RESEARCH

Use of Secondary Prevention Drug Therapy in Patients With Acute Coronary Syndrome After Hospital Discharge

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ABSTRACT

BACKGROUND: Acute coronary syndrome includes life-threatening clinical conditions ranging from unstable angina to non-Q-wave myocardial infarction and Q-wave myocardial infarction that are a major cause of emergency medical care and hospitalization in the United States. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the management of patients with unstable angina and non-ST-segment elevation myocardial infarction (2002-2004) recommend (1) angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for ACE inhibitor intolerance, (2) beta-blockers, and (3) statins for long-term treatment of patients after an acute coronary event.

OBJECTIVE: To examine rates of use of 3 key evidence-based drug therapies (ACE inhibitors/ARBs, beta-blockers, and statins) after hospital discharge for patients with acute coronary syndromes (ACS).

METHODS: The study cohort was identified using medical claims from commercial health plans within a managed care organization located in the Mid-Atlantic states, with approximately 3.4 million members with medical benefits of whom 1.2 million members (35.3%) had pharmacy benefits. Members were included if they were (1) aged ≥ 18 years, (2) continuously enrolled with the same commercial plan from January 1, 2003, through December 31, 2005, (3) had any medical claims for hospitalization for ACS defined by *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 410.xx (acute myocardial infarction) or 411.1 (intermediate coronary syndrome) during the sample identification period from July 1, 2003 through June 30, 2004, and (4) had no medical claims for ACS hospitalizations from January 1, 2003, through June 30, 2003, in any of 10 diagnosis fields on an inpatient hospital claim. Pharmacy claims for ACE inhibitors, ARBs, beta-blockers, and statins were obtained for 18 months following each index date, defined as the earliest ACS diagnosis date during the identification period. Utilization was defined as the member having at least 1 pharmacy claim within each class from index date to 3 months post-index date. Five time periods were examined to assess therapy: -180 to 0 days (6 months prior), 0 to 90 days (3 months), 0 to 180 days (6 months), 0 to 365 days (12 months), and 0 to 548 days (18 months) following the index date. ACE inhibitors and ARBs were considered together (i.e., a patient had to have at least 1 pharmacy claim for an ACE inhibitor or an ARB). Logistic regression analyses were used to predict use of the 3 drug classes for patients with different clinical (diagnosis and prior use) and demographic (sex and age) characteristics.

RESULTS: The study cohort included 1,135 patients (0.27% of 424,526 continuously enrolled members) with ACS as defined by ICD-9-CM codes in medical claims from July 1, 2003, to June 30, 2004. Nearly 65% of the sample patients were men (n = 734 men and n = 401 women), with a mean (standard deviation [SD]) age of 63.8 (SD 13.1) years. Of the 1,135 members with ACS, 588 (51.8%) had at least 1 pharmacy claim for an ACE inhibitor or ARB, 725 (63.9%) for a beta-blocker, and 710 (62.6%) for a statin during the 3-month follow-up period; receipt of at least 1 prescription in all 3 classes was found in 339 (29.9%) of patients. Patients who were aged < 45 years, 65-79 years, and ≥ 80 years were significantly less likely than patients aged 45-64 years to receive statins ($P < 0.05$). In addition, patients who were aged ≥ 80 years were significantly less likely to receive ACE inhibitors/ARBs ($P = 0.003$), beta-blockers ($P < 0.001$), or all 3 classes ($P = 0.002$). Women were less likely than men to receive statins ($P = 0.004$) and all 3 drug classes ($P = 0.012$). Patients with intermediate coronary syndrome were significantly less likely than those with acute myocardial infarction to receive any of the study drugs ($P < 0.001$). Those patients who had used ACE inhibitors/ARBs, beta-blockers, statins, and all 3 drug classes during the 6 months prior to the index diagnosis of ACS were more likely than those without prior use (odds ratios of 12.2, 9.4, 8.3, and 4.9, respectively, $P < 0.001$) to have these medications continued after ACS diagnosis.

CONCLUSION: At 3 months following the index ACS hospitalization, the majority of the patients were not receiving the 3 guideline medication therapies. ACS patients with intermediate coronary syndrome and those aged 80 years or older were less likely to be receiving any of the 3 therapies, and women were less likely than men to receive statin therapy.

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What is already known about this subject

- There is evidence of decreased cardiovascular morbidity and mortality from secondary prevention therapies (ACEIs or ARBs, beta-blockers, and statins) alone and in combination in patients after acute coronary syndromes (ACS).
- Previous research has documented rates of use of the following secondary prevention therapies in patients with ACS at hospital discharge: 57% to 81% for ACE inhibitors, 71% to 79% for beta-blockers, and 35% to 91% for statins.

