Health and Economic Benefits of Increased β-Blocker Use Following Myocardial Infarction

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Context β-Blockers are underused in patients who have myocardial infarction (MI), despite the proven efficacy of these agents. New evidence indicates that β-blockers can have benefit in patients with conditions that have been considered relative contraindications. Understanding the consequences of underuse of β-blockers is important because of the implications for current policy debates over quality-of-care measures and Medicare prescription drug coverage.

Objective To examine the potential health and economic impact of increased use of β-blockers in patients who have had MI.

Design and Setting We used the Coronary Heart Disease (CHD) Policy Model, a computer-simulation Markov model of CHD in the US population, to estimate the epidemiological impact and cost-effectiveness of increased β-blocker use from current to target levels among survivors of MI aged 35 to 84 years. Simulations included 1 cohort of MI survivors in 2000 followed up for 20 years and 20 successive annual cohorts of all first-MI survivors in 2000-2020. Mortality and morbidity from CHD were derived from published meta-analyses and recent studies. This analysis used a societal perspective.

Main Outcome Measures Prevented MIs, CHD mortality, life-years gained, and cost per quality-adjusted life-year (QALY) gained in 2000-2020.

Results Initiating β-blocker use for all MI survivors except those with absolute contraindications in 2000 and continuing treatment for 20 years would result in 4300 fewer CHD deaths, 3500 MIs prevented, and 45 000 life-years gained compared with current use. The incremental cost per QALY gained would be $4500. If this increase in β-blocker use were implemented in all first-MI survivors annually over 20 years, β-blockers would save $18 million and result in 72 000 fewer CHD deaths, 62 000 MIs prevented, and 447 000 life-years gained. Sensitivity analyses demonstrated that the cost-effectiveness of β-blocker therapy would always be less than $11 000 per QALY gained, even under unfavorable assumptions, and may even be cost saving. Restricting β-blockers only to ideal patients (those without absolute or relative contraindications) would reduce the epidemiological impact of β-blocker therapy by about 60%.

Conclusions Our simulation indicates that increased use of β-blockers after MI would lead to impressive gains in health and would be potentially cost saving.

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SEVERAL CLINICAL TRIALS AND OBservational studies have demonstrated that β-blocker use after myocardial infarction (MI) is an effective approach to reducing morbidity and mortality.[1-3] Although the efficacy of β-blockers was proven nearly 2 decades ago,[4-6] they remain underused. Recent surveys indicate that β-blockers are prescribed to as few as 40% of eligible patients in some health plans,[7] and they are particularly underused in women and elderly patients.[2,3,8,9] Even among elderly patients who are considered "ideal" candidates for treatment, only about half are prescribed β-blockers on discharge.[3] Several studies have pointed out that underuse of β-blockers has important health consequences, yet there has been a dearth of concrete, quantitative evidence on the economic consequences of such underuse.[10]

We sought to examine the health and economic impact of increased β-blocker use following MI using a computer model that simulates coronary heart disease (CHD) in the US population (the Coronary Heart Disease Policy Model). The CHD Policy Model has been used for numerous studies for more than a decade[11] and has been extensively validated by comparing its output to published statistics.[12]

We also examined the implications of recent data from the National Cooperative Cardiovascular Project (CCP) suggesting that patients with conditions that traditionally have been considered relative contraindications to β-blockers can benefit from their use.[2] Because of this new evidence, the 1999 guidelines from the American College of Cardiology and American Heart Association (ACC/AHA)[13] recommend the

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judicious use of β-blockers in these patients as "probably beneficial."

Understanding the consequences of underusing β-blockers is important because of the implications for current policy debates over quality-of-care measures. β-Blocker use is measured as a quality indicator in the most common performance measurement system for managed care plans, HEDIS (Health plan Employer Data and Information Set).[10] It also is used to illustrate the more general problem of underuse of effective treatments.[14] The underuse of β-blockers also has implications for the current debate over Medicare prescription coverage since the majority of β-blocker recipients are eligible for Medicare.

