SPECIAL ARTICLE

Full Coverage for Preventive Medications after Myocardial Infarction

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ABSTRACT

BACKGROUND

Adherence to medications that are prescribed after myocardial infarction is poor. Eliminating out-of-pocket costs may increase adherence and improve outcomes.

METHODS

We enrolled patients discharged after myocardial infarction and randomly assigned their insurance-plan sponsors to full prescription coverage (1494 plan sponsors with 2845 patients) or usual prescription coverage (1486 plan sponsors with 3010 patients) for all statins, beta-blockers, angiotensin-converting–enzyme inhibitors, or angiotensin-receptor blockers. The primary outcome was the first major vascular event or revascularization. Secondary outcomes were rates of medication adherence, total major vascular events or revascularization, the first major vascular event, and health expenditures.

RESULTS

Rates of adherence ranged from 35.9 to 49.0% in the usual-coverage group and were 4 to 6 percentage points higher in the full-coverage group ($P<0.001$ for all comparisons). There was no significant between-group difference in the primary outcome (17.6 per 100 person-years in the full-coverage group vs. 18.8 in the usual-coverage group; hazard ratio, 0.93; 95% confidence interval [CI], 0.82 to 1.04; $P=0.21$). The rates of total major vascular events or revascularization were significantly reduced in the full-coverage group (21.5 vs. 23.3; hazard ratio, 0.89; 95% CI, 0.90 to 0.99; $P=0.03$), as was the rate of the first major vascular event (11.0 vs. 12.8; hazard ratio, 0.86; 95% CI, 0.74 to 0.99; $P=0.03$). The elimination of copayments did not increase total spending ($66,008 for the full-coverage group and $71,778 for the usual-coverage group; relative spending, 0.89; 95% CI, 0.50 to 1.56; $P=0.68$). Patient costs were reduced for drugs and other services (relative spending, 0.74; 95% CI, 0.68 to 0.80; $P<0.001$).

CONCLUSIONS

The elimination of copayments for drugs prescribed after myocardial infarction did not significantly reduce rates of the trial's primary outcome. Enhanced prescription coverage improved medication adherence and rates of first major vascular events and decreased patient spending without increasing overall health costs. (Funded by Aetna and the Commonwealth Fund; MI FREEE ClinicalTrials.gov number, NCT00566774.)

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The use of medications based on solid clinical evidence has contributed substantially to reductions in cardiovascular morbidity and mortality.[1,2] For patients with acute myocardial infarction, prescribing of these highly effective therapies is now nearly universal at the time of hospital discharge in the United States,[3,4] but important gaps in care persist thereafter. Some patients never fill their first prescriptions,[5] and most have poor adherence to medication regimens over time.[6]

Drug costs are central among the many factors that contribute to medication underuse.[7,8] A third of Americans report that they did not fill a prescription or reduced the dose in the past year because of out-of-pocket costs.[9] Even among those with insurance, medication utilization varies according to the comprehensiveness of patients' insurance coverage.[8,10] Accordingly, the elimination of out-of-pocket costs for evidence-based therapies may promote the appropriate use of medication[11] and reduce rates of preventable events.[12] Observational studies suggest that this strategy increases targeted medication use,[13,14] but its effect on actual health outcomes and spending has not been rigorously assessed.

Methods

Study Design

The Post-Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) trial was an investigator-initiated, cluster-randomized, controlled policy study. Details of the study design have been published previously.[15] The trial protocol was designed and written by the academic investigators and conducted in collaboration with the sponsor, Aetna, which administered the changes in study-benefit design. The academic authors analyzed the trial data using an independent copy of the study database and vouch for analytic accuracy and completeness as well as the fidelity of the report to the study protocol. The study was monitored by an independent data and safety monitoring committee.

Study Population

Patients were eligible for inclusion in the study if they received both medical and prescription drug benefits through Aetna, a large commercial insurer in the United States, and if they had been discharged from the hospital with a principal or secondary diagnosis code of *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) 410 (except when the fifth digit was 2) and a length of stay of 3 to 180 days. This algorithm had a positive predictive value of 97%, a sensitivity of 96%, and a specificity of 99% for myocardial infarction.[15,16] Patients were excluded if they were enrolled in a health savings account, since these plans already offered full coverage for the study medications, or if they were 65 years of age or older at the time of hospital discharge, since Medicare was the primary health insurer for such patients.