What this study adds

- In an analysis of real-world use of secondary prevention therapies in the 90 days following a hospitalization for ACS, we found exposure rates of 52% for ACE inhibitors or angiotensin II receptor blockers (ARBs), 64% for beta-blockers, and 63% for statins; these rates are lower than those reported in some studies.
- Only 30% of the patients had at least 1 pharmacy claim in all 3 key drug classes in the 90-day period following the ACS hospitalization.
- At 3 months after discharge, patients with intermediate coronary syndrome and those aged 80 years or older were less likely to be receiving any of the 3 therapies, and women were less likely than men to receive statin therapy.
- During 18 months of follow-up, 65% of ACS patients had at least 1 pharmacy claim for an ACE inhibitor or ARB, 76% for a beta-blocker, 77% for a statin, and 46% for all 3 medication classes.

Note: *A commentary on the subject of this article appears on pages 312-15 of this issue, and an editorial appears on pages 316-17.*

Cardiovascular (CV) disease continues to be the number one cause of morbidity and mortality in the United States.[1] Unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction are life threatening CV disorders that are major causes of emergency medical care and hospitalizations in the United States.[2,3] Guidelines recommend that physicians aggressively manage these diseases to reduce the risk of morbidity and mortality in these patients. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the management of patients with unstable angina and non-ST-segment elevation myocardial infarction recommend angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, statins, and antiplatelet therapy for long-term treatment of patients after an acute coronary event.[2,3]

Numerous clinical trials have demonstrated the value of long-term management with ACE inhibitors, beta-blockers, statins, and aspirin (ASA) in reducing the risk of CV events and mortality in patients after acute coronary syndromes (ACS).[2,3] Unfortunately, there is evidence that these therapies are neither consistently prescribed when appropriate nor adhered to by patients.[4-7] It has been shown that use of medications after discharge from hospital is enhanced when the prescription is written at discharge, but it is not known whether long-term adherence is improved.[8,9] The present study was conducted to evaluate the use of guideline-recommended pharmacotherapy for patients within a managed care organization (MCO) who have had an ACS.

Study Objectives

The study objectives were to examine (1) rates of exposure to the 3 key evidence-based therapies (ACE inhibitors/ARBs, beta-blockers, and statins) after hospital discharge for patients with ACS and (2) clinical and demographic factors associated with exposure to these drugs.

Methods

Study Population

Medical and pharmacy claims data were obtained from an MCO located in the Mid-Atlantic states with approximately 3.4 million members with medical benefits, of whom 1.2 million members (35.3%) had pharmacy benefits. The study cohort was obtained from the population of members with continuous enrollment within the same commercial plan from January 1, 2003, through December 31, 2005, for medical and pharmacy benefits (N=424,526). Continuous enrollment within the same plan meant that if members switched from one plan to another within the MCO, they were excluded. Members were included in the cohort if they had at least 1 medical claim for hospitalization from July 1, 2003, through June 30, 2004, with diagnosis of ACS using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes of 411.1 (intermediate coronary syndrome) and 410.xx (myocardial infarction [MI]). The health plan's database included a separate file consisting of all inpatient hospitalizations, identified using a combination of room and board revenue codes with length-of-stay (difference between the first and final dates of service) of at least 1 day. In the medical claims database, each patient had up to 10 diagnosis codes for each hospitalization. Patients were included if the ACS code was anywhere within these 10 diagnosis fields; 76.7% of ACS diagnoses were primary, and 88.8% were primary, secondary, or tertiary. Each patient was assigned an index date, which represented the first date of one of the above diagnoses from July 1, 2003, through June 30, 2004. Patients were excluded if they had any inpatient admissions for ACS diagnoses from January 1, 2003, through June 30, 2003 (n=73), or were aged younger than 18 years (n=1) on their index date (Figure).

The medical claims dataset contained the following fields: unique de-identified patient number, ICD-9-CM codes for ACS hospitalizations, date of hospital discharge, patient age (as of index date), and patient sex. The pharmacy claims dataset contained the following fields: unique de-identified patient number, patient sex, prescription number, date filled, drug name, drug strength, MCO paid quantity, and number of paid days supplied. All data conformed to Health Insurance Portability and Accountability Act (HIPAA) patient privacy standards, and the dataset was delivered to the researchers with de-identified patient information. The University of Maryland Institutional Review Board assigned exempt status to the research protocol.

