Original Article

Long-Term Cost-Effectiveness of Providing Full Coverage for Preventive Medications After Myocardial Infarction

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Background—Adherence to drugs that are prescribed after myocardial infarction remains suboptimal. Although eliminating patient cost sharing for secondary prevention increases adherence and reduces rates of major cardiovascular events, the long-term clinical and economic implications of this approach have not been adequately evaluated.

Methods and Results—We developed a Markov model simulating a hypothetical cohort of commercially insured patients who were discharged from the hospital after myocardial infarction. Patients received β-blockers, renin–angiotensin system antagonists, and statins without cost sharing (full coverage) or at the current level of insurance coverage (usual coverage). Model inputs were extracted from the Post Myocardial Infarction Free Rx Event and Economic Evaluation trial and other published literature. The main outcome was an incremental cost-effectiveness ratio as measured by cost per quality-adjusted life year gained. Patients receiving usual coverage lived an average of 9.46 quality-adjusted life years after their event and incurred costs of $171 412. Patients receiving full coverage lived an average of 9.60 quality-adjusted life years and incurred costs of $167 401. Compared with usual coverage, full coverage would result in greater quality-adjusted survival (0.14 quality-adjusted life years) and less resource use ($4011) per patient. Our results were sensitive to alterations in the risk reduction for post-myocardial infarction events from full coverage.

Conclusions—Providing full prescription drug coverage for evidence-based pharmacotherapy to commercially insured post-myocardial infarction patients has the potential to improve health outcomes and save money from the societal perspective over the long-term.

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Clinical practice guidelines recommend that all post-MI patients receive treatment with β-blockers, renin–angiotensin system antagonists (angiotensin-converting enzyme inhibitors [ACEI] or angiotensin receptor blockers [ARB]), statins, and aspirin, unless a contraindication exists, for secondary prevention.[1] Although the rates of prescribing secondary prevention drugs at hospital discharge after acute MI have improved substantially,[2] long-term adherence to these drugs remains far from optimal.

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Several interventions that could effectively improve adherence to chronic preventive medications have been identified and evaluated in clinical trials.[3–5] Among these, removing financial barriers to medication filling by reducing patient out-of-pocket costs has attracted much attention,[6–12] supported by the Post Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) trial.[13] In this study, eliminating

copayments for β-blockers, ACEIs, ARBs, and statins prescribed to post-MI patients not only improved adherence but also reduced rates of major vascular events (although not revascularization) without increasing overall health spending.

Because MI FREEE was of relatively short duration (ie, a median follow-up period of 394 days) and most secondary prevention drugs are intended for life-long use, the better understanding of long-term implications of this strategy is needed. Accordingly, we conducted a cost-effectiveness analysis to evaluate the health and economic effect of providing full prescription drug coverage for evidence-based pharmacotherapy to post-MI patients over their lifetimes.

Methods

Study Setting and Background

MI FREEE was a clustered-randomized policy trial that evaluated whether providing full prescription drug coverage for secondary prevention drugs prescribed to patients after acute MI improved adherence, clinical outcomes, and health spending compared with usual

WHAT IS KNOWN

- Adherence to evidence-based pharmacotherapy after myocardial infarction (MI) remains suboptimal.
- The Post Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) trial demonstrated that eliminating patient medication copayments to post-MI patients not only improved adherence but also reduced rates of major vascular events (although not revascularization) without increasing overall health spending over a relatively short duration.

WHAT THE STUDY ADDS

- We developed a Markov model simulating a hypothetical cohort of commercially insured patients who were discharged from the hospital after MI.
- Using model inputs from the MI FREEE trial and other published literature, we concluded that the elimination of patient copayments for evidence-based pharmacotherapy after MI improves health outcomes and saves money from the societal perspective over a lifetime horizon.
- The model-estimated average cost reduction of $4011 per patient in this study suggests that society could potentially save almost $2 billion over the patient's lifetime for the 525 000 Americans who will experience their first MI every year.