Randomization and Study Procedures

Randomization occurred at the level of plan sponsor (i.e., the employer, union, government, or association that sponsors a particular benefits package) so that all eligible employees of a given plan sponsor received the same coverage after randomization. Plan sponsors were categorized into blocks on the basis of whether they were nationally based (a Fortune 500 company with more than 3000 employees or a governmental plan sponsor) and the baseline average copayments required for study medications. All plan sponsors were contacted by mail before the initiation of the study or as soon as they began providing benefits through Aetna and were given the opportunity to opt out of study participation. Plans that did not opt out were randomly assigned to full coverage (full-coverage group) or usual pharmacy benefits (usual-coverage group) with the use of a random-number generator, and all subsequently eligible patients of that plan sponsor were assigned to the same group.

Pharmacy benefits for patients in the full-coverage group were changed so that they had no cost sharing for any brand-name or generic statin, beta-blocker, angiotensin-converting–enzyme (ACE) inhibitor, or angiotensin-receptor blocker (ARB) for every prescription after randomization. All copayments and coinsurance were waived at the point of care (i.e., the pharmacy), as was any contribution to a patient's deductible. The date on which a patient was assigned to a study group was defined as the randomization date. Because the identification of patients was based on claims submitted by hospitals to Aetna, there was a lag between hospital discharge and randomization.

Upon ascertainment of eligibility, all patients were contacted by mail and phone and told of the importance of taking their medications as prescribed (see Appendix A in the Supplementary Ap-

pendix, available with the full text of this article at NEJM.org). Patients in the full-coverage group were also informed of the change in their pharmacy benefits. Medication choices and treatment decisions were left entirely to the discretion of the treating physicians and their patients. Because all patients, at a minimum, received their usual level of prescription-drug coverage, no specific patient-level written informed consent was sought. This study was approved by the institutional review board at Brigham and Women's Hospital.

STUDY OUTCOMES

We evaluated medication adherence by calculating the mean medication possession ratio (i.e., the number of days a patient had a supply of each medication class available, divided by the number of days of eligibility for that medication). Ratios were multiplied by 100 to generate absolute adherence percentages. We also calculated the proportion of patients who had full adherence (defined as a medication possession of ≥80%) to each and to all three study medication classes throughout follow-up.[17] Different agents within a therapeutic class were considered interchangeable. Patients who did not fill a particular prescription after randomization were considered to be nonadherent. In addition, we evaluated adherence among patients who filled at least one prescription during follow-up. In post hoc analyses, we measured adherence to drugs for which copayments were unchanged (i.e., clopidogrel, oral hypoglycemics, inhaled bronchodilators, proton-pump inhibitors, and antidepressants).

The primary clinical outcome was a composite of the first readmission for a major vascular event (fatal or nonfatal acute myocardial infarction, unstable angina, stroke, or congestive heart failure) or coronary revascularization (coronary bypass, stenting, or angioplasty). Prespecified secondary clinical outcomes included the rate of total major vascular events or revascularization, allowing for the occurrence of more than one event per patient and the time to the first major vascular event (i.e., the primary composite outcome excluding revascularization). In the recurrent events analysis, we excluded transfers between institutions (defined as readmission ≤2 days after the previous discharge), counted only one diagnosis per treatment episode, and counted each specific outcome (e.g., stroke) only one time per patient. All outcomes were assessed by applying validated algorithms with specificities of at least 95% to Aetna's databases of health care utilization.[15] This source contains complete data for filled prescriptions, procedures, physician encounters, hospitalizations, and inpatient deaths.

