ORIGINAL RESEARCH

Difference in Medication Adherence Between Patients Prescribed a 30-Day Versus 90-Day Supply After Acute Myocardial Infarction

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BACKGROUND: Evidence-based medication adherence rates after a myocardial infarction are low. We hypothesized that 90-day prescriptions are underused and may lead to higher evidence-based medication adherence compared with 30-day fills.

METHODS AND RESULTS: We examined patients with myocardial infarction treated with percutaneous coronary intervention between 2011 and 2015 in the National Cardiovascular Data Registry. Linking to Symphony Health pharmacy data, we described the prevalence of patients filling 30-day versus 90-day prescriptions of statins, β-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and $P2Y_{12}$ inhibitors after discharge. We compared 12-month medication adherence rates by evidence-based medication class and prescription days' supply and rates of medication switches and dosing changes. Among 353 259 patients with myocardial infarction treated with percutaneous coronary intervention, 90-day evidence-based medication fill rates were low: 13.0% (statins), 12.3% (β-blockers), 14.6% (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers), and 9.7% ($P2Y_{12}$ inhibitors). Patients filling 90-day prescriptions were more likely older (median 69 versus 62 years) with a history of prior myocardial infarction (25.0% versus 17.9%) or percutaneous coronary intervention (30.3% versus 19.5%; $P<0.01$ for all) than patients filling 30-day prescriptions. The 12-month adherence rates were higher for patients who filled 90-day versus 30-day supplies: statins, 83.1% versus 75.3%; β-blockers, 72.7% versus 62.9%; angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, 71.1% versus 60.9%; and $P2Y_{12}$ inhibitors, 78.5% versus 66.6% ($P<0.01$ for all). Medication switches and dosing changes within 12 months were infrequent for patients filling 30-day prescriptions—14.7% and 0.3% for 30-day $P2Y_{12}$ inhibitor fills versus 6.3% and 0.2% for 90-day fills, respectively.

CONCLUSIONS: Patients who filled 90-day prescriptions had higher adherence and infrequent medication changes within 1 year after discharge. Ninety-day prescription strategies should be encouraged to improve post–myocardial infarction medication adherence.

Key Words: adherence ■ evidence-based medications ■ myocardial infarction

Evidence-based medications (EBMs), such as statins, β-blockers, angiotensin-converting enzyme inhibitors (ACEis)/angiotensin receptor blockers (ARBs), and $P2Y_{12}$ inhibitors, are recommended for at least 12 months for patients after an acute myocardial infarction (MI),[1] yet the rates of medication adherence post-MI are low. Nearly 1 in 7 patients with stented MI are not adherent to $P2Y_{12}$ inhibitor therapy by 30 days after index MI discharge.[2] In another study of patients post-MI, only 74% of patients filled all their prescribed EBMs by 6 months after the index MI admission.[3] Patients who are post-MI with EBM nonadherence have higher readmission risk and lower event-free survival compared with adherent patients.[4,5]

Nonstandard Abbreviations and Acronyms

ARBs	angiotensin receptor blockers
EBM	evidence-based medication
NCDR	National Cardiovascular Data Registry

The 90-day prescription fills may provide the advantage of increasing medication adherence because of the longer prescription supply and need for fewer refills, yet the impact of 90-day prescription fills on post-MI medication adherence has never been evaluated. In addition, there is contradictory data on whether 90-day prescriptions of antihypertensives or oral hypoglycemics filled through mail order pharmacies may be associated with increased medication adherence when compared with patients filling 90-day prescriptions of these medications through store or retail pharmacies.[6,7] However, this relationship of EBM adherence and 90-day prescription fills at mail order versus store pharmacies has never been examined among patients post-MI. We therefore hypothesized that (1) 90-day prescription fills are associated with higher adherence to EBMs than 30-day fills, but are underused in patients post-MI; (2) relatively few patients have within-class EBM switches or dosing changes that justify not receiving 90-day prescriptions; and (3) patients with 90-day fills through a mail order pharmacy will have improved rates of medication adherence compared with patients with 90-day fills through a store pharmacy.

METHODS

Data Sources

The authors cannot make data and study materials available to other investigators for purposes of reproducing the results because of licensing restrictions. Interested parties, however, could obtain and license the data by contacting the NCDR (National Cardiovascular Data Registry).