METHODS

Modeling Approach

We used the CHD Policy Model, a computer-simulation, state-transition (Markov cohort) model of CHD in US residents aged 35 through 84 years. The model includes variables for CHD event rates, case fatality rates, and costs, which were modified to reflect the impact of increased β-blocker use. The model has been used extensively in other studies.[11,12,15-25] Details of the model are described elsewhere[12] and in the online Technical Appendix (available at: http://www.jama.com), as recommended.[26]

To determine the costs and health outcomes associated with increased use of β-blockers following MI, we designed 2 different cohort analyses. First, we estimated the costs and outcomes of treating patients who were discharged following MI in 2000 and then followed up for 20 years (the "single-cohort" model). Second, we estimated the costs and outcomes of treating 20 successive annual cohorts of patients with a first MI, starting in 2000 (the "multicohort" model). The single-cohort model provides an estimate of the health and economic impact to one cohort over time. The multicohort model provides a long-term estimate of the public health impact if this increase were sustained in each new cohort of patients with MI. We did not analyze strategies such as providing β-blockers only to "high-risk" patients because, as we discuss below, recent evidence suggests that the vast majority of patients with MI can benefit from β-blockers.

Table 1. Summary of Variables*

Variable	Best Estimate	Range for Sensitivity Analyses	References
β-Blocker eligibility	92%	60% (upper limit NA)	2, 3, 13
β-Blocker use rates	44%	59% (lower limit NA)	3, 28-30
Withdrawal rates			
Among patients with no relative contraindications	12%	NA	4-6
Among patients with relative contraindications	30%	50% (lower limit NA)	4-6
CHD event rate reductions with β-blocker use			
Myocardial infarction	27%	NA	4, 31
Sudden death from cardiac arrest	32%	NA	31
Mortality	22%	NA	3, 31
Effectiveness	3 y full benefits, then 3 y reduced (7%), then 1% benefits for 14 y	3, 6, or 20 y full benefits	4, 39
QALY reductions due to β-blockers	0%	1% for 3 y (lower limit NA)	32, 35
β-Blocker costs			
Per person per year	$432	$52-$600	37 (inflated)
Years of costs	20	6 only (upper limit NA)	4
Discount rate	3%	0%-10%	26

*NA indicates not applicable; QALY, quality-adjusted life-year.

Our primary goal was to model the incremental costs and benefits of increasing β-blocker use among patients with MI from current to target use (ie, all patients without absolute contraindications). We also modeled the impact of increasing β-blocker use from no use to current use to provide a context for our results and to enable comparisons to areas with different baseline rates. We reviewed the literature to develop point estimates and ranges for model inputs (TABLE 1 and online Appendix).

We conducted the analysis from a societal perspective. Costs and outcomes were discounted at 3% (range, 0%-10%).[26] All costs were adjusted to year 2000 using the 1999 Medical Services Consumer Price Index and the assumption of a continued inflation rate of 3% for 1999-2000.

Patients Eligible for Treatment

The proportion of patients who survive MI and who are appropriate candidates for β-blockers remains unresolved. Many believe that there are few absolute contraindications to β-blocker treatment (ie, atrioventricular block >first degree, heart rate <60/min, asthma, or allergy/intolerance). However, a variety of conditions traditionally have been considered relative contraindications (eg, diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, and congestive heart failure[13]), for which the potential risks must be weighed against the potential benefits.

Two recent studies using the CCP database found that use of β-blockers in patients with relative contraindications was associated with improved survival. Gottlieb et al[2] reported that β-blocker use remained associated with an approximately 40% decrease in 2-year mortality for many of the subgroups often considered to have relative contraindications, and that the absolute benefit among these groups was similar or greater than among "ideal" patients. Krumholz et al[3] found that 1-year mortality rates were similar among high- and low-risk patients. In addition, recent trials have demonstrated a survival benefit of β-blocker

use for patients with congestive heart failure.[27]

Based on this evidence, our primary analysis assumed that all patients with MI without absolute contraindications would be eligible for β-blocker use (92%). In sensitivity analyses, we assumed that only 60% of such patients would be eligible (based on the definition of ideal patients by the ACC/AHA as those without absolute or relative contraindications).[13] We also conducted stratified analyses by age (≥65 vs <65 years) because a higher percentage of nonelderly patients will be ideal candidates (60% of nonelderly patients[28] vs 31% of elderly patients[3]).

Rates of Use

Current Use. We estimated current use in 2000 by examining trends from 1990-1998. We estimated that use of β-blockers increased from 30% among all patients with MI in 1990[29,30] to 37% in 1994-1995 based on the CCP data[3] and then extrapolated this trend to estimate that 44% of patients with MI in 2000 will receive β-blockers. In sensitivity analyses, we assumed that current use could be as high as 59% (based on the average of 80% among ideal patients in managed care plans reported in recent HEDIS surveys[7] and a similar increase in use among patients with relative contraindications).