We evaluated the effect of the intervention on health care spending by patients and insurers using the allowed amounts appearing in the insurers' claims data for prescription medications, nondrug medical services (i.e., physician visits, emergency room admissions, hospitalizations, and outpatient procedures), and the combination of these two factors after the assignment of the patient to a study group. We evaluated cardiac-specific spending on the basis of relevant codes for coronary artery disease, congestive heart failure, stroke, hypertension, hyperlipidemia, arrhythmia, and other diseases of the heart and circulatory system.

STATISTICAL ANALYSIS

We planned to recruit 7500 patients over a 1.5-year period and to follow them for a minimum of 1 year in order to achieve a power of 90% to detect a between-group difference of 20% in the relative risk of the primary outcome. Because of slower-than-anticipated enrollment, the trial steering committee accepted a recommendation from the independent data and safety monitoring committee that equivalent power could be obtained if a total of 1000 primary outcome events were to occur. The steering committee then adapted the trial by extending enrollment by 15 months and reducing minimum follow-up to 3 months.

All analyses were performed on the basis of the intention-to-treat principle. We used generalized estimating equations with adjustment for the cluster and block-randomized design to compare rates of medication adherence and health spending. We used an identity link function with normally distributed errors to compare medication possession ratios and used a logit link function with binary distributed errors to compare rates of full adherence. Health spending was evaluated with the use of a log-link function with variances proportional to the mean.[18] In these analyses, data from patients were censored on the date of death or loss of insurance eligibility or at the end of the study period on November 30, 2010, whichever came first.

The primary clinical outcome and rates of major vascular events were evaluated as the time to the first event after randomization. The exposure

time was calculated as the time from randomization to the date of an outcome event, loss of insurance eligibility, or the end of the study period. We used Cox proportional-hazards models to estimate hazard ratios and 95% confidence intervals. We adjusted for clustering using a robust sandwich estimator for the covariance matrix.[19] The rate of total major vascular events or revascularization was compared with the Cox model extension, which allows for the estimation of multiple correlated failure times, as described by Wei and colleagues.[20] In additional analyses, we adjusted for age, sex, and differences in rates of coexisting illnesses between the study groups.[21] Subgroup analyses were performed according to age, sex, baseline copayment levels, presence or absence of coexisting illnesses, and patterns of medication use before randomization.

RESULTS

PATIENTS

Of the 6768 potentially eligible patients, 913 (13.5%) were excluded because their plan sponsors declined to participate. Thus, 5855 patients from 2980 plan sponsors were enrolled (Appendix B in the Supplementary Appendix). Plan sponsors had a median enrollment of 1 patient (range, 1 to 340). The plan sponsor with the largest number of enrolled patients was assigned to the usual-coverage group; 325 plan sponsors (10.9%) were nationally based.

Assignment to a study group occurred a median of 49 days after hospital discharge; 95% of patients were assigned within 100 days after discharge. A total of 133 patients (4.7%) in the full-coverage group and 151 (5.0%) in the usual-coverage group lost insurance eligibility between the time of hospital discharge and randomization, so data from these patients were not included in the follow-up analyses. The median duration of follow-up after randomization was 394 days (interquartile range, 201 to 663).

The baseline characteristics of the patients were well balanced between the two study groups (Table 1). The average age was 54 years, and three quarters of the patients were men. More than half the patients had filled prescriptions for the study drugs before their index hospitalization. Among patients who filled prescriptions between the time of hospital discharge and randomization, average copayments were similar in the two study groups.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Full Prescription Coverage (N=2845)	Usual Prescription Coverage (N=3010)
Age — yr	53.6±7.6	53.7±7.6
Male sex — no. (%)	2152 (75.6)	2248 (74.7)
Medication use before hospitalization — no. (%)†		
ACE inhibitor or ARB	1541 (54.2)	1588 (52.8)
Beta-blocker	1841 (64.7)	1965 (65.3)
Clopidogrel	1541 (54.2)	1637 (54.4)
Statin	1735 (61.0)	1828 (60.7)
Warfarin	180 (6.3)	178 (5.9)
Coexisting illness — no. (%)†		
Congestive heart failure	769 (27.0)	876 (29.1)
Chronic obstructive pulmonary disease	446 (15.7)	495 (16.4)
Diabetes	976 (34.3)	1047 (34.8)
Hypertension	2027 (71.2)	2178 (72.4)
Previous myocardial infarction	445 (15.6)	523 (17.4)
Stroke	164 (5.8)	201 (6.7)
Procedure on index hospitalization — no. (%)		
Angiography	2695 (94.7)	2819 (93.7)
Percutaneous coronary intervention	1915 (67.3)	1988 (66.0)
Coronary-artery bypass grafting	508 (17.9)	544 (18.1)
Comorbidity score‡	0.22±0.39	0.23±0.39
No. of days from hospital discharge to randomization	48.9±23.0	48.4±22.2
Copayment before randomization — U.S. $§		
ACE inhibitor or ARB	13.48±11.74	13.35±10.82
Beta-blocker	12.64±11.15	12.83±12.97
Statin	24.98±22.06	24.92±20.80

