Original Investigation

Multifaceted Intervention to Improve Medication Adherence and Secondary Prevention Measures After Acute Coronary Syndrome Hospital Discharge
A Randomized Clinical Trial

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IMPORTANCE Adherence to cardioprotective medication regimens in the year after hospitalization for acute coronary syndrome (ACS) is poor.

OBJECTIVE To test a multifaceted intervention to improve adherence to cardiac medications.

DESIGN, SETTING, AND PARTICIPANTS In this randomized clinical trial, 253 patients from 4 Department of Veterans Affairs medical centers located in Denver (Colorado), Seattle (Washington); Durham (North Carolina), and Little Rock (Arkansas) admitted with ACS were randomized to the multifaceted intervention (INT) or usual care (UC) prior to discharge.

INTERVENTIONS The INT lasted for 1 year following discharge and comprised (1) pharmacist-led medication reconciliation and tailoring; (2) patient education; (3) collaborative care between pharmacist and a patient's primary care clinician and/or cardiologist; and (4) 2 types of voice messaging (educational and medication refill reminder calls).

MAIN OUTCOMES AND MEASURES The primary outcome of interest was proportion of patients adherent to medication regimens based on a mean proportion of days covered (PDC) greater than 0.80 in the year after hospital discharge using pharmacy refill data for 4 cardioprotective medications (clopidogrel, β-blockers, 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors [statins], and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers [ACEI/ARB]). Secondary outcomes included achievement of blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) level targets.

RESULTS Of 253 patients, 241 (95.3%) completed the study (122 in INT and 119 in UC). In the INT group, 89.3% of patients were adherent compared with 73.9% in the UC group ($P = .003$). Mean PDC was higher in the INT group (0.94 vs 0.87; $P < .001$). A greater proportion of intervention patients were adherent to clopidogrel (86.8% vs 70.7%; $P = .03$), statins (93.2% vs 71.3%; $P < .001$), and ACEI/ARB (93.1% vs 81.7%; $P = .03$) but not β-blockers (88.1% vs 84.8%; $P = .59$). There were no statistically significant differences in the proportion of patients who achieved BP and LDL-C level goals.

CONCLUSIONS AND RELEVANCE A multifaceted intervention comprising pharmacist-led medication reconciliation and tailoring, patient education, collaborative care between pharmacist and patients' primary care clinician and/or cardiologist, and voice messaging increased adherence to medication regimens in the year after ACS hospital discharge without improving BP and LDL-C levels. Understanding the impact of such improvement in adherence on clinical outcomes is needed prior to broader dissemination of the program.

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Adherence to cardioprotective drug regimens, in particular 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEI/ARB), and antiplatelet agents following hospital discharge for acute coronary syndrome (ACS) has been found to be poor in several studies.[1-5] In addition, among those who were taking their cardiac medications, one-third of patients discontinued using at least 1 medication by 1 month.[2] Longer-term adherence continued to decline, and at 1-year following the index cardiac event, only approximately 60% of patients were still taking statin medications.[3] Cohort and population-based studies have shown that patients with lower adherence to cardioprotective drug regimens following acute myocardial infarction (MI) were associated with a higher 1-year and long-term mortality.[1,2,4,5]

We describe herein the results of a multisite, patient-level prospective randomized clinical trial testing the effect of a multifaceted patient-centered intervention to improve adherence to cardioprotective medication regimens (as determined by pharmacy refill data) vs usual care for veterans following hospitalization for ACS. The details of the protocol have been previously reported.[6] The intervention comprised pharmacist-led medication reconciliation and tailoring, patient education, collaborative care involving pharmacists, and automated telephone voice messaging calls.

Methods

Study Population and Recruitment

This study was conducted at 4 Department of Veterans Affairs (VA) medical centers (Denver, Colorado; Little Rock, Arkansas; Seattle, Washington; and Durham, North Carolina) and was approved by the institutional review board at each respective site. Written informed consent was obtained from each study participant. Recruitment began July 1, 2010, in Denver and Seattle; September 1, 2010, in Little Rock; and July 1, 2011, in Durham. Patients admitted with ACS as the primary reason for hospital admission and used the VA for their usual care were screened for eligibility. Acute coronary syndrome was defined as MI or unstable angina using standard definitions. Exclusion criteria included (1) patients admitted for primary noncardiac diagnosis who developed ACS as a secondary condition (eg, perioperative MI); (2) planned discharge to nursing home or skilled nursing facility; (3) irreversible, noncardiac medical condition (eg, metastatic cancer) likely to affect 6-month survival or inability to execute study protocol; (4) lack of telephone or cell phone; (5) VA not a primary source of care in the future; (6) fill medications at non-VA pharmacy; and (7) pregnancy.[7]