Authorization for this study and waiver of written informed consent were granted by Chesapeake Institutional Review Board. With permission from the American College of Cardiology, Symphony Health (a PRA Health Sciences Company) linked records from the National Cardiovascular Data Registry NCDR Acute Coronary Treatment and Intervention Outcomes Network (ACTION) and CathPCI Registries to the Symphony Health longitudinal pharmacy claims data set. The ACTION Registry is a quality improvement registry of consecutive patients with MI treated at 1127 hospitals in the United States, and the CathPCI registry is a quality improvement registry of consecutive patients treated with percutaneous coronary intervention (PCI) at 1712 hospitals in the United States. Both registries collect detailed patient demographics, clinical characteristics, and in-hospital treatments and outcomes via retrospective medical record review using a standardized set of data elements and definitions.[8,9] Symphony Health data contain prescriber information for 280 million patients and 1.8 million prescribers in the United States. The pharmacy claims capture is ≈92% of the retail and 68% of mail orders. It includes claims submitted to all payer types, including commercial plans, Medicare, and Medicaid. These are adjudicated claims collected from major US clearing houses as well as large national retail, mail order, and specialty pharmacy chains. All data were de-identified and linked via a compliant, anonymous unique identifier.

Study Population

We examined all ST-segment–elevation MI (STEMI) and non–ST-segment–elevation MI (NSTEMI) patients (ages 18 and older) treated with PCI in the linked data set between June 1, 2011 and September 31, 2015. We included all patients discharged alive after the index MI admission (n=1 150 541). We excluded patients who were transferred to another hospital or discharged to a skilled nursing facility (n=36 259) or were not discharged on any of the following: a statin, β-blocker, ACEi/ARB, or a P2Y$_{12}$ inhibitor (n=333 975). To determine 30-day versus 90-day fills via pharmacy fill data, we excluded patients who died within the first 90 days (n=10 867) or who did not have any pharmacy activity in the 90 days before the index admission (n=236 899) or during the

12-month follow-up period after the index admission (n=24 711). We also excluded patients who were not pharmacy eligible for at least 1 year following discharge (n=124 153) and those who could not be matched to a pharmacy fill for any of the drug classes of interest within 30 days of discharge (n=30 418). Patients who received prescription fills other than a 30-day or 90-day supply were not included. The final analysis population included 353 259 patients treated with PCI who were discharged on at least 1 EBM class and were matched to a pharmacy fill within 30 days of the index admission.

Definitions

We examined the proportion of patients filling a 30-day or 90-day supply of each of the 4 EBM drug classes of interest (ie, statins, β-blockers, ACEi/ARBs, or P2Y$_{12}$ inhibitors). The first prescription fill post-MI discharge was used to classify a 30-day versus 90-day supply. The first fill needed to occur within 30 days after discharge for patients with new prescriptions or within 90 days postdischarge for patients who were on the medication before admission.

We defined adherence for each EBM class as the proportion of days covered >80%, calculated by dividing the sum of days' supply of the medication available by the total number of days within the measured period (180 days for 6-month adherence and 360 days for 12-month adherence). If a patient filled a medication early and had overlapping days' supply of the same medication, the early fill was added to the prior fill to calculate days' supply covered. If the patient switched between medications of the same class (ie, "switching within class"), we stopped counting the existing supply of the first medication as of the day the alternative medication was filled and started counting the days' supply from the alternative medication fill. As long as patients filled medications within the same class, they were considered on therapy.

We defined a within-class medication switch during the 12-month (360 days) time period postdischarge as a switch in product within an EBM class (eg, metoprolol switched to carvedilol). We defined a dosing change within the 12-month (360 days) time period postdischarge as a change in dose or dose frequency of the same medication.

The pharmacy type was classified based on the location of the first dispensed fill in each class. Store pharmacies were any independent, chain retail, or grocery store pharmacies, and mail order pharmacies were any pharmacy that delivered prescription drugs through the mail or shipping companies.

Statistical Analysis

Among the population of patients who were discharged on at least 1 EBM class, we examined the

fill rates for each EBM class by prescription days' supply. We also evaluated the baseline patient demographics, clinical characteristics, and in-hospital characteristics by prescription days' supply. We defined 90-day fills as patients whose first EBM in the class was filled as a 90-day prescription. A t test assuming unequal variance was used for continuous variables, and a χ^2 test was used for categorical variables.