* Plus–minus values are means ±SD. There was no significant between-group difference in any category. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

† Medication use before hospitalization and coexisting illnesses were assessed on the basis of all filled prescriptions and available diagnoses during the 12-month period preceding the index hospitalization. Medication use was defined as the filling of at least one prescription during this period.

‡ The comorbidity score ranges from 0 to 3.4, with higher scores indicating an increased risk of death. The score was calculated with the use of the Ontario acute myocardial infarction mortality prediction rules, which predict 30-day and 1-year mortality.[21] Each patient's score is calculated on the basis of published weights according to sex and the characteristics observed on the index hospitalization: shock, diabetes with complications, congestive heart failure, cancer, cerebrovascular disease, pulmonary edema, acute renal failure, chronic renal failure, and cardiac dysrhythmias. Because all patients in the trial were under the age of 65 years, weights according to age were not included in our calculations.

§ Included in this category are all patients who filled prescriptions after the index hospitalization and before randomization. Amounts represent average copayments for a 1-month supply of medication.

Table 2. Medication Adherence during Follow-up.*

Variable	Absolute Adherence†				Full Adherence‡			
	Full Prescription Coverage	Usual Prescription Coverage	Absolute Difference (95% CI)	P Value	Full Prescription Coverage	Usual Prescription Coverage	Odds Ratio (95% CI)	P Value
		percentage points			*no./total no. (%)*			
All patients§								
ACE inhibitor or ARB	41.1±39.8	35.9±38.1	5.6 (3.4–7.7)	<0.001	789/2845 (27.7)	689/3010 (22.9)	1.31 (1.14–1.49)	<0.001
Beta-blocker	49.3±37.5	45.0±36.6	4.4 (2.3–6.5)	<0.001	873/2845 (30.7)	758/3010 (25.2)	1.32 (1.16–1.49)	<0.001
Statin	55.1±37.7	49.0±37.3	6.2 (3.9–8.5)	<0.001	1097/2845 (38.6)	950/3010 (31.6)	1.37 (1.20–1.56)	<0.001
All three medication classes	43.9±33.7	38.9±32.7	5.4 (3.6–7.2)	<0.001	344/2845 (12.1)	268/3010 (8.9)	1.41 (1.18–1.67)	<0.001
Patients who filled at least one prescription								
ACE inhibitor or ARB	66.5±29.6	60.8±30.7	5.8 (3.6–8.1)	<0.001	789/1759 (44.9)	689/1775 (38.8)	1.28 (1.10–1.49)	0.002
Beta-blocker	65.0±28.9	61.0±28.9	4.0 (2.1–5.9)	<0.001	873/2159 (40.4)	758/2224 (34.1)	1.31 (1.14–1.50)	<0.001
Statin	70.5±27.0	65.0±28.4	5.5 (3.6–7.5)	<0.001	1097/2223 (49.3)	950/2267 (41.9)	1.36 (1.18–1.56)	<0.001
All three medication classes	67.4±15.5	62.9±26.3	4.5 (2.5–6.4)	<0.001	344/1385 (24.8)	268/1389 (19.3)	1.36 (1.12–1.65)	0.002

* Plus–minus values are means ±SD. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.
† Absolute adherence was calculated with the use of a medication possession ratio (i.e., the number of days for which patients had a supply of each medication class available divided by the number of days they were eligible for that medication). Ratios were multiplied by 100 to generate absolute adherence percentages. Values are for mean medication possession.
‡ Full adherence was defined as having a supply of medications available on at least 80% of days during follow-up. Patients who did not fill a particular prescription after randomization were considered to be nonadherent.
§ Patients who lost eligibility before randomization or who did not fill a prescription after randomization were considered to be nonadherent.