Study Procedures

Eligible patients with ACS were randomized using blocked randomization stratified by study site in a 1:1 ratio to INT or UC. The allocation sequence was concealed until a patient consented to participate and was generated centrally using the graphical user interface implemented for the study. The multifaceted intervention comprised the following 4 main components, which were previously described in greater detail[6]:

1. *Medication Reconciliation and Tailoring:* Within 7 to 10 days of hospital discharge, a pharmacist met with patients via an in-person clinic visit or telephone call to address medication problems or adverse effects and reconciled differences in medications between the prehospital and postdischarge regimens. The pharmacist also provided patients with a pill box for those who did not have one and instructed the patient on how to fill the pill box. One month later, the pharmacist called the patient to assess any interim new medications as well as adverse effects to medications and/or adherence issues. At that point, the pharmacist attempted to synchronize refill dates of cardiac medications so that refill would all occur on the same date or as close as possible. The pharmacist answered any other questions related to medications, emphasizing the importance of continuing to take medications as prescribed.
2. *Patient Education:* Patients received education about medications at the point of hospital discharge but also continued to receive education following hospital discharge to ensure retention of the information by study pharmacist. This occurred at the 1-week and 1-month visit following discharge during interactions with the pharmacist. Thereafter, educational messages were provided through automated voice messages and pharmacist telephone calls when requested by the patient.
3. *Collaborative Care:* The pharmacist notified the patient's primary care clinician and/or cardiologist (if the patient had one) that the patient was enrolled in the adherence intervention by having them cosign the pharmacists' initial enrollment note in the computerized medical record. This enrollment note included the pharmacists' contact information so that the primary care clinician/cardiologist could reach them for questions or clarifications.
4. *Voice Messaging:* The voice messaging system contacted patients at regularly scheduled intervals. There were 2 types of calls: medication reminder and medication refill calls. The medication reminder calls occurred monthly. The medication refill calls were synchronized to when a medication refill was due. The calls occurred 14 days prior to the refill due date, 7 days prior to the refill due date, and on the due date. During months 2 through 6 of the intervention, patients received both medication reminder (monthly) and medication refill calls (timed to refill due dates) for the 4 medications of interest. During months 7 through 12 of the intervention, patients only received medication refill calls.

Study Visit Overview

The baseline visit occurred prior to hospital discharge when patients were randomized to intervention or usual care. Consistent with usual practices at each site, patients in both groups received standard ACS hospital discharge instructions (eg, numbers to call, follow-up appointments, diet and exercise advice), a discharge medication list, and educational information about cardiac medications. For patients randomized to intervention, an appointment for an in-person visit or telephone consultation with a pharmacist was scheduled by study

personnel within 7 to 10 days of discharge. Both intervention and usual care patients were scheduled for a 12-month clinic visit. At this visit, 3 BP measurements were taken in standard fashion by someone blinded to study group assignment (eg, after 5 minutes of rest and 2 minutes apart between measurements). The final BP was based on the mean value of the latter 2 measurements. In addition, patients were referred for laboratory blood draw to assess low-density lipoprotein cholesterol (LDL-C) levels. If a patient had a value checked within 3 months and the dose of antilipemic medication(s) did not change, this value was used as the end-of-study LDL-C measurement for outcomes assessment.

Analysis

We planned to recruit 280 patients over an 18-month period and to follow patients for 12 months to have 80% power to detect a difference of 15% in the proportion of patients who were adherent to their cardioprotective medications. Because of the slower than anticipated enrollment, a fourth site (Durham) was added to the initial 3 sites and enrollment was extended for another 3 months. Recruitment ended on March 31, 2012, and the last date of follow-up was March 31, 2013.