The adherence analysis evaluated the population of patients alive at 12 months after the index discharge, further excluding 5247 patients (1.5%) who died between 91 and 365 days after the index admission, resulting in an analysis population of 348 012 patients treated with PCI. In addition to calculating proportion of days covered, we also calculated the unadjusted and adjusted relative risks/probability of being adherent at 12 months after the index discharge by EBM class and prescription days' supply. We adjusted for age, sex, race, insurance type, household income, education level, history of prior MI, prior heart failure, prior coronary artery bypass grafting, prior PCI, diabetes mellitus, hypertension, dyslipidemia, smoking status, MI type (STEMI versus NSTEMI), and stent type (drug-eluting stents versus presumed bare metal stents). The adjusted relative risks were calculated using a modified Poisson regression model using the SAS GENMOD procedure. As patients who filled a 90-day prescription at discharge are not at risk for nonadherence until after day 90, a sensitivity analysis examined 1-year adherence censoring the first 90 days postdischarge.

Finally, among 12-month survivors who filled a 90-day supply, we analyzed the percentage of patients filling prescriptions at mail order or store pharmacies by EBM class. We then examined the percentage of adherent patients (proportion of days covered >80%) at 12 months by EBM class and pharmacy type.

RESULTS

A total of 353 259 patients had an acute MI and were treated with PCI before being discharged on 1 or more EBM classes (ie statin, β-blocker, ACEi/ARB, or P2Y$_{12}$ inhibitor). Most of these discharge EBMs were new prescriptions never filled in the 90 days prior the index MI: 73.1% for statins, 75.3% for β-blockers, 66.1% for ACEi/ARBs, and 93.9% for P2Y$_{12}$ inhibitors. Within each EBM class, the majority of patients filled their first prescription as a 30-day supply: 87.0% for statins, 87.7% for β-blockers, 85.4% for ACEi/ARBs, and 90.3% for P2Y$_{12}$ inhibitors (Table 1). The 90-day fills were infrequent (≤20.0% for all classes) even when this was a continuation of a medication filled before the index MI. Nearly all (n=303 039; 85.8%) patients filled

more than 1 EBM class. Among patients who filled a 30-day prescription initially, the majority persisted with 30-day fills in the next 3 months (Table S1). At the patient level, 283 087 patients (80.1%) filled all their EBMs in 30-day supplies, 25 851 patients (7.3%) filled all their EBMs in 90-day supplies, and 44 321 patients (12.5%) filled some of their EBMs as a 30-day supply and others as a 90-day supply.

Table 2 compares the demographic and clinical characteristics between patients who filled exclusively 30-day versus exclusively 90-day supplies in their first fill of all EBM classes. Patients who filled 90-day supplies were older, more likely White, and less likely to have commercial insurance than those patients who filled only 30-day supplies (all $P<0.01$). Patients who filled a 90-day supply were also more likely to have a past medical history of hypertension, dyslipidemia, diabetes mellitus, and a history of a prior MI or prior revascularization (all $P<0.01$). The median hospital length of stay was 3 days (25th, 75th percentiles=2, 4) for both groups. Patients who filled a 90-day supply were more likely to have presented with a NSTEMI and were slightly more likely to be treated with drug-eluting stents compared with patients who filled only 30-day supplies (all $P<0.01$).

Table 1.   Proportion of Patients Filling a 90-Day Fill by Evidence-Based Medication Class*

Drug Class	90-d Fill/Total Fill (n/N Patients)	Proportion With 90-d Fill (%)
Overall		
Statins	35 662/273 332	13.0
β-blockers	33 911/276 323	12.3
ACEi/ARBs	27 122/185 764	14.6
P2Y$_{12}$ inhibitors	27 142/280 269	9.7
New prescription at discharge†		
Statins	21 758/199 695	10.9
β-blockers	21 616/208 178	10.4
ACEi/ARBs	14 551/122 870	11.8
P2Y$_{12}$ inhibitors	24 375/263 112	9.3
Home medications re-prescribed at discharge‡		
Statins	13 904/73 637	18.9
β-blockers	12 295/68 145	18.0
ACEi/ARBs	12 571/62 954	20.0
P2Y$_{12}$ inhibitors	2 767/17 157	16.1

ACEi indicates angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers.

*This table is demonstrating patients whose first evidence-based medication in the class was filled as a 90-day prescription.

†New prescription at discharge=patients without exposure to that evidence-based medication class in the 90 days before the index myocardial infarction event but who were discharged on that class.

‡Home medications re-prescribed at discharge=patients filling that evidence-based medication class in the 90 days before the index myocardial infarction, although we cannot detect whether they were discharged on the same or different agent within the class.