levels of insurance coverage.[13,14] The trial included a total of 5855 individuals who received health and pharmacy benefits from Aetna, a large health insurer in the United States. Patients randomized to receive full prescription drug coverage had no cost sharing (ie, copayments, coinsurance, and deductibles) for any brand-name or generic statins, β-blockers, and ACEI or ARB for every prescription after randomization until the end of the trial. Patients randomized to receive usual prescription drug coverage had no change in their existing benefits and faced average monthly copayments of $12 to $25 per drug. Randomization occurred at the level of the plan sponsor (ie, 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, and plan sponsors were categorized into blocks on the basis of whether they were nationally based (a Fortune 500 company with >3000 employees or a governmental plan sponsor) and the baseline average copayments required for study medications. Over a median follow-up period of 394 days, full coverage improved adherence by 4% to 6% points across the 3 drug classes (statins, β-blockers, and ACEI or ARB), reduced rates of first major vascular events and total major vascular events or revascularization, but did not significantly reduce rates of the primary composite outcome of first major vascular events or revascularization. Patient out-of-pocket spending for drug and nondrug spending was reduced by an average of $499 (*P*<0.001), and overall health spending remained unchanged ($66 008 for intervention patients and $71 778 for controls [relative spending 0.89; 95% confidence interval {CI} 0.50–1.56; *P*=0.68]).

Using data from MI FREEE, we developed a Markov state-transition model to evaluate the incremental cost and quality-adjusted life expectancy that would result from full or usual prescription drug coverage for secondary prevention drugs prescribed to post-MI patients. Our model simulated the prognosis of a hypothetical cohort of commercially insured patients who were discharged from the hospital after acute MI and were prescribed guideline-recommended secondary prevention drugs. We did not explicitly model the use of clopidogrel because our analysis focused on the use of drugs intended for lifelong use, and the appropriate length of treatment with antiplatelet agents other than aspirin remains controversial.[15] Patients were followed as they transitioned in 1-month cycles through a series of health states over the course of their lifetimes (Figure 1). In each cycle, patients were at risk for reinfarction, stroke, being hospitalized for congestive heart failure (CHF), with the potential of dying from any of these conditions, or undergoing revascularization. Throughout the patients' lifetimes, they were also at risk for dying of other causes. Our model did not consider potential adverse drug effects as a result of improved adherence. Based on guidelines from the Panel on Cost-Effectiveness Analysis in Health and Medicine of the US Public Health Service, we assumed a societal perspective, lifetime horizon, and a discount rate of 3% per year for both health benefits and costs.[16] The analysis was performed using TreeAge Pro Suite 2013 software (TreeAge Software, Williamstown, MA). The analysis was exempt from approval by an institutional review board.

Model Inputs

The model parameters are summarized in Table 1 and are described in greater detail below.
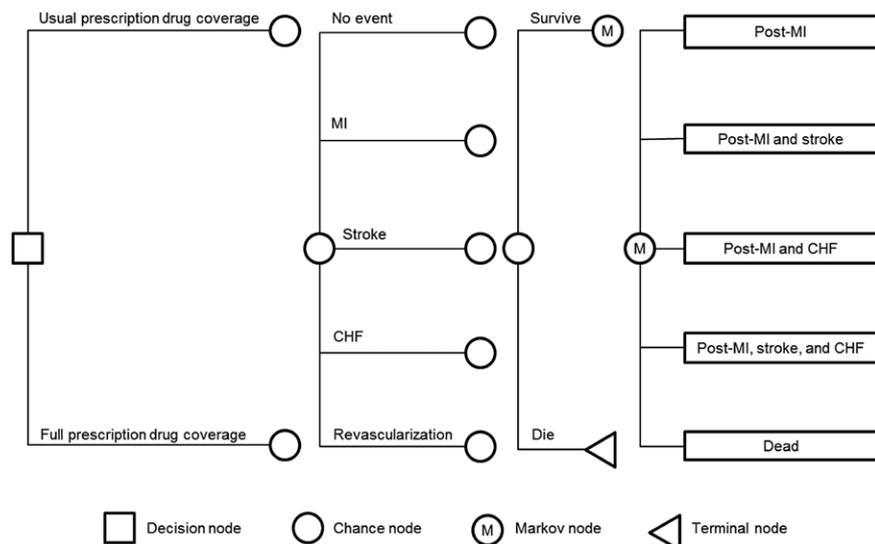
Figure 1. Cost-effectiveness model structure comparing full and usual prescription drug coverage. At the decision node, patients were assigned to usual or full coverage. Patients entered the model in the post-myocardial infarction (MI) health state. In each cycle, patients had a chance of having reinfarction, having stroke, being hospitalized for congestive heart failure (CHF), with the potential of dying of these conditions, or undergoing repeat revascularization. Repeat revascularization was modeled as a transient health state. All patients had a chance of dying of other causes from any Markov health state at any time throughout the patients' lifetime. The dead state was modeled as a terminal (ie, absorbing) health state.