Withdrawal Rates. We estimated that a proportion of patients initiating β-blockers would withdraw from treatment, thereby incurring 6 months of costs but no benefits. In 3 large β-blocker trials, the proportion of patients who were randomized to receive β-blockers and who withdrew from treatment due to cardiopulmonary complications ranged from 7.7% to 12.5%.[4-6] Since these trials included ideal β-blocker recipients, we assumed that, conservatively, 12% of ideal patients would withdraw from treatment due to adverse effects. We assumed that a higher percentage of patients with relative contraindications to β-blockers would withdraw (30%, upper range of 50%). We made the conservative assumption that all patients who withdrew from treatment would do so in the first year and hence experience none of the benefits of β-blocker treatment.

Impact of β-Blocker Use on CHD Events and Mortality

Our primary data sources for treatment effectiveness were meta-analyses of clinical trials[1,31] and data from the CCP.[2,3] We estimated that β-blocker treatment, when begun within days or weeks after MI and continued for several months or years, would reduce 1-year mortality by 22%.[3,31] We estimated that β-blocker treatment would reduce the 1-year risk of a recurrent MI and revascularization by 27% and the risk of sudden death due to cardiac arrest by 32%.[4,31] We assumed that the beneficial effect of β-blockers is independent of other medications.[2,3]

We modeled the effects of β-blocker treatment on event rates and mortality (as described above) to be constant for the first 3 years and then decline to a 7% rate reduction for the next 3 years, followed by a 1% event rate reduction for the remaining 14 years. These estimates were based on the effects seen in the longest-term clinical trial,[4] but they are conservative because the benefits of β-blockers may persist at a higher level for a longer period. In sensitivity analyses, we examined the effect of assuming 3 years of full effectiveness followed by no further benefits but 20 years of costs, 6 years of benefits and costs, or 20 years of full effectiveness and costs.

Although β-blocker use may improve quality of life, we made the conservative assumption that it would decrease quality of life due to adverse effects. We used sensitivity analysis to model the change to quality of life as a result of β-blocker use. The model already incorporates the utilities (quality-adjusted life-years [QALYs]) associated with CHD.[23] Since we are not aware of any studies conducted to measure the quality of life associated specifically with β-blockers after MI, we based our estimate of a 1% decrement in quality of life on studies of similar agents.[32-35]

Costs

The most commonly used β-blockers are atenolol and metoprolol.[36] We used the maximum dosages to provide a conservative cost assumption (atenolol, 100 mg once a day, and metoprolol, 100 mg twice a day). The average wholesale price in 1998 for one hundred 100-mg tablets was $97 for atenolol and $65 for metoprolol (generic), based on a review of all relevant prices.[37] Therefore, we calculated a weighted average cost of $432/y. As a conservative assumption, we assumed that the drugs would be taken for 20 years even though the benefits beyond year 7 would be small. For an upper estimate, we assumed a cost of $600/y based on prices for brand-name drugs (Tenorim for atenolol [$564/y] and Lopressor for metoprolol [$500/y]). For a lower estimate, we assumed a cost of $52/y based on Medicare reimbursement rates.[37] Drug costs are even lower in large-volume contracts (eg, $13/y through Veterans Affairs) (Audrey Lee, PharmD, oral communication, VA Pharmacy Research Service, March 28, 2000).

The averted costs of treatment for MIs and CHD mortality have been estimated for the CHD Policy Model and described in detail elsewhere[23] and in the online Appendix. We did not include the costs of the following: adverse effects due to β-blockers since serious sequelae are infrequent and would not add significantly to the costs; the incremental costs of office visits, laboratory tests, and pharmacy costs that may be associated with β-blocker use because these would be minimal; and the possible increased costs due to substitution of higher cost or less effective treatments.[10]

RESULTS

Base-Case Results

Single Cohort Followed Up for 20 Years. We evaluated the impact of extending β-blocker therapy to all MI survivors in the United States without absolute contraindications in 2000 and continuing treatment for 20 years (TABLE 2). Compared with current use, this strategy would result in an esti-

Table 2. Epidemiological Impact of Increasing β-Blocker Use in the Single Cohort (n = 406 000)*

β-Blocker Use	CHD Deaths	MIs	Life-Years	Incremental CHD Deaths	Incremental MIs	Incremental Life-Years	Life-Years Saved per Person Treated
Zero	183 000	165 600	3 994 000	. . .	. . .	. . .	. . .
Current†	177 700	161 400	4 049 000	−5300	−4200	55 000	0.31
Target‡	173 400	157 900	4 094 000	−4300	−3500	45 000	0.23

*Projected for years 2000-2020 in absolute (undiscounted) numbers. Numbers are rounded. CHD indicates coronary heart disease; MI, myocardial infarction; and ellipses, not applicable.
†Current use is 44% of the post-MI population.
‡Target population is 92% of the post-MI cohort (80% with withdrawals).

