilization or adherence in members post-MI.

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At a time when the cost of healthcare remains a priority, disease management (DM) programs have been advocated as a means of improving management and outcomes for many chronic diseases.[1,2] One such chronic condition, coronary heart disease (CHD), continues to be the number one cause of death for men and women in the United States, accounting for 1 of every 5 deaths in 2004. About 35% of the deaths due to CHD are caused by myocardial infarction (MI). The prevalence of MI is estimated to be around 7.9 million, with 157,000 deaths each year. Within the first year after MI, about 18% of men and 23% of women will die.[3] The cost to manage cardiovascular (CV) disease is large, with estimates of the direct and indirect costs of CV disease in the United States to be $431.8 billion in 2007. These statistics contribute to the popularity of CV DM programs among managed care organizations (MCOs). Independent evaluations of the effectiveness of DM programs are important to assess the value of these programs to MCOs.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have developed evidence-based treatment guidelines (2000-2001) for the secondary prevention of MI.[4,5] Recommended pharmacotherapy includes an antiplatelet agent, a β-blocker, an angiotensin-converting enzyme (ACE) inhibitor, and a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin). Additional research has documented a 75% reduction in all-cause mortality with a combination regimen of statins, aspirin, β-blockers, and ACE inhibitors.[6] Throughout this article, secondary prevention refers to the use of ACC/AHA guideline-recommended pharmacotherapies in patients after MI.

Despite the strong evidence that using these medications decreases the risk of CV complications and death, audits of current practice often reveal suboptimal control of CV risk factors and underuse of antiplatelet agents, β-blockers, and lipid-lowering agents in patients with CHD.[7-9] One US study that evaluated patients with coronary artery disease found rates of β-blocker use of 40% in 2001.[8]

The effectiveness of pharmacologic treatment is directly related to the physician's choice of therapy and patient adherence with the given medication regimen. Simpson et al found that if physicians prescribed medications after MI according to evidence-based guidelines, patients were more likely to adhere to these prescriptions in the 1-year study period.[7] After a patient has sustained an acute

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MI, failure to comply with even some aspects of the recommended regimen can lead to complications, rehospitalizations, or mortality. Horwitz et al found that patients who did not adhere well to their treatment regimen (defined as taking less than 75% of the prescribed medication) were 2.6 times more likely than those with higher adherence to die within a year follow-up after an MI.[10] Therefore, early intervention that optimizes the patient's treatment regimen and adherence to that regimen decreases risk for further complications and death.

Based on the published literature, there is room to improve post-MI drug therapy management and decrease overall CV morbidity and mortality. DM programs aim to do just that. A meta-analysis of 12 clinical trials published by McAlister et al showed that DM programs improved processes of care (patients were more likely to be prescribed efficacious drugs) and there was a reduction in hospital admissions for patients with CHD.[11] However, the design of each study varied with different endpoints, there were no measurements of medication adherence, and/or many of the results were self-reported. Ofman et al examined the clinical and economic impact of 6 trials of DM programs[12] and found that only 1 study reported a decrease of reinfarction rates,[13] and there was no improvement in provider adherence to guidelines in the trials.

Several different measures can be used to evaluate CV DM programs, such as decreasing the rate of reinfarction, improving quality of life, or clinical markers that have shown benefit in reducing CV morbidity or mortality. One such surrogate marker is use of secondary prevention regimens. These endpoints are easily measured and analyzed by MCOs with access to administrative, medical, and pharmacy claims data.

The objective of this retrospective, controlled study was to evaluate the effectiveness of a DM program in increasing provider adherence to recommended post-MI CV pharmacotherapy, as well as increasing patient adherence to these regimens. We hypothesized that members enrolled in the CV DM program would be more likely to be prescribed recommended secondary prevention regimens and to adhere to these regimens.