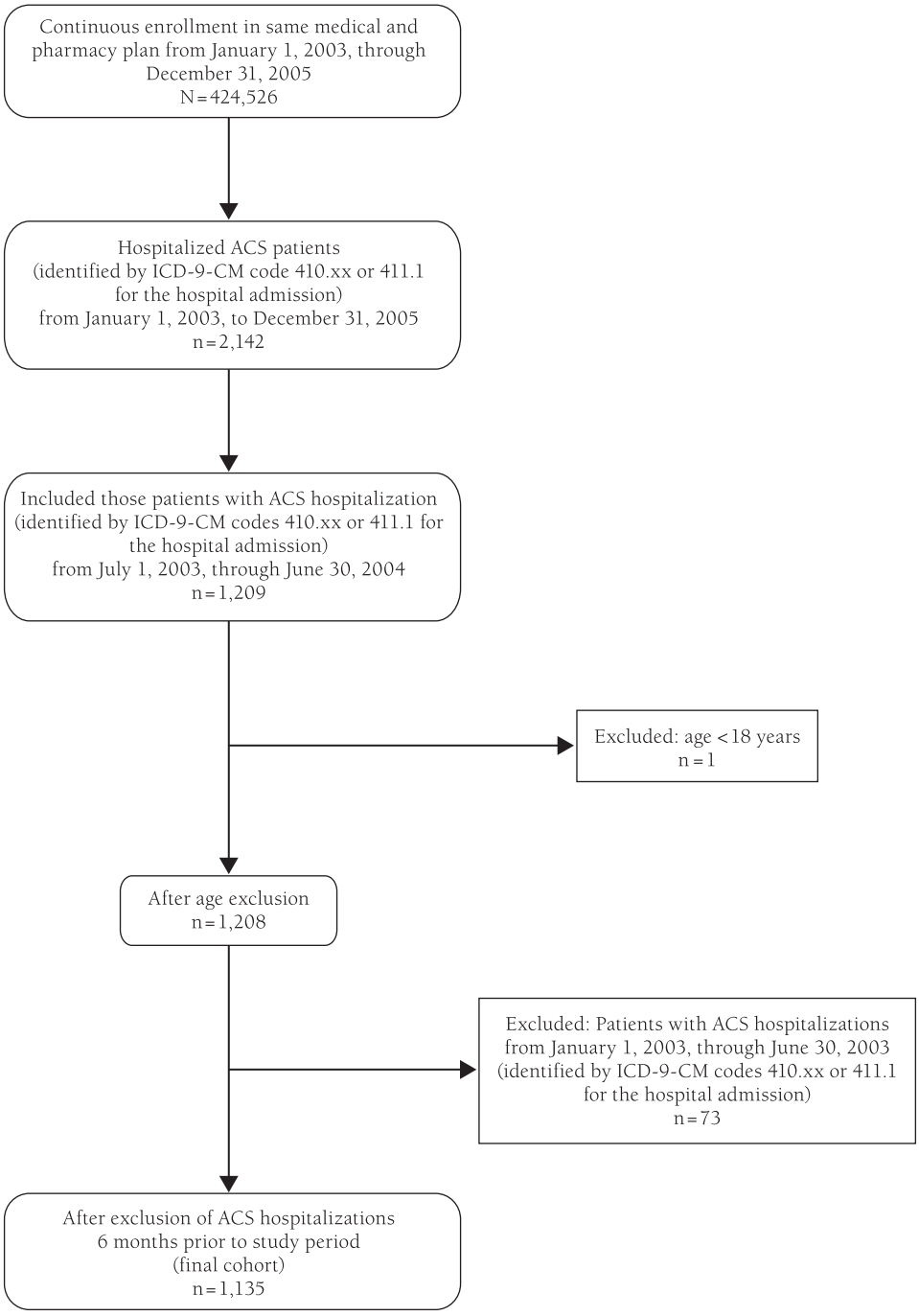
Pharmacy Claims Analysis

Pharmacy claims for ACE inhibitors, ARBs, beta-blockers, and statins were identified by drug name (Appendix) from 6 months before through 18 months following each patient's index date. Utilization was defined as having at least 1 pharmacy claim for any agent in a class during the first 3 months following the index date (defined as day 0). Five time periods were examined to assess use of therapy: -180 to 0 days (6 months prior), 0-90 days (3 months), 0-180 days (6 months), 0-365 days (12 months), and 0-548 days (18 months) following index date. ACE inhibitors and ARBs were considered together (i.e., a patient was considered to have received the target drug therapy if there was at least 1 pharmacy claim for an ACE inhibitor or an ARB). Patients were defined as receiving treatment per guidelines if they had at least 1 pharmacy claim for (1) an ACE inhibitor or ARB, (2) a beta-blocker, and (3) a statin, filled at any time within 3 months following the patient's index date.

Pharmacy Benefits

There was some variation in the design of pharmacy benefits for these MCO members during the 3-year time period of this study from January 1, 2003, through December 31, 2005. However, the predominant pharmacy benefit plan during the period of this study was a 3-tier copayment plan with a mail-order pharmacy option and copayments per 30-day supply of $10 for generic

FIGURE 1 Population of Approximately 1.2 Million Members



ACS=acute coronary syndromes; ICD-9-CM= International Classification of Diseases, Ninth Revision, Clinical Modification.