Table 1.   Model Parameters

Parameter	Base-Case Estimate	Sensitivity Analyses Range Tested	Distribution	Reference
Patients' age, y	54	50–80	Not assigned	13
Post-MI event rates under usual prescription coverage (per year)*		50% to 200% of base-case rates	Beta	13, 17, 18
MI	0.07			
Stroke	0.03			
CHF	0.05			
Repeat revascularization	0.09			
Event-related mortality of post-MI events		50% to 200% of base-case rates	Beta	19–21
MI	0.08			
Stroke	0.07			
CHF	0.11			
Risk reduction of post-MI events by full prescription drug coverage			Lognomal	13
MI	0.16	0.00–0.30		
Stroke	0.31	0.04–0.50		
CHF	0.13	0.00–0.30		
Repeat revascularization	−0.06	−0.24 to 0.10		
Utility of post-MI events (≤1 month)		50% to 200% of base-case utility loss	Gamma	22–27
MI	0.770			
Stroke	0.600			
CHF	0.570			
Repeat revascularization	0.824			
Utility of post-MI events (>1 month)		50% to 200% of base-case utility loss	Gamma	22–27
MI	0.850			
Stroke	0.650			
CHF	0.840			
Repeat revascularization	1.000			
Post-MI event-related costs ($)		50% to 200% of base-case costs	Gamma	13
MI	27 796			
Stroke	29 104			
CHF	17 318			
Repeat revascularization	9172			
Cost of ongoing care after post-MI events ($ per month)		50% to 200% of base-case costs	Gamma	13, 28
MI	437			
Stroke	1524			
CHF	348			

Values presented are for a 54-year-old patient (or post-MI year 0). CHF indicates congestive heart failure; and MI, myocardial infarction.

*Varied by year.

Post-MI Event Rates and Effect of Full Coverage

We obtained rates of post-MI events (ie, reinfarction, stroke, hospitalization for CHF, and repeat revascularization) under usual coverage from MI FREEE,[13] pooled data from the Framingham Heart Study, Atherosclerosis Risk in Community study, and Cardiovascular Heart Study of the National Heart, Lung, and Blood Institute,[17] and the Arterial Revascularization Therapies Study.[18] We obtained the risk reduction for post-MI events from full coverage from MI FREEE.[13] Consistent with other cost-effectiveness analyses of the long-term effect of health interventions,[28] we made a conservative assumption that the benefit of full coverage was constant for 5 years after the start of this enhanced coverage and then decreased in a linear fashion over the next 5 years to null. We chose a 5-year cutpoint somewhat arbitrarily based on the fact that the longest follow-up in MI FREEE was just over 4 years. Because the long-term effect of full coverage has yet to be determined, we varied this assumption widely in our sensitivity analyses.

Mortality

We obtained case fatality rates related to post-MI events from population-based cohort studies of patients who were hospitalized for MI,[19] stroke,[20] and CHF.[21] We obtained total mortality rates from the 2006

United States Life Table.[29] We modeled the long-term excess mortality after MI using pooled data from the Framingham Heart Study, Atherosclerosis Risk in Community study, and Cardiovascular Heart Study of the National Heart, Lung, and Blood Institute.[17]

Quality of Life

We assigned a utility weight to each health states that reflected the preference for, or desirability of, that health state. All utility values were taken from studies that used standardized methods (ie, the time-tradeoff or standard gamble technique). Specifically, we used EQ-5D scores collected from coronary heart disease patients in the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease database to define the utilities for MI.[22] We used a time trade-off score collected from stroke patients in the quality-of-life substudy of Global Use of Strategies to Open Occluded Coronary Arteries trial and an EQ-5D score collected from stroke patients in the Medicare Expenditure Panel Survey to define the utilities for stroke.[23–25] We used standard gamble scores directly elicited from the general public to define the utilities for CHF.[26] We used a pooled EQ-5D score taken from the percutaneous coronary intervention arms of the Arterial Revascularization Therapies Study and the Stent or Surgery trial to define the utility for repeat revascularization.[27] For patients with multiple conditions, the utilities for the associated conditions were multiplied together. We assumed that a stroke, for example, reduced a patient's quality of life by same percentage, regardless of whether CHF also is present.