Table 2.   Characteristics of Patients Initially Filling a 30-Day Versus 90-Day Supply of Medications*

	30-d Fill, N=283 087	90-d Fill, N=25 851	P Value
Demographics			
Median age, y	62 (54–71)	69 (60–75)	<0.01
Female	32.2	33.0	0.01
White	87.2	90.5	<0.01
Commercial insurance	46.0	30.0	<0.01
High school education or less	31.8	28.5	<0.01
Household income <$30 000	14.0	16.4	<0.01
Prior medical history			
Current or recent smoker	36.0	25.1	<0.01
Hypertension	71.8	79.1	<0.01
Dyslipidemia	59.8	68.9	<0.01
Diabetes mellitus	30.2	34.2	<0.01
Dialysis-treated kidney disease	1.6	1.9	<0.01
Prior MI	17.9	25.0	<0.01
Prior HF	6.8	10.2	<0.01
Prior CABG	8.9	16.5	<0.01
Prior PCI	19.5	30.3	<0.01
Prior stroke	0.2	0.2	0.18
In-hospital characteristics			
STEMI	43.6	36.8	<0.01
Treated with DES	75.6	77.6	<0.01

Continuous variables presented as median (25th–75th percentile) and categorical variables presented as frequency percentage. CABG indicates coronary artery bypass graft; DES, drug-eluting stent; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

*This table represents those patients who filled exclusively a 30-day vs exclusively a 90-day supply in their first fill of all evidence-based medication classes.

Among the 348 012 (98.5%) patients who survived to 12 months after discharge for whom 1-year medication adherence was analyzed, 90-day fill rates were similarly low, ranging from 9.7% for P2Y$_{12}$ inhibitors to 14.6% for ACEi/ARBs (Table S2). At 12 months, medication adherence rates were significantly higher for patients with initial 90-day than those with 30-day fills, regardless of medication class ($P<0.01$ for all classes; Figure 1). The risk ratios in Table 3 demonstrate that patients who filled a 90-day prescription were more likely to achieve 12-month EBM adherence than patients who filled a 30-day prescription initially both before and after adjusting for demographic, socioeconomic, and clinical factors. As patients who initially filled a 90-day prescription were not at risk for nonadherence until after day 90, a sensitivity analysis censoring the first 90 days was performed and showed similar results (Table 3). In addition, a sensitivity analysis censoring
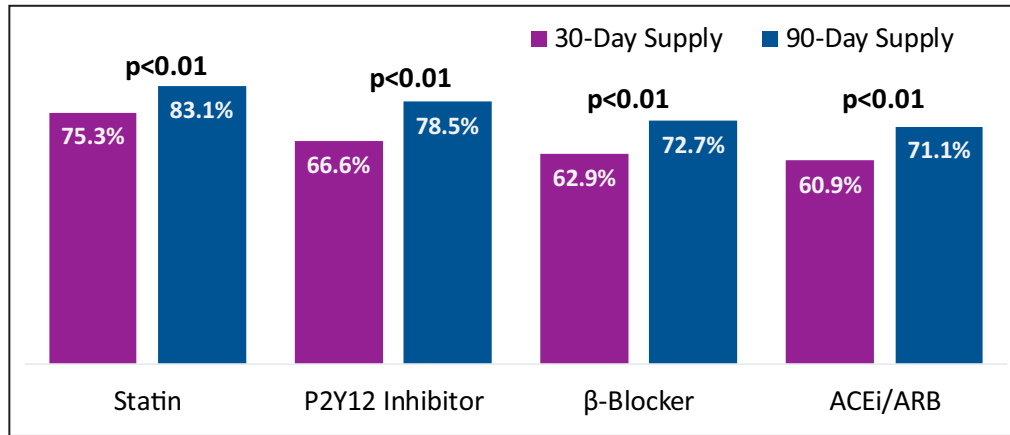
Figure 1. Adherence by evidence-based medication class and prescription days' supply at 12 months.
ACEi indicates angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers.

the first 90 days was performed to examine medication adherence rates at 12 months. Similar to Figure 1, medication adherence rates were significantly higher across all EBM classes for patients with initial 90-day fills compared with patients with 30-day fills (Figure S1).