Table 3. Costs, Outcomes, and Cost-effectiveness of Increasing β-Blocker Use in the Single Cohort*

	Total Costs and Effectiveness				Incremental Costs and Effectiveness		
β-Blocker Use	CHD Costs, $ in Millions	β-Blocker Costs, $ in Millions	Total Costs, $ in Millions	QALYs	Incremental Costs, $	Incremental QALYs	Cost per QALY Gained, $
Zero	18 200	0	18 200	3 086 000	. . .	. . .	. . .
Current†	17 700	630	18 400	3 129 000	181 000 000	42 000	4300
Target‡	17 400	1200	18 500	3 163 000	158 000 000	35 000	4500

*Numbers are rounded. Incremental costs and effectiveness for years 2000-2020 presented as absolute (undiscounted) numbers. Total costs and effectiveness discounted 3% from 2000. CHD indicates coronary heart disease; QALYs, quality-adjusted life-years; and ellipses, not applicable.
†Current use is 44% of the post-MI population.
‡Target population is 92% of the post-MI cohort (80% with withdrawals).

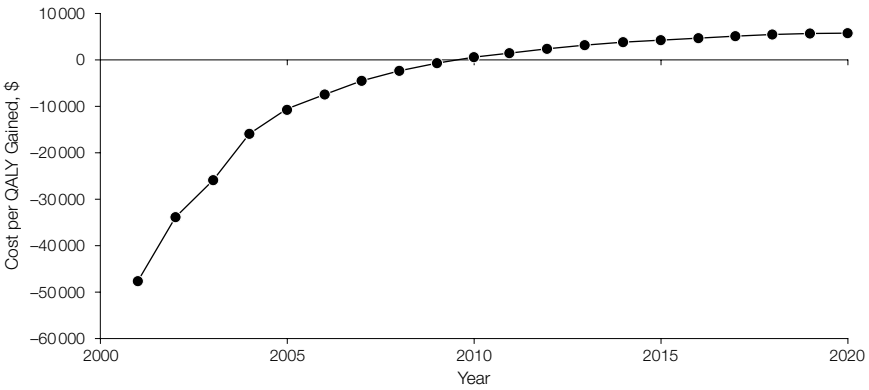
mated 4300 fewer CHD deaths, 3500 MIs prevented, and the addition of 45 000 life-years. The potential benefits of increasing β-blocker use from current to target rates are similar in magnitude (albeit slightly less) to the previously achieved benefits of increasing β-blocker use from none to current rates (Table 2).

The additional costs of β-blocker medication over 20 years were projected to be $570 million. However, because increased β-blocker use would decrease CHD treatment costs, the net cost was estimated to be only $158 million. The incremental cost per QALY gained would be $4500 (TABLE 3).

The magnitude of benefit was projected to be greatest during the first 3 years of treatment and to decrease thereafter. Because we assumed that β-blockers would remain fully effective for only the first 3 years, the annual number of life-years gained would peak in year 3 at 4900 and decline to 600 by year 20. Costs show a similar pattern, with estimated net savings for the first 3 years.

Multicohort Analysis. We also examined the effects of implementing increased β-blocker use in all first-MI survivors annually over 20 successive years (FIGURE 1). Increased β-blocker use would result in an estimated 72 000 fewer CHD deaths, 62 000 MIs prevented, and a gain of 447 000 life-years. Increased β-blocker use would be cost saving for the first 9 years. Over the entire period it also would be cost saving, saving a total of $18 million compared with current use.

Figure 1. Cost-effectiveness of Increasing β-Blocker Use in 20 Successive Annual Cohorts



Each data point indicates the cost or cost savings per quality-adjusted life-year (QALY) gained for each year, as all patients with a first MI over 20 successive years become eligible for β-blocker use (the multicohort model) (n=297 000 in 2001). Increasing β-blocker use from current to target levels would be cost saving each year until 2010 and would approach a steady state of cost per QALY gained of $5400 in 2020.

Sensitivity Analyses

Sensitivity analyses demonstrated that the cost-effectiveness of β-blocker therapy always would be less than $11 000 per QALY gained, even using unfavorable assumptions. They also demonstrated that, under several scenarios, increased β-blocker use would be cost saving (FIGURE 2 and online Appendix).