Costs

MI FREEE collected healthcare spending (ie, prescription drugs and nondrug medical services, such as physician visits, emergency room admissions, hospitalizations, and outpatient procedures) from the insurer's claims data. In MI FREEE, full coverage increased cardiovascular drug spending from $162 to $175 per month (ie, relative spending 1.08; 95% CI 1.01–1.15; P=0.02).[13] We used these data to estimate that full coverage increased cardiovascular drug spending across the 3 drug classes (statins, β-blockers, and ACEI or ARB). We obtained direct and indirect healthcare costs of ongoing care after post-MI events from a previous cost-effectiveness analysis of strategies to improve adherence to post-MI medications.[22] All costs were presented in 2012 US dollars and were inflated using the medical care component of the US Consumer Price Index.[30]

Outcomes

We calculated the incremental cost-effectiveness ratio of full coverage as the additional cost from this strategy compared with usual coverage divided by its additional health benefit. Health benefits were measured in quality-adjusted life years (QALYs) gained. Incremental cost-effectiveness ratios were calculated at multiple time horizons to provide a trajectory of summary measures over time.[31] To assess the robustness of our findings, we performed extensive deterministic sensitivity analyses. We obtained ranges tested from 95% CI when available; otherwise, we used from 50% to 200% of the base-case estimates. Two-way sensitivity analyses were performed by simultaneously altering relative drug spending and the risk reduction for post-MI events from full coverage. We also conducted a probabilistic sensitivity analysis, in which the model was run using a value of each parameter drawn randomly from the distribution assigned to that parameter. We used beta distributions for probabilities; lognormal distributions for relative risks; and gamma distributions for costs and utility decrements. We ran 10 000 iterations to generate a

cost-effectiveness acceptability curve showing the probability that full prescription drug coverage is cost-effective at varying willingness-to-pat thresholds, compared with usual prescription drug coverage.[32]

Model Validation

The estimated proportions of patients who had reinfarction, stroke, and hospitalization for CHF within 5 years after first MI were 19%, 5%, and 13%, respectively. The estimated median survival after MI was 20 years. All of these estimates correlated well with available observational data.[17]

Results

Base-Case Analysis

For patients receiving usual coverage, average quality-adjusted survival was 9.46 QALYs, and lifetime costs were $171 412 (Table 2). For patients receiving full coverage, average quality-adjusted survival was 9.60 QALYs, and lifetime costs were $167 401. Compared with usual coverage, full coverage improved quality-adjusted survival by 0.14 QALYs per patient and reduces costs by ≈$4011 per patient. Because it yielded greater health benefits at a lower cost, full prescription drug coverage dominated the strategy of usual prescription drug coverage. Both cumulative cost savings and QALY gained from full coverage increased with time after initial MI but began to plateau 10 years after initial hospital discharge, when the model had assumed that the effect of full coverage had fully dissipated (Table 3).

Sensitivity Analyses

Full coverage would remain dominant with a wide range of plausible estimates of model parameters, including age of the cohort, rates, mortality, utilities, and costs of post-MI events, and discount rate. Assuming the shortest duration of the health benefit from full coverage (ie, 1 year, which was shorter than the average duration of MI FREEE), full coverage had an incremental cost-effectiveness ratio of $15 021 per QALY gained. Table 4 summarizes 2-way sensitivity analyses of relative drug spending and the risk reduction of post-MI events from full coverage. Even under assumptions using the highest bound of 95% CI of relative drug spending and the lowest bound of 95% CI of the risk reduction of post-MI events from full coverage (Table 1), full coverage would be preferred at a conventional willingness-to-pay threshold of $100 000 per QALY gained.

The result of the probability sensitivity analysis is displayed in the cost-effectiveness acceptability curve (Figure 2). The curve indicates that full coverage was cost-saving compared with usual coverage in 56% of simulations and was cost-effective at a conventional willingness-to-pay threshold of $100 000 per QALY gained in 86% of simulations.

Table 2.   Base-Case Analysis Results

| Strategy | Cost, $ | | | QALYs | △Cost, $ | △QALYs | ICER, $ per QALY |
	Drug	Non-drug	Total				
Usual coverage	23 371	148 041	171 412	9.46	Reference	Reference	Reference
Full coverage	25 413	141 988	167 401	9.60	−4011	0.14	Dominant

ICER indicates incremental cost-effectiveness ratio; and QALY, quality-adjusted life year.

Table 3.   Cumulative Changes in Cost Savings and QALY Gained From Full Coverage Over the 30-Year Time Horizon

Post-MI Years	Cost Savings, $	QALY Gained, y
1	442	0.002
5	2568	0.03
10	3353	0.08
15	3759	0.11
20	3939	0.13
25	3999	0.13
30	4011	0.14

MI indicates myocardial infarction; and QALY, quality-adjusted life years.