MEDICATION ADHERENCE

In the usual-coverage group, rates of adherence were 35.9% for ACE inhibitors or ARBs, 45.0% for beta-blockers, 49.0% for statins, and 38.9% for all three medication classes (Table 2). In the full-coverage group, rates of adherence were increased by 5.6 percentage points (95% confidence interval [CI], 3.4 to 7.7) for ACE inhibitors or ARBs, by 4.4 percentage points (95% CI, 2.3 to 6.5) for beta-blockers, by 6.2 percentage points (95% CI, 3.9 to 8.5) for statins, and by 5.4 percentage points (95% CI, 3.6 to 7.2) for all three medication classes ($P<0.001$ for all comparisons). The odds of full adherence to the study medications increased by 31 to 41% ($P<0.001$) (Table 2). Rates of adherence to other medications for which copayments were not altered did not differ significantly between the two study groups (Appendix C in the Supplementary Appendix).

CLINICAL OUTCOMES

The primary outcome of a fatal or nonfatal vascular event or revascularization occurred in 562 patients in the usual-coverage group (rate per 100 person-years, 18.8), as compared with 493 patients in the full-coverage group (rate per 100 person-years, 17.6), a nonsignificant reduction (hazard ratio, 0.93; 95% CI, 0.82 to 1.04; $P=0.21$) (Table 3 and Fig. 1A). After adjustment for age and baseline coexisting illnesses, the results were similar (hazard ratio, 0.94; 95% CI, 0.83 to 1.06; $P=0.29$).

Prespecified secondary outcomes occurred in significantly fewer patients in the full-coverage group than in the usual-coverage group. Rates of total major vascular events or revascularization, which included all outcome events that occurred in each patient during the study, were reduced by 11% (hazard ratio, 0.89; 95% CI, 0.80 to 0.99; $P=0.03$) (Table 3). The hazard ratio for the first major vascular event was reduced by 14% (hazard ratio, 0.86; 95% CI, 0.74 to 0.99; $P=0.03$) (Table 3 and Fig. 1B). Among individual components of the composite outcomes, the elimination of copayments led to significant reductions in the rate of stroke (hazard ratio, 0.69; 95% CI, 0.50 to 0.96; $P=0.03$) (Appendix D in the Supplementary Appendix) and nonsignificant reductions in the rates of myocardial infarction or unstable angina (hazard ratio, 0.84; 95% CI, 0.70 to 1.02; $P=0.08$) (Appendix D in the Supplementary Appendix) and congestive heart failure (hazard ratio, 0.87; 95% CI, 0.70 to 1.08; $P=0.21$). The elimination of copay-

Table 3. Clinical Outcomes.

Outcome	Full Prescription Coverage (N=2845)		Usual Prescription Coverage (N=3010)		Hazard Ratio* (95% CI)	P Value
	no.	*rate/100 person-yr*	*no.*	*rate/100 person-yr*		
Fatal or nonfatal vascular event or revascularization†						
First event	493	17.6	562	18.8	0.93 (0.82–1.04)	0.21
Total events	622	21.5	729	23.3	0.89 (0.80–0.99)	0.03
First fatal or nonfatal vascular event	329	11.0	405	12.8	0.86 (0.74–0.99)	0.03
Individual components of outcome‡						
Myocardial infarction or unstable angina	187	6.0	236	7.1	0.84 (0.70–1.02)	0.08
Stroke	60	1.8	92	2.6	0.69 (0.50–0.96)	0.03
Congestive heart failure	150	4.8	182	5.4	0.87 (0.70–1.08)	0.21
Revascularization	293	9.8	298	9.1	1.06 (0.90–1.24)	0.51
Death from cardiovascular causes	57	1.7	72	2.0	0.85 (0.60–1.21)	0.36