The primary outcome was the proportion of patients who were adherent to cardioprotective medication regimens (β-blockers, statins, clopidogrel, and ACEI/ARB) in the year following hospitalization for ACS. Pharmacy data were obtained from the VA Central Data Warehouse (CDW), which included medication names and dates of medication refills and cancellations. Medication adherence was calculated based on the proportion of days covered (PDC) during the 365-day follow-up that a patient had a medication available, adjusted for inpatient days, medication cancellation dates, medication switches, medication fills prior to enrollment date, and death. The proportion was adjusted by excluding days from both the numerator and denominator and assuming that patients did not deplete their medication supply on those excluded days. All inpatient days were excluded. If a medication therapy was cancelled, the days between the cancellation date and the next within-class medication fill were excluded. If a patient switched medications within a class, the patients' medication supply was replaced with the new medication supply. If a patient died during follow-up, all days following the death were excluded. We applied this algorithm to the 180 days prior to the enrollment date to capture the existing medication supply at enrollment date, but only the days during the 365-day follow-up contributed to the final proportion. Adherence for each medication class ranged from 0 to 1.00 (perfect adherence) and was then averaged across all nonmissing classes of medications to derive the summary PDC. Adherent patients were defined based on a summary PDC greater than 0.80, as consistent with the literature.

The secondary outcomes were the proportion of patients reaching blood pressure (BP) goals (<140/90 mm Hg [<130/80 mm Hg for patients with diabetes or chronic kidney disease]) and LDL-C goals (<100 mg/dL [to convert to millimoles per liter, multiply by 0.0259]) at 12 months.[8] Tertiary outcomes included hospitalization for MI, coronary revascularization within the VA, and all-cause mortality. The occurrence of a MI hospitalization was based on *International Classification of Diseases, Ninth Revision* (*ICD-9*) code 410. Coronary revascularization procedures (ie, percutaneous coronary intervention [PCI] with or without stenting and coronary artery bypass graft surgery) were based on *ICD-9* and *Current Procedural Terminology* (CPT) codes. Mortality data were obtained from the VA vital status file.

We used an intent-to-treat approach for all analyses. Baseline traits were summarized as means and standard deviations for numeric variables or frequency counts and percentages for categorical variables. Unpaired *t* tests were used to compare continuous variables, and χ^2 tests were used to compare categorical variables across the intervention and usual care. We used a log-rank test to compare the hazard of first hospitalization for MI, revascularization, or death. We used a Wilcoxon rank sum test to compare PDCs between study arms. For all other outcomes, χ^2 tests and *t* tests were used for comparisons, as appropriate. In sensitivity analysis, we also assessed change in LDL-C level between baseline and follow-up visit, and LDL-C level at end of study by statin adherence. We also evaluated change in systolic BP and diastolic BP levels between baseline and follow-up visit.