METHODS

Background of Disease Management Program

The MCO outsourced the CV DM program to a vendor whose primary function was DM services. The CV DM program began at the MCO in August 2001 to assist members who were at increased risk of developing complications of heart disease. Only members whose employer had purchased the DM benefit were eligible to participate. Participation was based on criteria set by the DM service and relied on the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes in medical claims data. One of the qualifying *ICD-9-CM* codes was MI (410.xx). All members with this *ICD-9-CM* code in their medical claims (and whose employer had purchased the DM benefit) were automatically enrolled into the program. Members were recruited into the program on a rolling basis, typically within a month of discharge. The vendor promised to achieve several goals such as improvement in the use of secondary prevention pharmacotherapy and medication adherence, with its care management team providing specific information on the importance of taking prescribed medications.

Like other DM programs, this program was primarily nurse managed and relied heavily on telephone and mail communication with members. The initial assessment and follow-up assessment from the DM program occurred via telephone. One-time mailings included the welcome letter and disease-specific kits. Periodic mailings included patient-specific goals, disease-specific information, and a quarterly newsletter. The nurse had access to pharmacy claims and could see whether patients were on secondary prevention drugs and were refilling their prescriptions on time. Prescription claims information was verified by telephone. If patients were not on all of the secondary prevention pharmacotherapies, their physicians received a letter asking them to consider using these therapies for their patients.

Participation in the program was voluntary and there were no out-of-pocket costs to the members. Members who chose not to participate had to actively opt out of the program, or they would have continued to receive correspondence from the DM service.

Member Cohort

Medical and pharmacy claims data were obtained from a MCO located in the Mid-Atlantic States. This MCO had approximately 3.4 million members with medical benefits and 1.2 million members (35.3%) with pharmacy benefits. The study cohort was obtained from the population of members with continuous enrollment within the same commercial plan from January 1, 2002, through December 31, 2003, for medical and pharmacy benefits. Continuous enrollment within the same plan meant that if members switched from 1 plan to another within the MCO, they were not included. Members with a primary, secondary, or tertiary *ICD-9-CM* code for MI (410.xx) in their hospital discharge claims from January 1, 2002, to December 31, 2002, were obtained from medical claims data. The index date of the event (MI) was the member's discharge date. Members were included if they were between the ages of 18 and 64 years on their index date.

Table 1. Study Terms and Definitions

Term	Definition
Utilization	At least 1 pharmacy claim in the first year after the index date
Time to first fill	Number of days until the first prescription claim after the index date
Medication possession ratio	Percentage of time, calculated by adding the total days supply for all pharmacy claims within the class and dividing by the total possible days supply of prescription fills from the date when the prescription was originally dispensed; the denominator of total possible days supply consisted of the number of days from the first fill until the last fill, plus days supply of last fill

Patients were excluded if they were pregnant (extracted from *ICD-9-CM* codes), or if they actively opted out or were enrolled in the DM program for less than 1 month. Note that members aged 65 years and older on their index date were not included because they were no longer eligible for DM services once they were eligible for Medicare.

Members were placed into either the active group (patients automatically enrolled in the DM program because their employer had purchased the benefit) or the control group (members whose employer did not purchase the DM benefit) by linking medical claims data with enrollment data from the DM service. Baseline characteristics included CHD risk factors, CV procedures (as proxy for severity), and respiratory diseases (as proxy for contraindications to selected secondary pharmacotherapy); these were retrieved using *ICD-9-CM* codes from January 1, 2001, to December 31, 2001. Members' sex and age on the index date also were determined.

Pharmacy claims data were captured for all ACE inhibitors, β-blockers, angiotensin II receptor blockers (ARBs), statins, and combination products containing drugs from these classes from the member's index date to 365 days after the index date. This ensured that each member had 1 year of prescription data to evaluate. Although ARBs were not mentioned in the guidelines available during the study period, we included them as part of secondary prevention for patients intolerant to ACE inhibitors. Utilization (measured by at least 1 pharmacy claim in a class within 1 year from the index date) was used as a proxy for provider prescribing according to accepted guidelines. The medications were not necessarily taken concomitantly, but showed that a prescriber placed the member on the recommended therapy. The time to the first fill also was analyzed. In addition, the study aimed to assess the impact of the DM program on members' medication adherence to the prescribed secondary prevention therapy.