The rates of medication switching within the same EBM class or dosing change within the 12 months postdischarge for patients who filled 30-day versus 90-day supplies are shown in Table 4. Most patients only had 1 medication change made during the year, with the majority of medication switches occurring in the first 3 to 4 months after the index MI discharge (Figure 2A). Similarly, the majority of dosing changes occurred within the first 3 to 4 months after the index

Table 3. RR of 12-Month Adherence (Proportion of Days Covered >80%) by Evidence-Based Medication Class

Drug Class	Unadjusted RR (95% CI) 30-d to 90-d	Adjusted* RR (95% CI) 30-d to 90-d
12-mo adherence		
Statins	0.91 (0.90–0.91)	0.95 (0.95–0.95)
β-blockers	0.87 (0.86–0.87)	0.94 (0.94–0.95)
ACEi/ARBs	0.86 (0.85–0.86)	0.94 (0.93–0.95)
P2Y$_{12}$ inhibitors	0.85 (0.84–0.85)	0.93 (0.92–0.93)
12-mo adherence (sensitivity analysis censoring first 90 d)		
Statins	0.88 (0.87–0.88)	0.96 (0.95–0.96)
β-blockers	0.89 (0.88–0.90)	0.97 (0.96–0.97)
ACEi/ARBs	0.89 (0.89–0.91)	0.96 (0.95–0.97)
P2Y$_{12}$ inhibitors	0.88 (0.87–0.89)	0.95 (0.95–0.96)

ACEi indicates angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; and RR, relative risk.

*Adjusted for age, sex, race, insurance type, household income, education level, history of prior myocardial infarction, prior heart failure, prior coronary artery bypass grafting, prior percutaneous coronary intervention, diabetes mellitus, hypertension, dyslipidemia, smoking status, myocardial infarction type (ST-segment–elevation myocardial infarction vs non–ST-segment–elevation myocardial infarction), and stent type (drug-eluting stent vs presumed bare metal stent).

MI discharge (Figure 2B). Table S3 represents the monthly percentage of overall within-class switches and dosing changes among patients who filled a 90-day supply and demonstrates that the majority of changes occurred within the first 4 months after the index MI discharge.

Within each EBM class, 99% of patients filling a 30-day prescription did so in store pharmacies. Mail order prescription fills were used infrequently among patients filling 90-day prescriptions: 8.8% for statins, 7.9% for β-blockers, 9.0% for ACEi/ARBs, and 6.4% for P2Y$_{12}$ inhibitors. Among patients filling a 90-day supply, rates of 12-month adherence were higher across all EBM classes among patients who filled their prescription at store pharmacies compared with mail order pharmacies (Table S4). Among patients who filled at store pharmacies only, those filling 90-day prescriptions were associated with higher 12-month adherence across all EBM classes compared with patients filling 30-day prescriptions: 81% versus 73% for statins, 70% versus 60% for β-blockers, 69% versus 59% for ACEi/ARBs, and 76% versus 63% for P2Y$_{12}$ inhibitors ($P<0.01$ for all).

DISCUSSION

In this nationwide study of patients with MI treated with PCI, we demonstrated that the filling of 90-day prescriptions on being discharged from an MI hospitalization were low across all EBM classes, even for those patients who were already prescribed these medications before the index MI admission. The 1-year adherence rates were significantly higher among those patients filling 90-day prescriptions compared with those filling 30-day prescriptions. Importantly, the majority of patients filling 30-day or 90-day prescriptions did not undergo a medication

Table 4. Medication Switches and Dosing Changes by Evidence-Based Medication Class Within 12 Months of Discharge

	Within-Class Switch* % of Patients			Dosing Change* % of Patients			Within Class Switch or Dosing Change
	Overall	1 Change	≥2 Changes	Overall	1 Change	≥2 Changes	
30-d fill							
Statins	15.1	11.1	4.0	16.4	12.4	4.0	28.9
β-blockers	23.2	11.1	12.2	17.8	11.9	5.9	36.0
ACEi/ARBs	15.6	11.0	4.6	23.4	15.5	8.0	35.0
P2Y$_{12}$ inhibitors	14.7	12.8	1.9	0.3	0.2	0.1	14.9
90-d fill							
Statins	13.4	10.0	3.4	14.4	11.1	3.3	25.6
β-blockers	21.3	9.7	11.6	14.9	10.4	4.5	32.3
ACEi/ARBs	13.3	9.5	3.8	18.7	13.1	5.6	29.0
P2Y$_{12}$ inhibitors	6.3	5.0	1.3	0.2	0.1	<0.1	6.4

ACEi indicates angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers.

*Medication switch included any switch between agents of different primary molecule within the same evidence-based medication class. A dosing change included a change in average daily dose or in strength of medication while remaining on the same molecule. A change in product with a different dose would be counted as a medication switch only. All results are reported as percentages among patients with a 90-day fill.

switch or dose change within EBM class during the follow-up year. Mail order prescription fills were infrequent among patients filling 90-day prescriptions and were not associated with higher medication adherence.