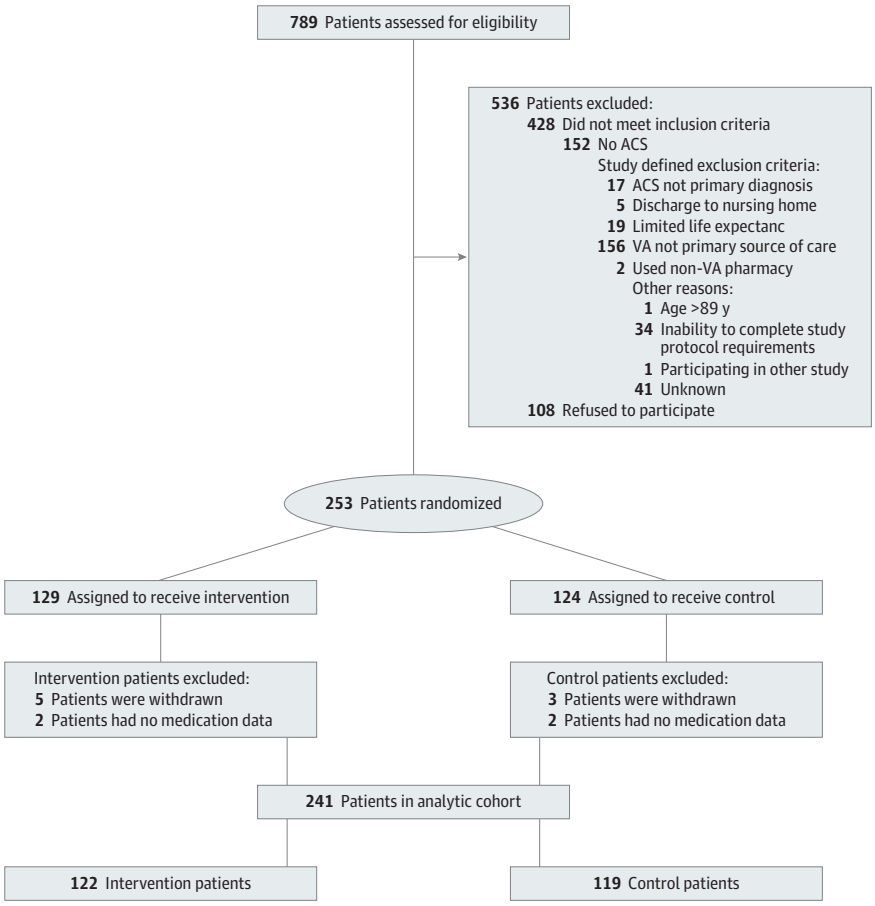
Cost Analysis

The cost analysis was conducted from the perspective of the VA health care system. Costs of the intervention were measured through direct observation of processes used by pharmacists at 3 sites for the 7 to 10-day follow-up visit and at 2 sites for the 1-year visit. A process flow diagram was used to identify typical processes, time required, and steps to complete. Resources were attached to each of these steps and then attached to input costs (wages and materials). Wage rates were based on national VA average wages for each job category plus a standard 30% fringe benefit rate. For intervention patients, the full cost of the intervention was assigned if they survived to 12 months, and a prorated cost based on the process flow model was assigned for patients with shorter survival. The VA's patient care costs were assessed using data from the VA Decision Support System (DSS) National Data Extract, which captured each patient's inpatient, outpatient, and pharmacy costs for up to 12 months following initial hospital discharge. Pharmacy costs were stratified to reflect ACS-related and non-ACS-related drugs and were standardized to reflect the cost per covered day to adjust for varying follow-up periods or number of study drug prescriptions. Median and interquartile ranges of costs and utilization were calculated for both the intervention and usual care group. We tested for differences in the distributions using a Wilcoxon rank sum test.

Data and Safety Monitoring

An Internal Safety Committee that comprised the study site principal investigators met quarterly to review adverse events. The committee reviewed each adverse event to determine whether the event was study related and to ensure compliance with local institutional review board reporting requirements. Further oversight was provided by Health Services Research and Development Service National Data Safety Management Board, which convened yearly.

Figure. Patient Flowchart



ACS indicates acute coronary syndrome; VA, Department of Veterans Affairs.

Results

Of 789 patients screened, 361 patients were potentially eligible and 253 patients were randomized—129 to intervention and 124 to usual care (**Figure**). The patients were predominantly male (approximately 98%), and the mean age was approximately 64 years. Baseline characteristics of the patients were comparable (**Table 1**). Almost half of the patients (approximately 45%) had diabetes, and two-thirds had a history of coronary artery disease. During the hospitalization, approximately 40% in each group underwent PCI. Usual care patients were more likely to undergo coronary artery bypass graft surgery (17.1% vs 6.7%; $P = .02$).

For the primary outcome of medication adherence based on the 4 classes of medications, a greater proportion of intervention patients were adherent compared with usual care patients (89.3% vs 73.9%; $P = .003$) (**Table 2**). The mean PDC for the 4 medications combined was greater for intervention patients (0.94 vs 0.87; $P < .001$). Furthermore, a statistically significant greater proportion of intervention patients were classified as adherent for statins (93.2% vs 71.3%; $P < .001$), ACEI/ARB (93.1% vs 81.7%; $P = .03$), and clopidogrel (86.8% vs 70.7%; $P = .03$). For β-blockers, the proportion of adherent patients was comparable between the 2 groups (88.1% vs 84.8%; $P = .59$). The PDC values for each class of medications are listed in Table 2 and demonstrated a 6% to 11% greater PDC in the intervention group except for β-blockers.

For the secondary outcomes, there was no statistically significant differences in the proportion of patients reaching BP ($P = .23$) or LDL-C level ($P = .14$) targets. There was a trend toward greater BP control (58.6% vs 48.9%), decline in systolic BP (−12 vs −4 mm hg), and decline in diastolic BP (−5 vs −3 mm hg) for intervention patients; however, these comparisons were not statistically significantly different (**Table 3**). For the LDL-C outcome, more than one-third (37%) of patients did not have a follow-up laboratory evaluation, which differed by study arm (33.6% [intervention] vs 40.3% [usual care]). Patients with missing LDL-C measurements were less adherent to statin medication compared with those with a follow-up laboratory evaluation (74% vs 96%; $P = .02$). There was no statistically significant difference in change in LDL-C level (−13 vs −12 mg/dL) between intervention and usual care. When change in LDL-C level was stratified by randomization group and adherence categories, adherent patients in the intervention (−15.5 mg/dL) and usual care (−13.1 mg/dL) groups had similar magnitudes of LDL-C level decline. Interestingly, nonadherent usual care patients also had a decline in LDL-C level (−9.3 mg/dL),