A higher withdrawal rate and restricting β-blockers to only patients without absolute or relative contraindications would have little effect on the cost-effectiveness ratios; however, these actions would have a large impact on the absolute benefits. For example, in the single-cohort analysis, restricting

β-blockers to only patients without absolute or relative contraindications would reduce the epidemiological impact of β-blocker therapy by about 60% (data not shown).

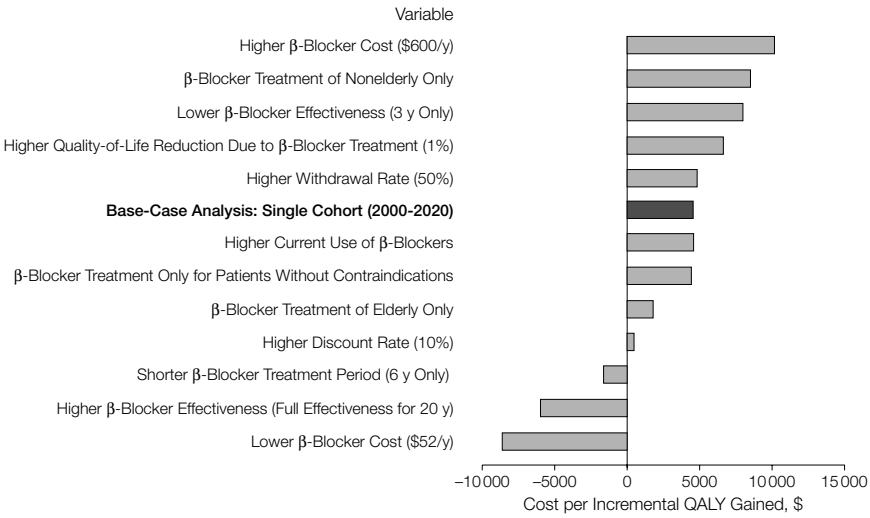
If brand-name rather than generic β-blockers are prescribed, the incremental cost per QALY gained would increase to $10 500 (FIGURE 3). However, β-blockers become cost saving if the costs drop to as little as $300 per person annually. This is significantly more expensive than the cost of discounted medications typically found in large organizations and programs such as Veterans Affairs.

COMMENT

Our results suggest that increased use of β-blockers after MI would lead to impressive gains in health and would potentially be cost saving if the increase were sustained over time, β-blockers were taken for only 6 years, or the costs of β-blockers were less than $300/y. These are reasonable scenarios; for example, consumers can purchase β-blockers on the Internet for only $103/y (eg, http://www.drugstore.com [accessed November 1, 2000]). By increasing β-blocker use in one cohort, the number of life-years saved over 20 years is 7 times larger than that of annual mammography screening for women aged 50 to 69 years in a similar size cohort and has a more favorable cost-effectiveness ratio.[38] In another example, by increasing β-blocker use among all patients having a first MI over the next 20 years, the number of deaths averted (n=72 000) would be similar to the size of the adult population of Ann Arbor, Mich. A particularly important finding is that restricting β-blockers only to ideal candidates (those without absolute or relative contraindications) would reduce the epidemiological impact of β-blocker therapy by about 60%. There has been controversy over whether β-blockers should be prescribed to individuals with relative contraindications, and this is one major reason for their underuse. Although clinical trials would need to be conducted to conclusively demonstrate the efficacy of β-blockers in these populations, the latest evidence and our analysis suggest that these patients can derive substantial benefits from β-blocker use at a reasonable cost. However, our results suggest that even if use were increased in only ideal patients, the benefits would be substantial.