* Hazard ratios have been adjusted for the cluster and block randomized design.
† First events are based on the first occurrence of any of the composite outcome events. Total events include all events in patients who may have had more than one component of the composite outcome. In this analysis, we excluded transfers between institutions, counted only one diagnosis per treatment episode, and counted each specific outcome (e.g., stroke) only one time per patient.
‡ Individual components are based on the first occurrence of these outcomes.

ments was not associated with a significant difference in the rate of coronary revascularization (hazard ratio, 1.06; 95% CI, 0.90 to 1.25; P=0.51). There was no evidence of heterogeneity in the clinical outcomes (Appendix E in the Supplementary Appendix).

HEALTH SPENDING

During follow-up in the full-coverage group, there were significant reductions in patients' out-of-pocket spending both for prescription drugs (relative spending, 0.70; 95% CI, 0.65 to 0.75; P<0.001) and for nondrug medical services (relative spending, 0.82; 95% CI, 0.72 to 0.94; P=0.005) (Table 4). In contrast, there was a significant increase in pharmacy spending by insurers (relative spending, 1.32; 95% CI, 1.14 to 1.52; P<0.001) but not for nondrug medical services (relative spending, 0.90; 95% CI, 0.52 to 1.58; P=0.72). The mean total spending was $66,008 in the full-coverage group and $71,778 in the usual-coverage group, a nonsignificant difference (relative spending, 0.89; 95% CI, 0.50 to 1.56; P=0.68). Although the effect of the intervention on cardiovascular-specific spending was similar to that for total spending and was not significant, the strength of the observed association was stronger (relative spending, 0.89; 95% CI, 0.77 to 1.02; P=0.08).

DISCUSSION

In this randomized policy trial involving 5855 patients who were discharged from the hospital after myocardial infarction, the elimination of copayments for statins, beta-blockers, ACE inhibitors, and ARBs did not significantly improve the primary outcome of the first major cardiovascular event or revascularization. The intervention increased medication adherence and reduced the rates of prespecified secondary clinical outcomes (first major vascular event and total major vascular events or revascularization). The enhanced coverage reduced patients' out-of-pocket spending for drug and nondrug services and did not significantly change total spending by insurers or overall costs.

Most activities that are aimed at boosting the quality of care for patients with myocardial infarction have focused on efforts to improve prescribing practices at the time of hospital discharge.[22,23] In contrast, reducing copayments for evidence-based medications, commonly known as value-based insurance design or evidence-based plan design,[11,24]