Discussion

Nonadherence to preventive therapies prescribed after MI has well-documented clinical and economic consequences. Efforts to improve adherence by selectively reducing patient copayments have demonstrated short-term benefits for improving health outcomes in a cost-effective manner.[9–11] Using data from MI FREEE,[13] we evaluated the long-term benefits of this strategy and found that, compared with the usual pharmacy benefits, the elimination of patient copayments for evidence-based pharmacotherapy after MI improves health outcomes and saves money from the societal perspective. These savings resulted from the acute and ongoing costs of care for major vascular events (ie, reinfarction, stroke, and hospitalization for CHF) avoided and more than offset the additional prescription drug costs resulting from improved adherence. Cost savings and gains in quality-adjusted survival appeared within the first year of initial MI and continued to increase over patients'

Table 4.   Incremental Cost-Effectiveness Ratio ($ per QALY) of Full Coverage by Relative Drug Spending and the Risk Reduction of Post-MI Events From Full Coverage

|	Relative drug spending		
	Lowest	Base-case	Highest
Risk reduction of MI			
Lowest	Dominant	Dominant	1390
Base-case	Dominant	Dominant	419
Highest	Dominant	Dominant	Dominant
Risk reduction of stroke			
Lowest	Dominant	28 769	58 130
Base-case	Dominant	Dominant	419
Highest	Dominant	Dominant	Dominant
Risk reduction of CHF			
Lowest	Dominant	Dominant	2031
Base-case	Dominant	Dominant	419
Highest	Dominant	Dominant	Dominant
Risk reduction of Revascularization			
Lowest	Dominant	Dominant	451
Base-case	Dominant	Dominant	419
Highest	Dominant	Dominant	Dominant

CHF indicates congestive heart failure; MI, myocardial infarction; and QALY, quality-adjusted life-year.

lifetimes. The average cost reduction of $4011 per patient would save society almost $2 billion over the patient's lifetime for the 525 000 Americans who will experience their first MI every year.[17]

Copayments are widely used to contain health spending in the US healthcare system. However, as the burden of cost sharing continues to grow, patients may increasingly avoid essential medical interventions.[6–8] Underuse of effective drugs is a major contribution to suboptimal disease control and poor outcomes. For example, studies of patients with a variety of chronic health conditions have indicated that a 10% increase in patient cost sharing is associated with a reduction of 2% to 6% in spending on prescription drugs and an increase in the use of other resources, such as emergency departments and inpatient services.[7] One logical response to these observations is to selectively eliminate cost-related barriers for evidence-based drugs. In this strategy, widely known as value-based insurance design (VBID) or evidence-based plan design, copayments, coinsurance, and deductibles are reduced or eliminated for drugs that are potentially life-saving and of high value (ie, providing important health benefits relative to costs).[9–11] VBID has implemented increasingly in the management of chronic health conditions, such as cardiovascular diseases, diabetes mellitus, and asthma.[12] The Patient Protection and Affordable Care Act of 2010 included a provision that "the Secretary may develop guidelines to permit a group health plan and a health insurance issuer offering group or individual health insurance coverage to utilize" VBID.[33]

A review of observational studies suggests that VBID is consistently associated with short-term improvements in adherence (average change of 3% over 1 year) that are cost-neutral for payers.[12] The hope that these changes in adherence should be translated into meaningful improvements in health and reduction in overall healthcare spending in the long-term, thus far, has been largely based on data from model-based economic evaluations.[22,34–36] For example, a previous cost-effectiveness analysis based on Medicare data showed that the elimination of patient cost sharing for secondary prevention drugs would save both lives (0.35 QALYs) and money ($2500) per post-MI Medicare beneficiary.[22] However, the critical limitation of these analyses is their reliance on data generated from policies that increased cost sharing for evidence-based drugs to estimate what would be expected to happen if copayments were reduced instead. MI FREEE filled this knowledge gap by demonstrating the ability of VBID not only to improve adherence but also to reduce actual rates of major vascular events (although not revascularization) without increasing overall healthcare spending, but was of relatively short duration.[13] Given that most secondary prevention drugs are intended for life-long use, the findings from our analysis are likely to be more representative of the real-world effect of VBID. In the current policy climate where efforts to improve healthcare quality must be coupled with efforts to contain costs, our analysis extended the growing evidence that VBID is a promising approach that could be easily scaled to large populations to improve the quality of care for post-MI patients.