TABLE 1 Patient Characteristics and Key Findings

Cohort of Members With Acute Coronary Syndromes	n = 1,135
Male, number (%)	734 (64.7)
Age in years, number (%)	
<45	40 (5.5)
45-64	418 (56.9)
65-79	208 (28.3)
≥80	68 (9.3)
Female, number (%)	401 (35.3)
Age in years, number (%)	
<45	24 (6.0)
45-64	161 (40.1)
65-79	111 (27.7)
≥80	105 (26.2)
Mean age [SD] range, years	63.8 [13.1]
	27-96
Index diagnosis, number (%)	
411.1 Intermediate coronary syndrome	846 (74.5)
410.xx Acute myocardial infarction	289 (25.5)
Initial	267 (92.4)
Subsequent	10 (3.5)
Unspecified	12 (4.2)
Health plan, number (%)	
HMO	207 (18.2)
PPO	322 (28.4)
POS	192 (16.9)
Traditional indemnity	303 (26.7)
Unknown	111 (9.8)
Number (%) receiving any of the 3 drug therapies in guidelines[a] within 3 months of index diagnosis	974 (85.8)

[a] *American College of Cardiology/American Heart Association (ACC/AHA) 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction (2002) and ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction (2004).*[2,3]

HMO = health maintenance organization; POS = point-of-service; PPO = preferred provider organization.

drugs, $20 for preferred brand drugs, and $35 for non-preferred brand drugs. A 90-day supply could be obtained from community pharmacies or mail order for copayments of $20, $40, $70; fewer than 5% of members used mail order. No Medicare+ Choice (Medicare Advantage) plans were offered by the MCO during the study period; 68.5% of Medicare-eligible members (n = 38,749) had the same pharmacy benefits as other commercial members, and 31.5% (n = 17,812) had a senior pharmacy benefit program that provided coverage up to $1,100 in annual expenditures and then discounted price (i.e., 100% copayment) after $1,100 maximum annual benefit.

Statistical Analysis

Statistical analysis included calculations of percentages for discrete variables and means and standard deviations (SD) for continuous variables. Logistic regression analyses were used to predict use of each of the 3 drug classes (at least 1 claim in 3 months of follow-up) for patients with different clinical (i.e., diagnosis and prior use) and demographic (i.e., sex and age) characteristics. Statistical significance was set at an accepted alpha ($P<0.05$). Statistical analysis was performed with Minitab Statistical Software (Minitab, Release 13 Minitab, Inc., State College, Pennsylvania).

Results

Member Demographics

The study cohort included a total of 1,135 patients (0.27% of the member population with continuous enrollment in medical and pharmacy plans) with ACS as defined by ICD-9-CM codes from medical claims data from July 1, 2003, to June 30, 2004. Nearly 65% of the sample patients were men (n = 734 men and n = 401 women), with a mean (SD) age of 63.8 (13.1) years (Table 1). The majority of members were aged between 45 and 64 years (n = 579, 51.0%) followed by those aged 65-79 years (n = 319, 28.1%), those aged 80 years and older (n = 173, 15.2%), and those aged 44 or younger (n = 64, 5.6%). There were disproportionate differences in sex by age category. Proportionately fewer women were aged between 45 and 64 years (40.1%) than were men (56.9%), and more women (26.2%) than men (9.3%) were aged 80 years or older. Almost 75% of the cohort had intermediate coronary syndrome. Of the remaining 25% with acute MI, 92.4% were coded as having an initial MI. PPO and traditional indemnity enrollees constituted 28.4% and 26.7% of the sample, respectively. About 10% of the cohort had an unknown health plan, which included members with a discount program.

Drug Use for Secondary Prevention

Of the 1,135 members with acute coronary syndromes, 588 (51.8%), 725 (63.9%), and 710 (62.6%) patients had at least 1 pharmacy claim for an ACE inhibitor/ARB, beta-blocker, and statin, respectively during the first 90 days post index (Table 2). Of the patients who received therapy at any time during 18 months of follow-up, approximately 80% had their first claim within the first 90-days post-index date. For example, the percentage of study patients with at least 1 pharmacy claim was 79.6% (588 at 90 days/739 at 18 months) for ACE inhibitor/ARBs, 84.6% for beta-blockers, and 81.7% for statins. Of all study patients, 397 (35.0%), 412 (36.3%), and 429 (37.8%) patients had claims for ACE inhibitors or ARBs, beta-blockers, and statins, respectively, both during the 6 months prior to and within the 3 months after ACS discharge. These patients accounted for 67.5% (397/588), 56.8% (412/725), and 60.4% (429/710) of patients with at least 1 pharmacy claim for ACE inhibitors/ARBs,

TABLE 2 Utilization of Secondary Prevention Drug Therapies in Patients With ACS (N = 1,135) 6 Months Prior and After 3, 6, 12, and 18 Months of Follow-up[a]

	ACE Inhibitor or ARB	Beta-blocker	Statin	All 3 Drugs
Post ACS discharge use, n (%)				
3 months	588 (51.8)	725 (63.9)	710 (62.6)	339 (29.9)
6 months	666 (58.7)	785 (69.2)	787 (69.3)	426 (37.5)
12 months	708 (62.4)	834 (73.5)	834 (73.5)	484 (42.6)
18 months	739 (65.1)	857 (75.5)	869 (76.6)	525 (46.3)
Pre ACS discharge use, n (%)				
6 months prior	495 (43.6)	486 (42.8)	510 (44.9)	210 (18.5)
Post ACS discharge use for patients with prior use, n (%)[b]				
3 months	397 (80.2)	412 (84.8)	429 (84.1)	128 (61.0)
Post ACS discharge use for patients without prior use, n (%)[c]				
3 months	191 (29.8)	313 (48.2)	281 (45.0)	211 (22.8)