Table 1 lists the terms and definitions used. Adherence was evaluated by examining the medication possession ratio (MPR).[14] The MPR represents the percentage of time that a member "possesses" medication. It was calculated by adding the total days supply for all pharmacy claims within the class and dividing by the total possible days supply of prescription fills from the date when the prescription was originally dispensed. The denominator of total possible days supply consisted of the number of days from the first fill until the last fill, plus days supply of last fill. For example, a patient had an MI on June 26, 2002 (index date), and had 4 prescription refills for a statin within 365 days from the index date: first on July 1, 2002, for a 30-day supply; second on August 1, 2002, for a 90-day supply; third on December 20, 2002, for a 90-day supply; and fourth on March 31, 2003, for a 30-day supply. The numerator for the MPR calculation would be 30 + 90 + 90 + 30 = 240 days. The denominator would be the number of days between the first fill on July 1, 2002, and the last fill plus days supply, April 30, 2003 (March 31, 2003 + 30 days), which is 304 days. The MPR for this patient is 240/304 or 0.79. We chose to truncate the MPR at 1.0 to prevent overestimation of MPR (eg, last fill greater than the days supply remaining in the evaluation period). Medications within the same class were considered together. For example, if a patient switched from one ACE inhibitor to another, both were included for MPR calculations. In addition, the days supply of the last prescription of the first ACE inhibitor was truncated to coincide with the fill date of the second ACE inhibitor.

The data set contained the following fields: unique de-identified patient number, patient sex, patient age on index date, prescription number, date filled, drug name, drug strength, and number of paid days supplied. All data conformed to Health Insurance Portability and Accountability Act patient privacy standards, and the data set was delivered to the researchers with de-identified patient information. The protocol was approved by the University of Maryland institutional review board.

Statistical Analysis

Descriptive analysis was reported for sociodemographic and clinical characteristics of the active and control groups. Categorical values such as demographic data and utilization were compared with the χ^2 test. The Mann-Whitney test and

the 2-tailed Student *t* test were used to determine differences in the lengths of time to the first fill and the MPR, respectively. *P* values of <.05 were considered significant.

RESULTS

In 2002, 387 (48%) of members with a discharge diagnosis of MI in 2002 met the inclusion and exclusion criteria, with 250 (65%) members in the active group and 137 (35%) members in the control group. The mean age was 53.2 ± 7.2 years, and there were 3 times as many men as women. Both groups were similar with regard to baseline characteristics, except for prevalence of hypertension (Table 2). Patients in the control group were more likely to have hypertension (66.0% in the active group vs 77.4% in the control group, *P* = .02).

Table 2. Baseline Characteristics and Patient Demographics[a]

Characteristic	Active Group (n = 250)	Control Group (n = 137)	*P*
Male	191 (76.4)	104 (75.9)	.914
Age, mean ± SD, y	53.0 ± 7.3	53.6 ± 7.1	.45
Asthma	22 (8.8)	10 (7.3)	.61
Cerebrovascular disease	11 (4.4)	11 (8.0)	.14
Coronary artery bypass graft	95 (38.0)	51 (37.2)	.88
Chronic heart failure	66 (26.4)	35 (25.5)	.86
Chronic obstructive pulmonary disease	35 (14.0)	24 (17.5)	.36
Diabetes mellitus	57 (22.8)	41 (29.9)	.12
Hypercholesterolemia	194 (77.6)	117 (85.4)	.07
Hypertension	165 (66.0)	106 (77.4)	.02
Obesity	33 (13.2)	28 (20.4)	.06
Peripheral vascular disease	22 (8.8)	8 (5.8)	.30

[a]Values represent number (percentage) unless otherwise specified.

There were no statistical differences in utilization of ACE inhibitors, ARBs, β-blockers, and statins between the active and control groups (Table 3). A majority of the patients had at least 1 prescription in each of these classes. Angiotensin-converting enzyme CE inhibitors had the lowest rate of utilization (64.8% for the active group vs 66.4% for the control group, *P* = .75) and statins had the highest rate of utilization (83.2% for the active group vs 83.2% for the control group, *P* = 1.00). Overall utilization of the combination regimen of ACE inhibitors, β-blockers, and statins occurred in only about 50% of the members in each group; again, there was no statistical differences between the groups. When ARBs were considered as an alternative to ACE inhibitors in the combination regimen, use increased about 5 percentage points in both groups.