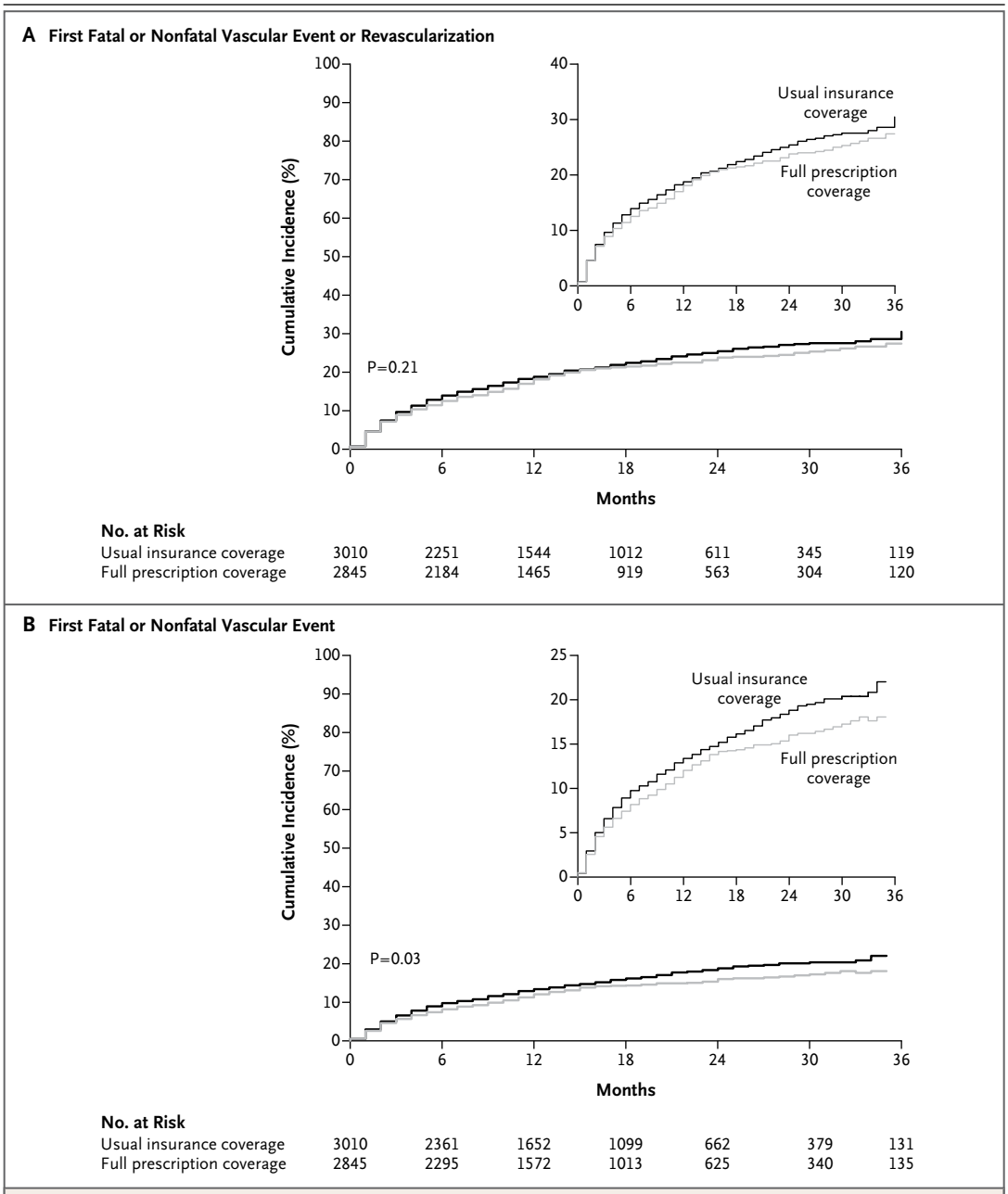

Figure 1. Cumulative Incidence of Outcomes.

Panel A shows the cumulative incidence of the primary outcome (first fatal or nonfatal acute myocardial infarction, unstable angina, stroke, congestive heart failure, or coronary revascularization). Panel B shows the cumulative incidence of the first fatal or nonfatal acute myocardial infarction, unstable angina, stroke, or congestive heart failure.

aims to increase long-term medication use. However, data are lacking from randomized, controlled studies evaluating the effectiveness of this strategy on clinically relevant outcomes for any condition.[13,14,25] Although the changes in medication use that we observed were modest, the simultaneous increases in adherence to multiple drug classes with synergistic effects may have been sufficient to reduce the rate of major vascular events and is consistent in magnitude with effects that would be expected from published economic models.[12,26] The nonsignificant reduction in the primary out-