[a] *Number (%) with at least 1 pharmacy claim in the time periods indicated:*
6 months prior ACS = 6 months before index date through index date
3 months post ACS = index date through 3 months after index date
6 months post ACS = index date through 6 months after index date
12 months post ACS = index date through 12 months after index date
18 months post ACS = index date through 18 months after index date

[b] *As a percentage of patients with use of the drug class in the 6 months prior to the index ACS hospitalization.*

[c] *As a percentage of patients without use of the drug class in the 6 months prior to the index ACS hospitalization.*

ACE = angiotensin-converting enzyme; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker

beta-blockers, and statins, respectively, within 3 months after ACS discharge (Table 2). A little less than one half of the patients who had no use of beta-blockers or statins during the 6 months prior to the index date were receiving them at 3 months, 48.2% and 45.0%, respectively. The percentages of use for ACE inhibitors and all 3 drug classes in patients without prior use were less than 30%. Although more than 85% of patients had at least 1 claim for any of the 3 classes, only 339 (29.9%) of patients had at least 1 pharmacy claim in *all* 3 classes in the 3 months after ACS discharge; of these patients 37.8% (128/339) had received at least 1 claim in all 3 drug classes within 6 months prior to ACS discharge.

More than 50% of patients aged 45-64 years and aged 65-79 years had at least 1 claim for an ACE inhibitors/ARB, beta-blocker, or statin (Table 3). Within 3 age classes, younger than 45 years, 65-79 years, and 80 years and older, the drug class with the highest prevalence of use was beta-blockers (rates of 57.8%, 62.7%, and 48.0%, respectively). Statins were the most commonly used class in patients aged between 45 and 64 years at 73.2%. Patients with intermediate coronary syndrome and acute MI had a higher use of beta-blockers and statins compared with ACE inhibitors/ARBs. Similarly, patients in HMO, PPO, and POS plans had a higher use of beta-blockers and statins compared with ACE inhibitors/ARBs. In the traditional indemnity plan, the use of each of the 3 classes was about 48%.

Patients in both of the older age categories (aged 65-79 and aged 80 and older) were less likely than patients in the 45-64 year group to receive beta-blockers and statins ($P = 0.002$ for aged 65-79 vs. aged 45-64 and $P < 0.001$ for aged 80 years and older vs. aged 45-64 years, Table 4). Additionally, patients aged 80 years and older were less likely than younger patients to receive ACE inhibitors/ARBs, or all 3 drug classes ($P = 0.003$ and $P = 0.002$, respectively). Patients who were aged younger than 45 years were less likely to receive statins and all 3 drug classes compared with those aged 45-64 years ($P = 0.032$ and $P = 0.049$, respectively). Women were significantly less likely than men to receive statins ($P = 0.004$). Patients who had used a therapy before index diagnosis of ACS were more likely to have that therapy continued after ACS diagnosis. Patients who had used ACE inhibitors or ARBs, beta-blockers, statins, and all 3 drug classes within 6 months before the index diagnosis of ACS were 12.2, 9.4, 8.3, and 4.9 times as likely to have these medications continued after ACS diagnosis, respectively ($P < 0.001$ for all 4 equations). Patients with intermediate coronary syndrome were significantly less likely than patients with acute MI to receive any of the therapies ($P < 0.001$ all comparisons). There were no differences in exposure to therapies based on health plan type except that patients enrolled in a traditional indemnity health plan were less likely to receive statins compared with patients in the HMO plan ($P < 0.018$). Hosmer-Lemeshow goodness-of-fit tests

TABLE 3 Number and Percent of Patients Using Secondary Prevention Drug Therapies in 3 Months of Follow-up After ACS Discharge, by Patient Subgroup

	ACE Inhibitor or ARB	Beta-blocker	Statin	All 3 Drug Classes	N of Cases
Age in years, n (%)					
<45	30 (46.9)	37 (57.8)	32 (50.0)	13 (20.3)	64
45-64	320 (55.3)	405 (69.9)	424 (73.2)	214 (37.0)	579
65-79	176 (55.2)	200 (62.7)	193 (60.5)	88 (27.6)	319
≥80	62 (35.8)	83 (48.0)	61 (35.3)	24 (13.9)	173
Sex, n (%)					
Male	396 (54.0)	478 (65.1)	505 (68.8)	250 (34.1)	734
Female	192 (47.9)	247 (61.6)	205 (51.1)	89 (22.2)	401
Prior use, n (%)					
ACE inhibitor or ARB	397 (80.2)	345 (69.7)	333 (67.3)	211 (42.6)	495
Beta-blocker	277 (57.0)	412 (84.8)	342 (70.4)	181 (37.2)	486
Statin	293 (57.5)	350 (68.6)	429 (84.1)	197 (38.6)	510
All 3 drug classes	169 (80.5)	179 (85.2)	176 (83.8)	128 (61.0)	210
Index diagnosis, n (%)					
411.1—intermediate coronary syndrome	408 (48.2)	503 (59.5)	503 (59.5)	204 (24.1)	846
410.xx—acute myocardial infarction	180 (62.3)	222 (76.8)	207 (71.6)	135 (46.7)	289
Health plan, n (%)					
HMO	109 (52.7)	139 (67.1)	145 (70.0)	68 (32.9)	207
PPO	178 (55.3)	212 (65.8)	235 (73.0)	114 (35.4)	322
POS	117 (60.9)	132 (68.8)	129 (67.2)	75 (39.1)	192
Traditional indemnity	147 (48.5)	188 (48.5)	145 (47.9)	58 (19.1)	303
Unknown	37 (33.3)	54 (48.6)	56 (50.5)	24 (21.6)	111