Despite this, there are numerous barriers to the more widespread implementation of this adherence enhancing strategy.
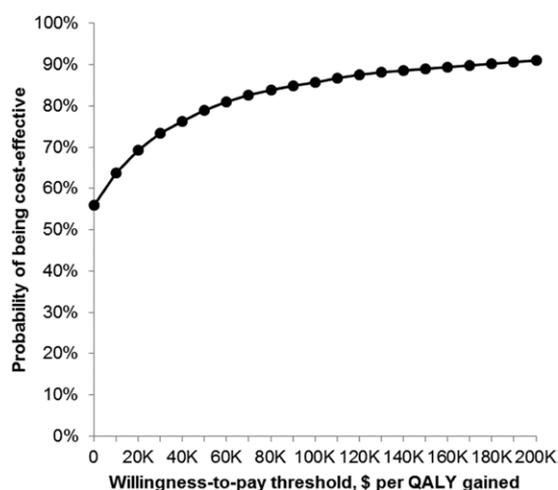
Figure 2. Cost-effectiveness acceptability curve for full coverage.

For example, although all VBID plans lower copayments for high-value medications, these insurance designs can be designed in numerous different ways based on the way in which the benefit design is structured and the programs that are concurrently offered with it. And, the optimal design has yet to be conclusively established. Recent evidence from a large-scale observational study suggests that VBID plans that are more generous, target high-risk patients, offer wellness programs, do not offer disease management programs, and make the benefit available only for medication ordered by mail have a significantly greater effect on adherence than plans without these features.[37] Interestingly, maintaining copayment tiers to create incentives for the preferential use of therapeutically equivalent generic medications does not seem to influence the ability of VBID plans to increase adherence, although the effect of this strategy on health spending remains unknown.

Further, payers have the greatest incentive to adopt plans using VBID when they have a reasonable change of benefiting from the reductions in spending on medical care that are averted by better medication adherence. The likelihood of this happening is threatened by the fragmented nature of the US healthcare system, whereby certain types of benefits like prescription drugs are carved out and where patients and employers frequently change who provides them with benefits (a process known as churn). As a result, with the exception of integrated systems and for high-risk conditions like post-MI care where improved quality maybe achieved quickly, payers face the possibility that they will bear the cost of therapy whereas other payers reap the savings from averted clinical events. These issues will need to be addressed before VBID becomes more widely adopted.[38]

It is important to note that our model was built using the clinical trial of relatively young individuals who had been discharged from the hospital after MI and who were covered by a large commercial insurer.[13] Therefore, our results may not be fully generalizable to patients with other conditions or to those who receive health insurance through other means, such as Medicare. That said, it is reassuring that our results are robust to wide variations in model inputs, including patient characteristics and event costs that may differ based on the type of insurance that patients may have or that may change as patients transition from commercial to public insurance. It is similarly reassuring that even under those scenarios that providing full coverage had only a small effect on post-MI event rates (or in other words assuming that the results of MI FREEE were a significant overestimate of the true effect), the strategy still appeared cost-effective at a standard willingness to pay threshold of $100 000 per QALY.

Our results should be interpreted in light of several other limitations. First, there is currently a paucity of data as regards to how long the health benefit by full prescription drug coverage lasts beyond the time horizon of MI FREEE. To address this limitation, we extensively varied our assumption and confirmed the robustness of our results. Second, greater adherence to post-MI secondary prevention has the potential to increase the risk of adverse events (eg, renal failure associated with ACEI or ARB use), which we did not incorporate into our model. Although these outcomes are relatively rare, including them would likely have reduced the cost-saving from full coverage that we observed. Third, our analysis did not consider the effect of providing full coverage for clopidogrel, and thus our results are not necessarily generalizable to this drug. MI FREEE and the current analysis both sought to evaluate the effect of copayment elimination independent of other cointerventions. Because the appropriate length of treatment with antiplatelet agents other than aspirin remains controversial, for the insurance coverage being evaluated to have been truly evidence-based, we would have to have provided full coverage for clopidogrel for only 1 year only and then have returned coverage to usual levels. Doing so would have influenced clinical decision-making and would have confounded our assessment of the relationship between selective copayment reduction and improvements in medication adherence. As a consequence, we limited our attention to those agents intended for lifelong use. Consistent with this, there are numerous adherence interventions that could be possibly effective but were not incorporated in our analysis.[3–5] Although our analysis focused on a policy-oriented intervention, it could be potentially attractive to combine it with other patient- or provider-oriented interventions aiming at improving adherence.

In conclusion, our analysis suggests that providing full prescription drug coverage for evidence-based pharmacotherapy to commercially insured post-MI patients could simultaneously save lives and money from the societal perspective and that the magnitude of such savings could be substantial. Future research should assess the long-term, real-world effectiveness of this strategy.