In the present study, patients who were post-MI infrequently used 90-day fills across all EBM classes. This was consistent in medications such as P2Y$_{12}$ inhibitors in which dosing changes are not anticipated, as well as in medications, such as β-blockers and ACEi/ARBs, with antihypertensive effects that may require dose titrations. Importantly, we also demonstrated that medication switching or dose titration were infrequent in the first year post-MI and observed only slightly higher rates among patients filling 30-day versus 90-day prescriptions. Similarly, consideration of whether patients are new to an EBM class did not explain why 90-day prescriptions are underprescribed at the time of discharge after an MI given than 80% to 84% of patients recently on an EBM class were still given a 30-day prescription. There are several potential reasons why patients who are post-MI may be predominately filling 30-day prescriptions after discharge. Many electronic health records are set to a default 30-day prescription fill for all prescriptions that are printed.[10] In addition, many prescription drug plans will not cover 90-day prescription fills for many medications, although this policy is beginning to change for many prescription drug plans as there is increasing awareness that 90-day prescription fills may lead to increased adherence.[11,12] Although we demonstrated that the majority of patients filling a 30-day or 90-day prescription will not undergo a product or dosing change after discharge, providers may prescribe 30-day supplies because of concern that a 90-day prescription fill could result in prescription waste, increased costs to the patient, or a potential for the patient to continue to take the wrong medication or dose if switched after discharge.

Provider prescribing practices and concerns for medication switching, dose titration, and prescription waste may be one of the reasons why so few patients who are post-MI and treated with PCI received 90-day prescription fills. Interestingly, we found that among those patients filling 30-day prescriptions, >9 of 10 patients did not have a medication or dose change within the first month, and generally 2 of 3 patients did not have a change in their EBM class during the year following their index MI discharge. If there were medication or dosing changes, the majority of patients just had 1 change, and these changes typically occurred early after discharge. In addition, prior studies have demonstrated that 90-day fills of medications, such as statins, antihypertensives, selective serotonin reuptake inhibitors, and oral hypoglycemics, are associated with comparable prescription waste but overall cost savings when compared with 30-day fills.[13] Even if the discharge provider is hesitant to send patients out with 90-day fills of the recommended EBMs, the follow-up outpatient providers should feel reassured in converting patients who are on stable regimens of post-MI EBMs from 30-day to 90-day fills. As most of these medications are recommended by the current guidelines for at least 1 year,[1] discharging providers and postdischarge outpatient providers should consider prescribing 90-day fills or converting 30-day to 90-day fills to potentially mitigate the risks of hospital readmission and cardiovascular mortality.

We also demonstrated that 1-year adherence rates were significantly higher for patients filling 90-day prescriptions compared with those filling 30-day
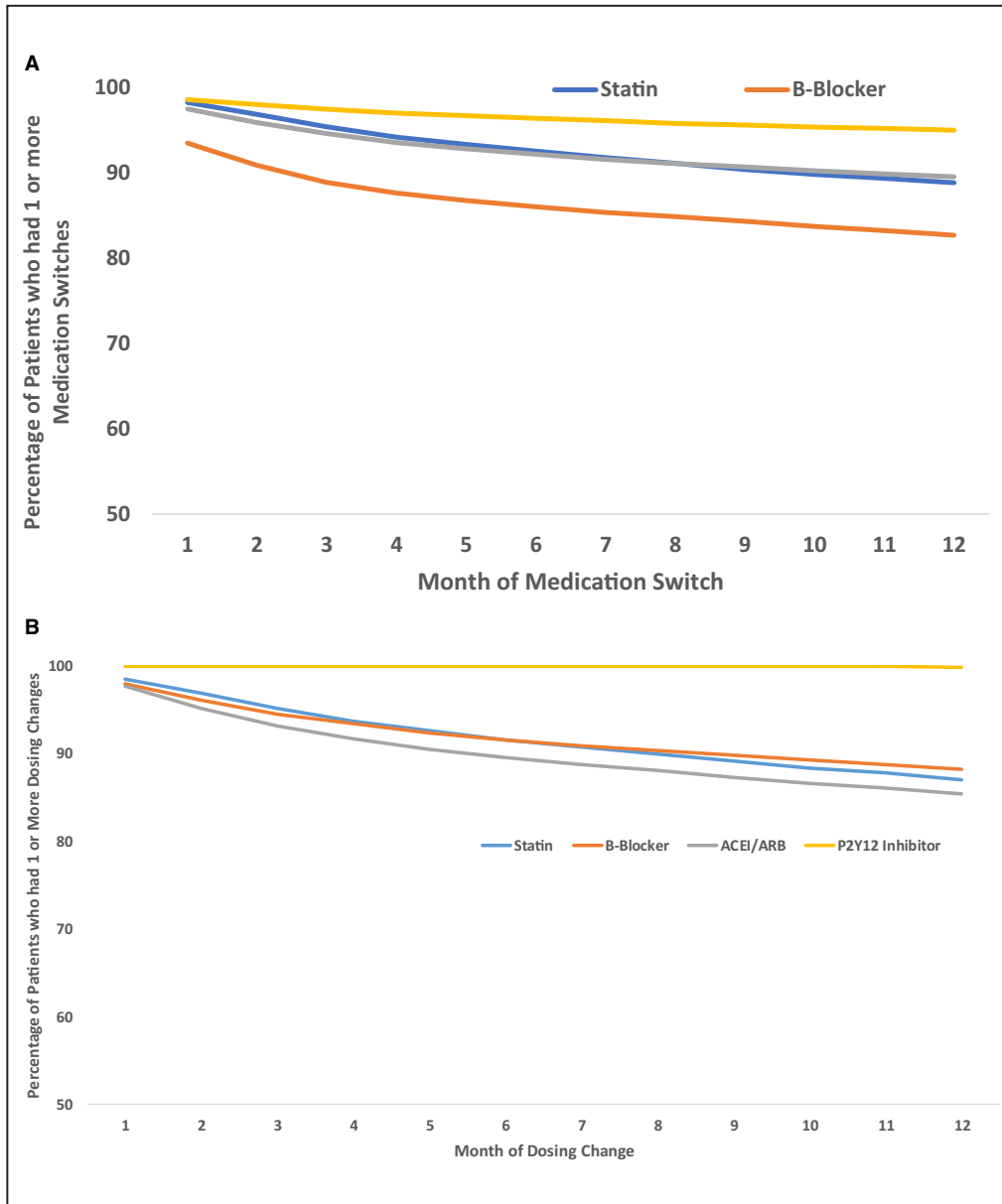
Figure 2.   Illustration of months during which medication switches or dosing changes occurred among patients prescribed a 90-day fill.