The mean time to first fill was within 1 month of discharge for ACE inhibitors, β-blockers, and statins in both the active and control groups (Table 4). However, the mean time to first fill for ARBs was considerably longer, with means in the 3- to 4-month range. There were no differences in the mean time to first fill between members that participated in the DM program and members in the control group. Based on the median data, at least half of the members filled their prescriptions within a couple of days after the index date. There were no differences between the active and control groups for time to first fill for any of the drug classes.

All of the MPRs for each of the drug classes were between 70% and 80% (Table 5). There were no statistically signifi-

Table 3. Utilization of Secondary Pharmacotherapy in the First Year After Myocardial Infarction[a]

Drug Class	Active Group (n = 250)	Control Group (n = 137)	*P* (χ^2 Test)
ACE inhibitor	162 (64.8)	91 (66.4)	.75
β-Blocker	204 (81.6)	114 (83.2)	.69
Statin	208 (83.2)	114 (83.2)	1.00
ARB	31 (12.4)	20 (14.6)	.55
ACE inhibitor + β-blocker + statin	127 (50.8)	72 (52.6)	.74
ACE inhibitor or ARB + β-blocker + statin	139 (55.6)	80 (58.7)	.50

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.
[a]Values represent number (percentage).

Table 4. Time to First Fill After Hospital Discharge of Patients With Myocardial Infarction

	No. of Days				
	Active Group (n = 250)		Control Group (n = 137)		
Drug Class	Mean ± SD (Median)	Range	Mean ± SD (Median)	Range	*P*
ACE inhibitor	23.4 ± 54.6 (2)	0-340	33.7 ± 66.1 (1)	0-307	.93
β-Blocker	19.2 ± 54.1 (1)	0-351	19.4 ± 48.7 (1)	0-325	.48
Statin	21.7 ± 47.5 (1.5)	0-263	30.6 ± 57.6 (2)	0-294	.21
ARB	122 ± 111 (84)	0-334	94 ± 107 (53)	0-322	.30

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

cant differences between the active and control groups with regard to medication adherence.

DISCUSSION

Disease Managment programs have been advocated as an effective strategy for managing high-cost chronic illnesses. They have become increasingly popular as MCOs strive to stay competitive by managing costs while providing the highest level of care to their members.[1,2,12] This real-world study failed to show a difference in medication utilization and adherence to secondary prevention pharmacotherapy for members enrolled in a CV DM program compared with members receiving usual care in the first year after an MI. Data in the literature state that this period is critical for the initiation and continuation of secondary prevention medications. This study did not show the positives outcomes seen in some previous studies.[11,13,15] However, many of the previous studies were not controlled and relied on patient recall to determine medication adherence. The effectiveness of these DM programs was scrutinized mainly because specific outcomes were not delineated, data were irretrievable or proprietary, resources were limited for conducting research, and organizations might be reluctant to publicize negative results.[2,12,16]

Although there were no statistical differences between the CV DM and usual care groups, the usual care group had at least as good as and most often greater actual numbers for utilization and MPR. Overall, the majority of patients were receiving at least 1 of the recommended pharmacotherapies, but about half of them were not receiving appropriate triple regimens. The adherence rates were in the 70% range, which is slightly below the industry standard of an MPR of at least 80%.

The short median and mean times to first fill implies that members were filling their medications within days of discharge from the hospital after an MI. Because it took about a month to automatically enroll patients, the real comparisons of the CV DM program and usual care are (1) medication utilization by the remaining 50% of members who did not fill prescriptions early and (2) adherence using MPR as a proxy. The only difference found between the groups was that the rate of hypertension was higher in the control group. This may have biased the results in favor of increased utilization and adherence with ACE inhibitors and/or β-blockers in the control group.