Sources of Funding

References

1. Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW, Lloyd-Jones DM, Minissian M, Mosca L, Peterson ED, Sacco RL, Spertus J, Stein JH, Taubert KA; World Heart Federation and the Preventive Cardiovascular Nurses Association. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation*. 2011;124:2458–2473. doi: 10.1161/CIR.0b013e318235eb4d.

2. McGovern PG, Jacobs DR Jr, Shahar E, Arnett DK, Folsom AR, Blackburn H, Luepker RV. Trends in acute coronary heart disease mortality, morbidity, and medical care from 1985 through 1997: the Minnesota heart survey. *Circulation*. 2001;104:19–24.

3. Haynes RB, Yao X, Kripalani S, Garg A, McDonald HP. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008;2:CD000011.

4. Cutrona SL, Choudhry NK, Fischer MA, Servi A, Liberman JN, Brennan TA, Shrank WH. Modes of delivery for interventions to improve cardiovascular medication adherence. *Am J Manag Care*. 2010;16:929–942.

5. Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC, Coker-Schwimmer EJ, Rosen DL, Sista P, Lohr KN. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. *Ann Intern Med*. 2012;157:785–795. doi: 10.7326/0003-4819-157-11-201212040-00538.

6. Goldman DP, Joyce GF, Escarce JJ, Pace JE, Solomon MD, Laouri M, Landsman PB, Teutsch SM. Pharmacy benefits and the use of drugs by the chronically ill. *JAMA*. 2004;291:2344–2350. doi: 10.1001/jama.291.19.2344.

7. Goldman DP, Joyce GF, Zheng Y. Prescription drug cost sharing: associations with medication and medical utilization and spending and health. *JAMA*. 2007;298:61–69. doi: 10.1001/jama.298.1.61.

8. Trivedi AN, Rakowski W, Ayanian JZ. Effect of cost sharing on screening mammography in Medicare health plans. *N Engl J Med*. 2008;358:375–383. doi: 10.1056/NEJMsa070929.

9. Fendrick AM, Smith DG, Chernew ME, Shah SN. A benefit-based copay for prescription drugs: patient contribution based on total benefits, not drug acquisition cost. *Am J Manag Care*. 2001;7:861–867.

10. Chernew ME, Rosen AB, Fendrick AM. Value-based insurance design. *Health Aff (Millwood)*. 2007;26:w195–w203. doi: 10.1377/hlthaff.26.2.w195.

11. Braithwaite RS, Rosen AB. Linking cost sharing to value: an unrivaled yet unrealized public health opportunity. *Ann Intern Med*. 2007;146:602–605.

12. Lee JL, Maciejewski M, Raju S, Shrank WH, Choudhry NK. Value-based insurance design: quality improvement but no cost savings. *Health Aff (Millwood)*. 2013;32:1251–1257. doi: 10.1377/hlthaff.2012.0902.

13. Choudhry NK, Avorn J, Glynn RJ, Antman EM, Schneeweiss S, Toscano M, Reisman L, Fernandes J, Spettell C, Lee JL, Levin R, Brennan T, Shrank WH; Post-Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) Trial. Full coverage for preventive medications after myocardial infarction. *N Engl J Med*. 2011;365:2088–2097. doi: 10.1056/NEJMsa1107913.

14. Choudhry NK, Avorn J, Glynn RJ, Toscano M, Glynn RJ, Rubino M, Schneeweiss S, Brookhart AM, Fernandes J, Mathew S, Christiansen B, Antman EM, Avorn J, Shrank WH. Rationale and design of the Post-MI FREEE trial: a randomized evaluation of first-dollar drug coverage for post-myocardial infarction secondary preventive therapies. *Am Heart J* 2008; 156:31–36.

15. Kushner FG, Hand M, Smith SC Jr, King SB III, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE Jr, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (updating the 2005 Guideline and 2007 Focused Update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:2271–2306. doi: 10.1161/CIRCULATIONAHA.109.192663.

16. Gold MR, Siegel JE, Russel LB, Weinstein MC. *Cost-Effectiveness in Health and Medicine*. New York, NY: Oxford University Press. 1996.

17. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18–e209. doi: 10.1161/CIR.0b013e3182009701.

18. Serruys PW, Ong AT, van Herwerden LA, Sousa JE, Jatene A, Bonnier JJ, Schönberger JP, Buller N, Bonser R, Disco C, Backx B, Hugenholtz PG, Firth BG, Unger F. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. *J Am Coll Cardiol*. 2005;46:575–581. doi: 10.1016/j.jacc.2004.12.082.

19. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med*. 2010;362:2155–2165. doi: 10.1056/NEJMoa0908610.

20. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, Copper LS, Shahar E. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke*. 1999;30:736–743.

21. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure. *JAMA*. 2003;290:2581–2587.

22. Choudhry NK, Patrick AR, Antman EM, Avorn J, Shrank WH. Cost-effectiveness of providing full drug coverage to increase medication adherence in post-myocardial infarction Medicare beneficiaries. *Circulation*. 2008;117:1261–1268. doi: 10.1161/CIRCULATIONAHA.107.735605.

23. Shrive FM, Manns BJ, Galbraith PD, Knudtson ML, Ghali WA; APPROACH Investigators. Economic evaluation of sirolimus-eluting stents. *CMAJ*. 2005;172:345–351. doi: 10.1503/cmaj.1041062.

24. Gore JM. Granger CB, Simoons ML, Sloan MA, Weaver WD, White HD, Barbash GI, Van de Werf F, Aylward PE, Topol EJ, Califf RM; the GUSTO-I Investigators. Stroke after thrombolysis. Mortality and functional outcomes in the Gusto-I trial. Global Strategies to Open Coronary Arteries. *Circulation*. 1995;92:2811–2818.

25. Ganz DA, Kuntz KM, Jacobson GA, Avorn J. Cost-effectiveness of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor therapy in older patients with myocardial infarction. *Ann Intern Med*. 2000;132:780–787.

26. Xie J, Wu EQ, Zheng ZJ, Croft JB, Greenlund KJ, Mensah GA, Labarthe DR. Impact of stroke on health-related quality of life in the noninstitutionalized population in the United States. *Stroke*. 2006;37:2567–2572. doi: 10.1161/01.STR.0000240506.34616.10.

27. Nichol G, Kaul P, Huszti E, Bridges JF. Cost-effectiveness of cardiac resynchronization therapy in patients with symptomatic heart failure. *Ann Intern Med*. 2004;141:343–351.

28. Hill RA, Boland A, Dickson R, Dündar Y, Haycox A, McLeod C, Mujica Mota R, Walley T, Bagust A. Drug-eluting stents: a systematic review and economic evaluation. *Health Technol Assess*. 2007;11:iii, xi–221.

29. Arias E. United States life tables, 2006. National Vital Statics Report. Volume 58, number 21. 2010.

30. US Department of Labor. US Consumer Price Index for Medical Care for All Urban Consumers. http://www.bls.gov/cpi/. Accessed December 1, 2013.

31. Ramsey S, Willke R, Briggs A, Brown R, Buxton M, Chawla A, Cook J, Glick H, Liljas B, Petitti D, Reed S. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force report. *Value Health*. 2005;8:521–533. doi: 10.1111/j.1524-4733.2005.00045.x.

32. Briggs A, Sculpher M, Claxton K. *Decision Modelling for Health Economic Evaluation*. Oxford: Oxford University Press; 2006.

33. *Patient Protection and Affordable Care Act of 2010*, Pub L No. 111–148. http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf. Accessed December 1, 2013.

34. Rosen AB, Hamel MB, Weinstein MC, Cutler DM, Fendrick AM, Vijan S. Cost-effectiveness of full medicare coverage of angiotensin-converting enzyme inhibitors for beneficiaries with diabetes. *Ann Intern Med*. 2005;143:89–99.

35. Braithwaite RS, Omokaro C, Justice AC, Nucifora K, Roberts MS. Can broader diffusion of value-based insurance design increase benefits from US health care without increasing costs? Evidence from a computer simulation model. *PLoS Med*. 2010;7:e1000234. doi: 10.1371/journal.pmed.1000234.

36. Ito K, Elkin E, Blinder V, Keating N, Choudhry N. Cost-effectiveness of full coverage of aromatase inhibitors for Medicare beneficiaries with early breast cancer. *Cancer*. 2013;119:2494–2502. doi: 10.1002/cncr.28084.

37. Choudhry NK, Fischer MA, Smith BF, Brill G, Girdish C, Matlin OS, Brennan TA, Avorn J, Shrank WH. Five features of value-based insurance design plans were associated with higher rates of medication adherence. *Health Aff (Millwood)*. 2014;33:493–501. doi: 10.1377/hlthaff.2013.0060.

38. Choudhry NK, Rosenthal MB, Milstein A. Assessing the evidence for value-based insurance design. *Health Aff (Millwood)*. 2010;29:1988–1994. doi: 10.1377/hlthaff.2009.0324.

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