A, Month the medication switch occurred among patients prescribed a 90-day fill. **B**, Month the dosing change occurred among patients prescribed a 90-day fill. ACEi indicates angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers.

prescriptions, even after censoring the first 90 days or limiting to in-store pharmacy fills. Other studies have shown that decreased medication adherence after an MI is associated with increased readmission risk and lower event-free survival[2–5] therefore, measures to improve post-MI medication adherence could have important patient outcome implications. Our study's finding that 90-day prescription fills of post-MI EBMs were associated with increased adherence to medication during the recommended minimum 1 year of follow-up should be considered by

policy makers and payers. Analyses of other patient populations and disease states have similarly demonstrated increased medication adherence associated with 90-day prescription fills. An observational study of >50 000 Medicaid patients prescribed statins, antihypertensives, selective serotonin reuptake inhibitors, or oral hypoglycemic medications found that patients prescribed 90-day fills of these medications had 20% higher adherence and 23% higher persistence compared with patients prescribed 30-day fills.[13] In a private insurer database, patients with 90-day prescription fills

had 40% lower nonadherence compared with patients with 30-day prescription fills for similar medications.[14] Our results, as well as the findings of other analyses on medication adherence and 90-day prescription fills, indicate that 90-day prescription strategies should be more frequently considered after an MI in efforts to enhance medication adherence.

We did find that mail order prescriptions fills were infrequent and not associated with increased medication adherence. Fewer than 10% of patients filled prescriptions via mail order in this MI study population. Mail order pharmacy users were not associated with greater adherence compared with store pharmacy users among patients given 90-day fills. Although prior studies have shown increased adherence associated with mail order pharmacies,[6,7] this association may be primarily driven by the length of prescription fill rather than who or which location filled the medication. Further work is needed to determine the association of mail order pharmacies in the post-MI population with medication adherence.