Table 1. Baseline Characteristics of the Study Population

Variable	Usual Care (n = 119)	Intervention (n = 122)	*P* Value
Age, mean (SD), y	64.0 (8.57)	63.8 (9.25)	.84
BMI, mean (SD)	30.6 (5.92)	31.1 (6.11)	.52
Male, No. (%)	116 (97.5)	120 (98.4)	.98
White race, No. (%)	89 (74.8)	100 (82)	.23
Diabetes mellitus, No. (%)	47 (39.5)	62 (50.8)	.10
Prior heart failure, No. (%)	13 (10.9)	17 (13.9)	.61
Peripheral arterial disease, No. (%)	10 (8.4)	14 (11.6)	.55
Chronic kidney disease, No. (%)	28 (23.5)	28 (23.0)	.99
Smoker, No. (%)	85 (71.4)	79 (65.3)	.38
Chronic lung disease, No. (%)	23 (19.3)	25 (20.5)	.95
Prior CAD, No. (%)	79 (66.4)	79 (64.8)	.90
Cerebrovascular disease, No. (%)	8 (6.7)	10 (8.2)	.85
Hypertension, No. (%)	106 (89.1)	113 (92.6)	.46
Hyperlipidemia, No. (%)	103 (86.6)	103 (84.4)	.78
Type of ACS, No. (%)			
STEMI	15 (12.6)	18 (14.8)	.88
NSTEMI	36 (30.3)	35 (28.7)	
Unstable angina	68 (57.1)	69 (56.6)	
In-hospital revascularization, No. (%)			
PCI	47 (39.8)	53 (43.8)	.62
Drug-eluting stent	37 (84.1)	30 (78.9)	.75
CABG	19 (17.1)	8 (6.7)	.02

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CABG, coronary artery bypass graft; CAD, coronary artery disease; NSTEMI, non–ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Table 2. Adherence Between Intervention and Usual Care Groups

Variable	Usual Care (n = 119)	Intervention, No. (%) (n = 122)	*P* Value	Absolute Difference in Proportions, % (95% CI)	NNT
Composite adherence (PDC >0.80), No. (%) [a]	88 (73.9)	109 (89.3)	.003	15 (5 to 26)	6.7
Average composite PDC, mean (SD)	0.87 (0.15)	0.94 (0.11)	<.001	NA	NA
Statin (n = 232)					
Adherent, No. (%)	82 (71.3)	109 (93.2)	<.001	22 (12 to 32)	4.5
PDC, mean (SD)	0.84 (0.21)	0.95 (0.12)	<.001	NA	NA
ACEI/ARB (n = 194)					
Adherent, No. (%)	76 (81.7)	94 (93.1)	.03	11 (1 to 22)	9.1
PDC, mean (SD)	0.89 (0.2)	0.95 (0.12)	.005	NA	NA
β-Blocker (n = 230)					
Adherent, No. (%)	95 (84.8)	104 (88.1)	.59	3 (−6 to 13)	33.3
PDC, mean (SD)	0.91 (0.16)	0.94 (0.13)	.11	NA	NA
Clopidogrel (n = 151)					
Adherent, No. (%)	53 (70.7)	66 (86.8)	.03	16 (2 to 30)	6.2
PDC, mean (SD)	0.83 (0.25)	0.91 (0.21)	.03	NA	NA

Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker; NNT, number needed to treat; PDC, proportion of days covered.

[a] Based on the 4 groups of cardiac medications of interest: β-blockers, statins, clopidogrel, and ACEI/ARB.

whereas nonadherent intervention patients had a LDL-C level increase (+15.4 mg/dL) (**Table 4**). Finally, there were no statistically significant differences between the 2 groups for rehospitalization for MI, revascularization, or death (Table 3).