ACE=angiotensin-converting enzyme; ACS=acute coronary syndrome; ARB=angiotensin II receptor blocker; HMO=health maintenance organization; POS=point-of-service; PPO=preferred provider organization.

indicated good model fit ($P=0.519$ for ACE inhibitors/ARBs, $P=0.953$ for beta blockers, $P=0.621$ for statins, and $P=0.899$ for use of all 3 therapy classes).

Discussion

Our study evaluated the rates of exposure to 3 evidence-based drug therapies after hospital discharge for patients with ACS in an MCO. We found that 588 (51.8%) of ACS patients had at least 1 pharmacy claim for an ACE inhibitor or ARB during the 3 months following discharge, 725 (63.9%) for beta-blockers, and 710 (62.6%) for statins. Several other studies have examined the proportion of hospitalized cardiac patients discharged on secondary prevention medications.[10-12] Birkhead et al. examined processes of care for patients discharged with MI during 2004 and 2005 in England and Wales. Using records extracted from a national audit database, this research found rates of use of 80.5% for ACE inhibitors, 74.1% for beta-blockers, and 91.3% for statins in a group of 57,508 patients during hospitalization.[12] Doyle et al. evaluated treatment for 1,356 cardiac ACS patients admitted to Intensive/Coronary Care units in Ireland. Use rates for ACE inhibitors, beta-blockers, and statins at hospital discharge were 57%, 79%, and 73%, respectively.[11] Austin et al. abstracted charts from hospital records to evaluate the use of statins at hospital discharge for 7,285 patients with acute MI between April 1, 1999, and March 31, 2001, in Canada. Patients who had relative contraindications to statin therapy, such as liver disease, cholestasis, or treatment with fibrates, were excluded from the analysis. Overall, 2,597 (35.6%) patients received a statin medication at discharge. The authors also reported the use of ACE inhibitors (58.2%) and beta-blockers (71.0%) at discharge.[10]

The percentage of use in these 3 studies ranged from 57%-81% for ACE inhibitors, 71%-79% for beta-blockers, and 35%-91% for statins.[10-12] Our reported use rates are lower than these ranges except for the Austin et al. study that showed an extremely low rate of statin use (36%) after hospital discharge (from April 1, 1999, through March 31, 2001).[10] Our lower exposure rates may be explained partly by a difference in methodology. Specifically, the previous studies noted the use of medications at discharge, but we report use based on pharmacy claims within 3 months of discharge for ACS. Patients may have been

TABLE 4 *Logistic Regression Analyses: Predictors of Using Secondary Prevention Drug Therapies During 3 Months of Follow-up[a] (n=1,135)*

Predictor Variable	ACE Inhibitor or ARB	Beta-blocker	Statin	All 3 Drug Classes
Age—odds ratio (95% CI)				
<45 yrs	0.84 (0.46-1.52) P=0.558	0.65 (0.36-1.19) P=0.168	0.53 (0.29-0.95) P=0.032	0.50 (0.25-1.00) P=0.049
45-64 yrs	1	1	1	1
65-79 yrs	0.83 (0.57-1.21) P=0.336	0.55 (0.38-0.80) P=0.002	0.55 (0.37-0.80) P=0.002	0.74 (0.50-1.08) P=0.119
≥80 yrs	0.47 (0.28-0.78) P=0.003	0.25 (0.15-0.42) P<0.001	0.27 (0.17-0.45) P<0.001	0.40 (0.23-0.72) P=0.002
Sex—odds ratio (95% CI)				
Male	1	1	1	1
Female	0.80 (0.59-1.08) P=0.150	0.97 (0.72-1.31) P=0.836	0.65 (0.48-0.87) P=0.004	0.66 (0.48-0.91) P=0.012
Prior use—odds ratio (95% CI)				
ACE inhibitor or ARB	12.23 (8.48-17.63) P<0.001	1.08 (0.78-1.50) P=0.633	0.75 (0.54-1.05) P=0.098	2.05 (1.43-2.92) P<0.001
Beta-blocker	0.85 (0.60-1.21) P=0.366	9.38 (6.31-13.94) P<0.001	1.52 (1.07-2.15) P=0.018	1.08 (0.74-1.58) P=0.695
Statin	0.59 (0.42-0.83) P=0.003	0.77 (0.55-1.06) P=0.112	8.25 (5.61-12.13) P<0.001	0.98 (0.68-1.41) P=0.915
All 3 drug classes	1.67 (0.96-2.90) P=0.067	1.10 (0.61-1.97) P=0.753	0.96 (0.54-1.73) P=0.899	4.92 (2.89-8.37) P<0.001
Index diagnosis—odds ratio (95% CI)				
411.1—intermediate coronary syndrome	0.36 (0.26-0.50) P<0.001	0.26 (0.19-0.37) P<0.001	0.40 (0.29-0.57) P<0.001	0.23 (0.16-0.32) P<0.001
410.xx—acute myocardial infarction	1	1	1	1
Health plan—odds ratio (95% CI)				
HMO	1	1	1	1
PPO	1.10 (0.72-1.67) P=0.671	1.03 (0.68-1.58) P=0.881	0.98 (0.63-1.52) P=0.926	1.07 (0.70-1.62) P=0.755
POS	1.25 (0.78-2.00) P=0.356	1.04 (0.64-1.68) P=0.878	0.65 (0.40-1.05) P=0.075	1.07 (0.68-1.70) P=0.763
Traditional indemnity	1.00 (0.61-1.65) P=0.995	1.31 (0.80-2.16) P=0.285	0.54 (0.33-0.90) P=0.018	0.62 (0.37-1.04) P=0.072
Unknown	0.69 (0.39-1.23) P=0.211	0.76 (0.43-1.35) P=0.348	(0.38-1.22) P=0.198	0.84 (0.45-1.56) P=0.587