Table 4. Drug and Nondrug Spending by Patients and Insurers during Follow-up.*

Outcome	Full Prescription Coverage (N=2845)	Usual Prescription Coverage (N=3010)	Relative Spending (95% CI)	P Value
	U.S. dollars			
Total spending				
Prescription drugs				
Insurer	4,847±15,835	3,921±6,606	1.32 (1.14–1.52)	<0.001
Patient	802±1,061	1,164±1,331	0.70 (0.65–0.75)	<0.001
Combined	5,649±16,384	5,085±7,583	1.17 (1.03–1.32)	0.02
Nondrug spending				
Insurer	59,878±634,988	66,076±617,412	0.90 (0.52–1.58)	0.72
Patient	480±815	618±1,480	0.82 (0.72–0.94)	0.005
Combined	60,358±635,098	66,693±617,756	0.90 (0.52–1.57)	0.72
Total spending				
Insurer	64,726±639,683	69,997±617,650	0.92 (0.55–1.56)	0.77
Patient	1,282±1,549	1,781±2,263	0.74 (0.68–0.80)	<0.001
Combined	66,008±639,970	71,778±618,055	0.89 (0.50–1.56)	0.68
Cardiovascular-specific spending				
Prescription drugs				
Insurer	2,271±2,408	1,822±2,058	1.31 (1.22–1.41)	<0.001
Patient	323±396	665±721	0.49 (0.46–0.53)	<0.001
Combined	2,594±2,688	2,488±2,659	1.08 (1.01–1.15)	0.02
Nondrug spending				
Insurer	15,457±39,386	17,516±52,895	0.86 (0.74–1.01)	0.06
Patient	203±316	235±349	0.91 (0.82–1.00)	0.05
Combined	15,661±39,509	17,750±52,993	0.86 (0.74–1.01)	0.06
Total spending				
Insurer	17,729±39,658	19,338±53,082	0.90 (0.78–1.04)	0.14
Patient	526±564	900±888	0.60 (0.56–0.64)	<0.001
Combined	18,254±39,839	20,238±53,250	0.89 (0.77–1.02)	0.08

* Plus–minus values are means ±SD.

come appears attributable to the lack of effect of the intervention on rates of coronary revascularization.

The intervention increased medication use for all the targeted classes, including those for which generic drugs are already commonly used. Similarly, we did not observe any modification in the effect on the basis of baseline copayment levels. Although patients with higher copayments might have been expected to benefit more, the elasticity of demand may not be linear. In addition, adherence to other medications, such as clopidogrel, for which copayments were not eliminated, was virtually identical in the two study groups.

Despite the improvements in adherence that we observed, overall adherence remained low. Consistent with previous studies,[6,27] less than half of patients in the full-coverage group were fully adherent to their prescribed therapies. Therefore, interventions to address other contributors to nonadherence (e.g., knowledge, attitudes, the complexity of prescribed regimens, and difficulties that patients have in accessing their medications) will be necessary to adequately address this problem.[28,29]

Providing more generous prescription drug coverage increased the insurer's pharmacy spending but did not significantly change spending for other

medical services, nor did it increase the insurer's total costs. An intervention that reduces patients' financial burdens without changing overall spending and with possible clinical benefits is a rarity in health care and suggests that eliminating cost sharing for secondary prevention after myocardial infarction may be cost-effective.[30]

Several limitations of our study should be acknowledged. We relied on administrative claims to identify patients and evaluate outcomes. The use of such data for the outcomes that were studied has been validated, and we did not adjudicate study events with medical records. We recruited patients with hospital discharge claims that take time to become available in administrative databases. During the resultant delay, some patients may have become nonadherent to their prescribed therapies. Although this approach increases the generalizability of our findings to other insurers that seek to institute similar plans, it may have diminished the observed effect of the intervention. We evaluated relatively young patients who had been discharged from the hospital after myocardial infarction and who were covered by a large national insurer, and our results may not be generalizable to patients with other conditions or to those who receive health benefits through other means. We do not report the effect of eliminating copayments on the rate of out-of-hospital deaths from cardiovascular causes, since such rates will be ascertained by means of data from death certificates recorded in the Centers for Disease Control and Prevention National Death Index (NDI), for which there is a lag between the date of death and its documentation in the NDI. The clinical outcomes we report include only verifiable deaths from cardiovascular causes (i.e., those that occurred during the course of a hospital admission).

In conclusion, in this randomized trial, the elimination of patient copayments for secondary prevention after myocardial infarction did not significantly reduce rates of the composite primary outcome. We did observe beneficial effects on secondary clinical outcomes, including rates of total major vascular events or revascularization procedures, as well as on rates of first major vascular events and patients' out-of-pocket spending. The intervention did not change overall health spending. This simple strategy may contribute to ongoing efforts to improve the quality of care for patients after myocardial infarction.

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