Over 12 months, each intervention patient received a mean of 3 hours 51 minutes of additional pharmacist time (valued at $62.02 hourly), 35 minutes of additional cardiologist time (valued at $186.97 per hour), and a pill box (valued at $5.00), for a total of $359.77 in costs directly related to the intervention. The difference in median cost for the 2 groups for all medications, ACS-related medications, and non-ACS–related medications was very small and not statistically different (Table 3). Median ACS-related medication costs were approximately $0.78 per covered day (IQR, $0.42 to $1.59), and median overall medication costs were $8 per covered day (IQR, $4.27 to $14.32). There were no statistically significant differences between the 2 groups in median number of VA outpatient visits (49 and 54, respectively) during the year (*P* = .11), which trans-

Table 3. Clinical Outcomes by Treatment Group

Variable	Usual Care (n = 119)	Intervention (n = 122)	*P* Value
Secondary prevention measures			
LDL-C <100 mg/dL, No./total[a] (%)	59/71 (83)	58/81 (72)	.14
LDL-C, mean (SD), mg/dL	76 (25)	80 (32)	.37
Change in LDL-C, mean (SD), mg/dL	−12 (31)	−13 (38)	.90
BP <140/90 mm Hg (<130/80 mm Hg for DM or CKD), No./total[a] (%)	46/94 (49)	58/99 (59)	.23
BP, mean (SD), mm Hg			
Systolic	132 (21)	130 (20)	.50
Diastolic	75 (12)	76 (12)	.50
Change in systolic BP	−4 (27)	−12 (27)	.07
Change in diastolic BP	−3 (18)	−5 (16)	.39
Clinical end points, No. (%)			
Mortality	9 (7.6)	11 (9.0)	.86
MI	5 (4.2)	8 (6.6)	.60
Revascularization	21 (17.6)	14 (11.5)	.24
Costs, median (IQR), $			
Cost of intervention	0	360	
Cardiac medication costs[b]	663 (359-1278)	722 (321-13 887)	.70
Total medication costs	2724 (1198-4766)	2887 (1698-4607)	.43
Total outpatient costs	11 691 (6323-20 584)	13 086 (6195-22 563)	.53
Total inpatient costs	14 287 (5439-23 983)	11 294 (5790-31 727)	.68
Total intervention, medication, outpatient, and inpatient costs	19 989 (9584-37 039)	19 901 (10 683-37 714)	.56

Abbreviations: BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction.

SI conversion factor: To convert LDL-C to millimoles per liter, multiply by 0.0259.

[a] Total number of patients with measurements.

[b] β-Blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, statins, and clopidogrel.

Table 4. Sensitivity Analysis of LDL-C Levels by Randomization Group and Adherence

	Usual Care		Intervention	
Variable	Not Statin Adherent	Statin Adherent	Not Statin Adherent	Statin Adherent
Patients, No.	33	82	8	109
Change in LDL-C level, mean (SD), mg/dL	−9.3 (39.1)	−13.1 (28.7)	15.4 (28.6)	−15.5 (38.2)
LDL-C level at end of study, mean (SD), mg/dL	88.3 (26.9)	72.3 (23.0)	114.4 (29.7)	77.4 (31.1)

Abbreviation: LDL-C, low-density lipoprotein cholesterol.

SI conversion factor: To convert LDL-C to millimoles per liter, multiply by 0.0259.

lated into similar costs. Furthermore, there were no differences in inpatient costs, stays, or costs per inpatient day between the 2 groups. Including the direct costs of the intervention, annual costs for intervention and usual care patients were similar.

Discussion

The objective of this study was to test the effectiveness of a multifaceted intervention to improve adherence to cardioprotective medications in the year after ACS hospital discharge. We found that our intervention comprising pharmacist-led medication reconciliation and tailoring, patient education, collaborative care involving pharmacists, and automated telephone voice messaging calls improved the proportion of adherent patients by approximately 15% and the mean adherence to the 4 medications combined by approximately 7%. There was no statistically significant difference in the secondary prevention measures or clinical outcomes over the 12 months of the study.

There have been few prior studies that have focused on improving medication adherence among patients discharged following ACS hospitalization. Smith et al[9] demonstrated that 2 mailed communications to patients after MI discharge improved adherence to β-blockers by 4.3%. Choudhry et al[10] showed reductions in adherence of 4% to 6% and in vascular events and revascularization with elimination of copayments for cardiovascular medications (ie, β-blockers, statins or ACEI/ARB) after MI discharge. Important differences should be highlighted for our study compared with these studies. First, we obtained informed consent from each study participant in contrast to prior studies where cluster randomization occurred and individual patient consent was not required. Because of this, the patients in our study were more adherent because they volunteered to participate in a study, and this is reflected in the high adherence rates in the usual care patients (PDC of 0.87). Next, we only followed up patients for 12 months after hospital discharge and did not see a statistically significant difference in clinical events. In the study by Choudhry et al,[10] the differences in clinical end points between full and usual prescription coverage began to diverge after 12 months. It will be important for us to continue to follow up patients longer to assess whether the higher adherence in the intervention group translates into improved clinical outcomes. Despite these differences, we were able to demonstrate a similar magnitude of improvement in adherence compared with the prior studies. Together, these stud-

ies provide an increasing evidence base of interventions to improve adherence to cardiac medication regimens after ACS discharge.