Perhaps the greatest barrier to implementing 90-day prescription strategies are restrictions placed on 90-day prescription fills by prescription drug plans and payers. These restrictions likely result because of concern for increased prescription waste and oversupply. Many Medicare prescription drug plans cover 30-day prescription supplies, but limit the filling of 90-day prescriptions to certain retail pharmacies or mail order pharmacies.[15] In addition, prescription drugs on a specialty tier are limited to 30-day supplies.[15] Other prescription drug plans, including Cigna and various Blue Cross Blue Shield prescription drug plans, will cover 90-day prescription supplies, particularly for stable medications, but will limit the filling of these medications to certain retail and mail order pharmacies.[16,17] After the North Carolina Medicaid program reduced the number of days of prescription supply that enrollees could fill from 100 to 34 days, a recent publication demonstrated a 2% (P=0.001) and 1.2% (P<0.001) drop in adherence for lipid-lowering therapies and antihypertensive therapies, respectively, among patients who were fully adherent at baseline.[18] Our hope is that by demonstrating increased medication adherence in the post-MI population using 90-day prescription strategies, many prescription drug plans will begin to change these policies and allow for wider coverage and promotion of 90-day supplies. Future strategies to increase medication adherence in the post-MI population should include (1) a focus on changing provider prescribing practices at the time of discharge and during outpatient follow-up, (2) increasing awareness among prescription drug plans and payers about the increased adherence associated with 90-day plans, and (3) adopting changes in electronic medical records to allow for automatic generation of 90-day prescription supplies instead of defaulting to 30-day prescription supplies.

Although our study uses a national cardiovascular registry data with in-depth clinical records of patients following a PCI and acute MI linked with longitudinal pharmacy claims data, there are several important limitations. As this is a retrospective, observational study, residual confounding cannot be excluded. The prescription fill database used for this analysis cannot account for drug samples or hospital-sponsored drugs distributed to patients at both the time of discharge or during outpatient follow-up visits. In addition, any restrictions from drug coverage plans on patient receipt of 90-day supplies is unknown and could not be accounted for in this analysis. Finally, as direct observation of medication ingestion was not possible, this analysis may have overestimated rates of medication adherence.

CONCLUSIONS

Most patients fill 30-day prescriptions rather than 90-day prescriptions of EBMs after an MI, yet patients who were post-MI who filled a 90-day supply of EBMs had higher adherence at 12 months after discharge. Only a minority of patients who were discharged with a 30-day or 90-day fill had a medication switch or dosing change within 12 months after discharge that might preclude consideration of longer duration fills. The 90-day prescription strategies should be encouraged among providers, payers, and prescription drug plans to improve post-MI medication adherence.

Supplementary Materials

Tables S1–S4
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Proportion of Patients who Converted to 90-day Prescription Fills within Three Months after the Index Prescription Fill.

	Converted to 90-day fills	**% out of n**
Statins	69,575/234,759	29.6%
Beta Blockers	74,549/239,097	31.2%
ACEi/ARB	46,688/156,769	29.8%
P2Y12 Inhibitors	67,327/249,650	27.0%

Table S2. Proportion of Patients Filling a 30-Day or 90-Day Supply by EBM Class Among Patients Surviving to Twelve Months.

	Total N	30-Day Fill % of Patients	90-Day Fill % of Patients
Overall			
Statins	269,919	87.0	13.0
β-Blockers	272,549	87.7	12.3
ACEi/ARBs	183,477	85.4	14.6
P2Y$_{12}$ Inhibitors	276,361	90.3	9.7

Table S3. Monthly Percentage of Overall Within-Class Switches and Dosing Changes That Occurred within the First 4 Months after the Index Prescription Fill among Patients who Filled a 90-Day Supply.

	Within-Class Switch* % of Patients				Dosing Change* % of Patients			
	Month 1	Month 2	Month 3	Month 4	Month 1	Month 2	Month 3	Month 4
Statins	16.0	12.3	12.7	10.2	12.1	11.7	13.3	11.0
β-Blockers	37.1	14.2	10.5	7.5	17.8	15.4	12.6	8.9
ACEi/ARBs	24.3	15.1	11.5	9.8	16.9	16.8	12.3	10.1
P2Y$_{12}$ inhibitors	30.6	11.4	9.9	8.2	18.2	4.5	9.1	13.6

Table S4. Rates of 12-Month Adherence (PDC > 80%) by EBM Class and Pharmacy Type among Patients who Filled a 90-Day Supply.

	Mail Order Pharmacy N (% Adherent)	Store Pharmacy N (% Adherent)	p
Statins	3,103 (76.0)	31,885 (81.2)	0.033
β-Blockers	2,653 (66.2)	30,665 (70.2)	<0.001
ACEi/ARBs	2,400 (67.0)	24,248 (68.8)	0.384
P2Y$_{12}$ inhibitors	1,715 (73.6)	24,848 (75.6)	<0.001

EBM = evidence based medication, PDC = proportion of days covered.

Store pharmacies include independent and chain retail stores and pharmacies within grocery or multi-purpose stores.

Figure S1. Adherence at 12-Months by EBM Class and Prescription Days-Supply after Censoring the First 90 Days after the Index MI Discharge.