[a] *Binary logistic regression analysis of 4 outcomes; dependent variable is >1 claim in therapy class from index date through 3 months after index date. Cells show odds ratio (95% CI), with reference category=1.*

Hosmer-Lemeshow goodness-of-fit for ACE inhibitors or ARBs (P=0.519), beta blockers (P=0.953), statin (P=0.621), all 3 drug classes (P=0.899)

ACE=angiotensin-converting enzyme; ACS=acute coronary syndrome; ARB=angiotensin II receptor blocker; CI=confidence interval; HMO=health maintenance organization; POS=point-of-service; PPO=preferred provider organization.

prescribed appropriate pharmacotherapy at discharge, but failed to fill the prescription. According to the AHA, an estimated 12% of patients are prescribed therapy but do not have their prescription filled.[13] In addition, a large percentage of our study patients received therapy prior to their ACS hospitalization and may have had enough medication supply to cover the first 3 months post discharge.

There is evidence of the benefits of combination therapy in decreasing cardiovascular mortality.[14] Although we did not look at combination therapy or whether these medications were taken concurrently, we report in our study that 339 (29.9%) of patients had at least 1 pharmacy claim in all 3 classes). A study of a nationwide registry of patients admitted to intensive care units for acute MI in France found that only 27% received an ACE inhibitor, antiplatelet agent, beta-blockers, and statin at discharge.[15] We did not evaluate antiplatelet therapy because much of this utilization is in the form of over-the-counter aspirin, which is not covered by the MCO.

Our study noted differences in the use of secondary prevention pharmacotherapy based on demographic variables. Patients in the higher age categories (65-79 years and ≥80 years) were less likely to receive beta-blockers and statins compared with patients in the 45-64 year category. Patients in the highest age category of ≥80 years were also less likely to receive ACE inihibitors/ARBs compared with patients in the 45-64 year category. Men were more likely than women to receive statins.

In an observational cohort of patients admitted with MI in 2004-2005, Birkhead et al. found that the proportion of patients not receiving secondary prevention drugs during hospitalization increased with age. There were 14.2% to 26% fewer patients using ACE inhibitors, beta-blockers, or statins in the age category ≥85 years compared with the younger group aged 55-64 years.[12] Austin et al. reported that patients who were not prescribed a statin after acute MI were older (mean age 70 years for those who were not prescribed a statin compared with 64 years for those prescribed a statin, $P<0.001$), and a higher percent was female (40% of those not prescribed a statin and 29% of those prescribed a statin were women, $P<0.001$).[10] Doyle et al. analyzed gender differences in 1,356 hospitalized cardiac ACS patients and noted far fewer women in the study, 28%, compared with men, 72%; and the average age was 6 years higher for women (69 years) than for men (63 years, $P<0.001$). The authors reported no difference in the use of ACE inhibitors and beta-blockers in men and women. However, they found a 6% difference between men and women in the use of statins, and the odds of being prescribed a statin were 35% higher for men than for women after adjustment for age and total cholesterol ($P=0.043$).[11]

Another study by Fonarow et al. found that among patients discharged from U.S. hospitals following an acute MI, patients who were prescribed lipid-lowering agents were significantly younger (average age 63.4 years) than patients not prescribed lipid-lowering agents (average age 70.1 years; $P<0.001$). Lipid-lowering treatment rates were 43.6% in patients aged <55 years, 33.4% in patients aged 65-74 years, 22.8% in patients aged 75-84 years, and 9.7% in patients aged older than 84 years. Women were also less likely to be treated with lipid-lowering medications (34.8% of men were discharged on lipid-lowering therapy vs. 26.8% of women).[16]