Our intervention included multiple components, all of which have been shown to improve adherence to medication regimens among patients with cardiovascular diseases.[11-14] While our study was conducted within an integrated health care delivery system, none of the components were unique to it and can be replicated in other health care settings. In our study, a pharmacist reconciled prehospital and posthospital medications within 7 to 10 days of discharge and contacted patients at 30 days to address any interim medication issues; contact thereafter was based on patient needs. The pharmacist notified the patient's primary care clinician and/or cardiologist of any interim changes and provided education to patients focusing on the importance of adherence. These findings add to a prior VA study[15] focused on collaborative care between primary care clinicians and specialists for patients with chronic stable angina by demonstrating that a multifaceted intervention, with 1 component involving collaborative care, improves adherence to secondary prevention medications. Finally, automated calls that were both educational and reminders about medication refills were delivered to patients. Delivery of these intervention components is likely facilitated within an integrated health care delivery system, but each of the components should be able to be implemented elsewhere. It will be important to replicate this intervention in other health care delivery systems as well as determine if a single component has the greatest impact on adherence.

The annual incremental program cost to the VA for the multifaceted intervention was modest at $360 per patient. Most of the costs were related to pharmacist time to review medications and to meet with the patient soon after ACS discharge. Increased medication adherence in our study did not lead to more medication costs for the intervention group. Including the costs of the intervention, median total VA costs over 12 months for the patients in the intervention were approximately the same as costs for usual care, suggesting that the intervention improved medication adherence without increasing VA costs. These results are in contrast to the study by Choudhry et al,[10] where there were higher medication costs for the insurance company but no difference in total health care spending between full and usual prescription coverage groups. We plan to continue follow-up of patients beyond the initial 12 months to assess whether there are differences in outcomes and costs in the longer term. In the interim, the modest costs associated with the intervention suggest that the intervention may be feasible to implement more broadly. Individual health care systems will need to weigh the costs and benefits of such an intervention to improve adherence.

There are several limitations that should be acknowledged. This study was conducted at 4 VA medical centers, which is predominantly composed of men and may not be generalizable to other patient populations. While prior studies have shown that male patients may be less adherent compared with female patients, adherence rates overall in this study for both groups were very high, and prior studies have not demonstrated a differential intervention effect in adherence by sex.[16] Second, we used pharmacy refill data to assess adherence in contrast to clinical trials that have traditionally used pill counts, although refilling a prescription does not mean the patient actually ingested the medication. However, the use of pharmacy refill data has been validated as a measure of adherence and used in multiple other adherence intervention studies.[16] Furthermore, in our assessment of adherence, we were able to account for medication discontinuation and hospitalized days in the VA, which improves our estimate of adherence. Third, we included all patients who consented to participate in the study regardless of their prior adherence behavior. Consideration should be given in the future about targeting patients who have exhibited nonadherence to medications because these patients may obtain a greater benefit with an adherence intervention. Finally, there was no statistically significant difference in the proportion of patients achieving BP and LDL-C level targets, which were the a priori secondary outcomes. However, our sensitivity analyses of the BP results suggest that intervention patients had greater declines in systolic and diastolic BPs. Regarding LDL-C, adherent patients were more likely to get follow-up LDL-C laboratory evaluations, and accordingly we saw declines in LDL-C levels in both intervention and usual care patients, which may have attenuated the intervention effect on LDL-C levels. Additional studies are needed to assess the association between adherence and these clinical outcomes in a larger patient sample.

In conclusion, we demonstrated an improvement in adherence to cardioprotective medications after ACS hospital discharge with use of a multifaceted intervention but not a change in LDL-C or BP levels. Additional studies are needed to understand the impact of the magnitude of adherence improvement shown in our study on clinical outcomes prior to broader dissemination of such an adherence program.

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