Unlike our study, a published report on a DM program in post-MI patients revealed an increase in medication adherence. A large open-access HMO partnered with a national provider of DM services and conducted a telephone-based case management program run by nurses designed for post-MI patients.[17] Specific outcomes included modification of lifestyle behaviors, adherence with therapy, and inpatient and emergency room utilization. Using self-reported adherence, the study found a 36% increase in adherence to β-blockers as well as a 52% increase in use of lipid-lowering agents after 12 months. Compared with a control cohort, claims for pharmacy utilization (cost) and overall costs for the active group were significantly reduced. Intuitively,

Table 5. Medication Possession Ratio for Secondary Pharmacotherapy in the First Year After Myocardial Infarction[a]

	Active Group (n = 250)	Control Group (n = 137)	
Drug Class	Mean ± SD	Mean ± SD	*P* (2-Sample *t* Test)
ACE inhibitor	70.7 ± 30.5	75.6 ± 30.0	.22
β-Blocker	72.8 ± 28.9	74.8 ± 26.9	.52
Statin	73.1 ± 26.5	78.4 ± 23.9	.065
ARB	76.7 ± 26.9	79.5 ± 30.0	.73

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.
[a]Values represent medication possession ratio as a percentage.

one would suspect that pharmacy costs would increase initially because of the increase of medication utilization, but this was not observed in the study.

Managed care organizations are in a unique position to conduct outcomes analyses. It is imperative that outcomes research continue in CV DM programs, as the costs to manage these patients remain high[18] and the resources spent to support such programs can be utilized elsewhere where the evidence shows consistent positive outcomes. Survey responses in the study by Fitzner et al[19] showed that MCOs who sponsor such programs consider improving clinical outcomes and reducing costs to be a priority; however, the majority of these same respondents (68%) occasionally or never requested outcomes data to ensure that these programs met their goals.[18]

The results of this study should be interpreted with some caution because of certain limitations in the dataset. Our dataset relied heavily on *ICD-9-CM* coding in identifying patients with MI. We have no way to evaluate the accuracy of the coding, which may be incomplete or inaccurate.

We obtained pharmacy claims data that indicate that the member filled the medication. Although filling a prescription does not ensure that members are actually taking the medication, there are data suggesting that analyzing pharmacy refills claims is an accurate measure of adherence to these regimens.[20] We examined utilization of combination therapy of ACE inhibitors or ARBs plus β-blockers and statins, which translates into at least 1 prescription filled for each medication within the 1-year study period. However, these fills do not imply that the medications were taken concomitantly. In addition, there are limitations inherent to the comparison: the active group had 65% of the study cohort and the control group had only 35%.

The employer group had to purchase the DM benefit, so there may be differences between the members who had this option (active group) and the members whose employer did not purchase the DM option (control group). Although there were few differences in the characteristics measured (Table 2), there may have been differences in other variables that were not measured. Medical and medication histories prior to the index date were not extracted. Therefore, it is unknown whether members in either group had a prior history of CHD or were dispensed secondary medications prior to their index date. This unknown factor may have resulted in inherent bias, as patients with a previous history of CHD may have been more likely to be on secondary prevention therapies. Lastly, although there was no benefit with respect to surrogate markers of drug use and adherence, it is unknown whether the DM program may have benefited members in other ways that were not measured in this study.

Take-away Points

This study provides real-world analysis of the effectiveness of a disease management (DM) program compared with usual care on utilization of secondary prevention therapies in a managed care organization (MCO).

- There has been very little published research using appropriate methodology to document the value of DM programs.
- Based on 3 measures, utilization, medication possession ratio, and time to first fill of the secondary prevention pharmacotherapies, there appeared to be no benefit of the DM program compared with usual care.
- The value of DM programs needs to be carefully evaluated when MCOs consider using them.

CONCLUSION

In our population, a CV DM program was not more effective than usual care in improving utilization of ACE inhibitors, statins, or β-blockers, or adherence in members post-MI. It is imperative that purchasers of DM services continue to monitor for improvement when providing these services, so that monetary and personnel resources are allocated appropriately in our high-cost healthcare environment.

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