In addition to demographic characteristics, we report differences in use rates based on index diagnosis. Patients with MI were more likely to receive secondary prevention therapy with ACE inhibitors/ARBs, beta-blockers, and statins compared with patients with ICS. A recent study, published last month, evaluated the patient characteristics associated with medical therapy at hospital discharge for ACS.[17] The use of optimal medical therapy (defined as discharge on antiplatelet/anticoagulant, beta-blocker, lipid-modifying agent, and ACE inhibitor in those without contraindications) was reported in 35.8% (2,091/5,833) of patients during October 2002-December 2003. This study found that patients who had a previous MI had a 35.0% rate of use of optimal medical therapy compared with a 30.9% rate for those without previous MI ($P=0.001$). The authors reported that patients presenting with ST-elevation MI and those with more extensive coronary artery disease, as reflected by prior MI or coronary revascularization, were more likely to be given aggressive medical treatment. Another study by Roe et al. found that high-risk clinical features, such as positive cardiac markers, were associated with use of ACE inhibitors, beta-blockers, and lipid-lowering agents ($P<0.05$).[18]

Limitations

Foremost among the study limitations is the absence of clinical information about these patients that might explain the reasons (e.g., medication intolerance or contraindication) that a given patient did not have a pharmacy claim for 1 or more of the 3 classes of drugs recommended for management of patients with ACS. This limitation may result in underestimates of appropriate use.

Second, we did not assess hospital utilization in the follow-up period after the index hospitalization. Some patients may have received medication during a rehospitalization; this medication would not be recorded in outpatient pharmacy claims. Other patients may have received physician samples during outpatient visits. Therefore, our rates of use of the 3 target medication classes may under-report actual use.

Third, 43.3% of our study population was aged 65 years or older, raising the possibility that pharmacy claims data were incomplete for Medicare-eligible members. The study MCO did not offer any Medicare+ Choice (Medicare Advantage) plans during the study period. Approximately 68.5% of Medicare-eligible members had the same pharmacy benefits as other commercial members, and 31.5% had a senior pharmacy benefits program that provided coverage up to $1,100 in annual expenditures and then discounted prices after $1,100 that were not funded

(i.e., 100% copayment). Because members had incentives to submit claims (i.e., to obtain discount prices) even after reaching the cap, we believe that the MCO's pharmacy claims are complete for Medicare-eligible members.

Fourth, it is possible that patients did not receive the 3 classes of guideline medication therapies concomitantly since only 1 pharmacy claim for each medication was required, and there was no requirement for concomitant use or overlap of the medications. Fifth, our data may under-report physician prescribing of the 3 guideline therapies because we did not examine medical records to determine if medications were prescribed but not dispensed to patients who failed to fill prescriptions. Sixth, we do not know the patient's complete medical history and whether this was their first ACS event.

Conclusion

The majority of patients with a diagnosis of ACS received therapy with at least 1 of the classes of secondary prevention medications. However, 70% of patients were missing at least 1 of the guideline medication therapies. The largest discrepancies in the use of guideline medications appear to be by age, sex, and index diagnosis. Those aged 65-79 years were less likely than those aged 45-64 to receive a beta-blocker or a statin, and those aged ≥80 years were less likely than younger patients to be receiving any of the therapies. Women were less likely than men to receive statin therapy. Patients with MI were more likely to receive any of the therapies compared with patients with intermediate coronary syndrome. Future research should attempt to explain the differences in use of these secondary prevention therapies by demographic factors, evaluate adherence and persistence, and determine cost-effective interventions to improve use of the 3 secondary prevention therapies.

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DISCLOSURES

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Appendix
List of Drugs for Which Pharmacy Claims Were Obtained

Beta Blockers

acebutolol
atenolol; atenolol with chlorthalidone
betaxolol
bisoprolol; bisoprolol with HCTZ
carvedilol
labetalol
metoprolol; metoprolol with HCTZ
nadolol
pindolol
penbutalol
propranolol; propranolol with HCTZ
sotalol
timolol; timolol with HCTZ

Statins

atorvastatin
atorvastatin with amlodipine
fluvastatin
lovastatin; lovastatin with niacin
pravastatin
rosuvastatin
simvastatin; simvastatin with ezetimibe

ACEIs and ARBs

benazepril; benazepril with HCTZ
benazepril with amlodipine
candesartan; candesartan with HCTZ
captopril; captopril with HCTZ
enalapril; enalapril with HCTZ
enalopril with felodipine
eprosartan
fosinopril; fosinopril with HCTZ
irbesartan; irbesartan with HCTZ
lisinopril; lisinopril with HCTZ
losartan; losartan with HCTZ
moexipril; moexipril with HCTZ
monopril; monopril with HCTZ
olmesartan; olmesartan with HCTZ
perindopril
quinapril; quinapril with HCTZ
ramipiril
trandolapril; trandolapril with verapamil
valsartan; valsartan with HCTZ