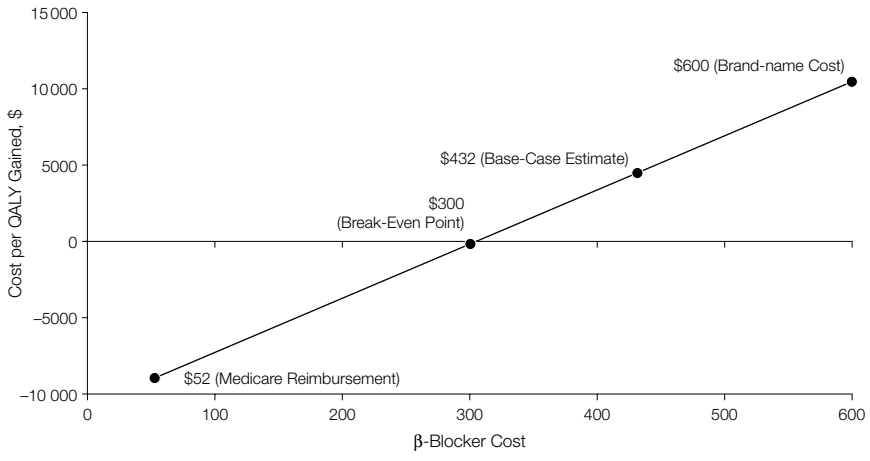
We reported in 1988 that β-blocker use following MI is relatively cost-effective.[39] The current study updates that analysis and also extends prior knowledge in several important ways. First, the prior study relied on a clinical decision analysis model. Such models are appropriate when more complex epidemiological models have not been developed, but they are limited because they cannot be validated easily against published data. Since that time, we have de-

Figure 2. Sensitivity Analyses



Each bar shows the cost or cost savings per quality-adjusted life-year (QALY) gained for each sensitivity analysis, based on the single-cohort analysis comparing current with target use of β-blockers. Base-case results (dark bar) are described in detail in Table 3.

Figure 3. Cost-effectiveness as a Function of β-Blocker Cost



Each point represents the cost or cost savings per quality-adjusted life-year (QALY) gained for representative β-blocker costs (brand-name drugs, average wholesale price of drugs [base-case], and Medicare reimbursement rates) as well as the break-even point for costs.

veloped and validated a sophisticated decision analytic model that incorporates an epidemiological model of the US population. This model enabled us to estimate future costs and outcomes over an extended period, thereby providing a public health perspective as well as a clinical perspective. Second, the prior study did not include the savings associated with reduced CHD events and mortality, a limitation we addressed in the current study. Third, the prior study was conducted when more patients were considered to have contraindications to β-blocker use. In the current study we used newly available data to examine the impact of extending β-blocker use to patients traditionally considered ineligible. Finally, the prior study was conducted when the policy landscape was quite different than it is today.

The reasons for underuse of β-blockers are complex.[3,40-43] In addition to concerns about β-blocker use in individuals with relative contraindications, reasons for underuse include concerns about the impact of β-blockers on quality of life[8,40] and the substitution of calcium channel blockers.[3,8] However, concerns about significant adverse effects have not been substantiated,[8,40,44,45] and the substitution of calcium channel blockers appears to be more of a result of the extensive marketing efforts for these drugs than any proven benefit.[8,36,46,47]

Another factor in underuse that has been much less prominent in the literature is the role of patient preferences. Patients may be reluctant to take a drug for 20 or more years that has a reputation for causing adverse effects such as sexual dysfunction.[33,34] Although patients who have their lives extended may gain an average of 4 to 5 years of life, the average gain in life-years for all patients is only a few months. Surprisingly, however, there has been little research on patients' preferences and their role in underuse of β-blockers. This is particularly surprising given that nonclinical factors that may reflect patient preferences, such as race/ethnicity, have been shown to be associated with β-blocker use.[2,3]

Understanding the consequences of underuse of β-blockers is important because of implications for current policy debates over quality-of-care measures and Medicare prescription drug coverage. Attempts to increase β-blocker use provide examples of both the success and failure of current efforts to improve health care quality. The inclusion of β-blocker use as a measure of quality of care in HEDIS has been associated with a large increase in use, particularly among plans that publicly report their results.[7] Although HEDIS covers only managed care plans and there are undoubtedly other causes for the increase in use, this result suggests that "what gets measured gets done."[48] Another example is the effort by the Health Care Financing Administration to implement a continuous quality improvement approach for Medicare beneficiaries with MI. Data feedback by peer review organizations resulted in a more than 50% relative increase in β-blocker use.[49]

However, despite the relative success of these efforts in increasing β-blocker use, there is still a long way to go. For example, use rates in managed care plans still range from 40% to 100%[7] and, even after the extensive efforts of the peer review organization demonstration, β-blocker use has been reported at 50% among all eligible patients and 68% among ideal patients.[49] These results suggest that quality improvement efforts to date may have "plucked the low-lying fruit," but that more extensive efforts will be required to encourage β-blocker use. This will require multiple strategies and the involvement of physicians, pharmacists and other health care providers, policymakers, and patients.[14,50]

Understanding the implications of the underuse of β-blockers is also important because of the relevance to the current debate over reform of Medicare prescription coverage. The majority of individuals eligible for β-blockers following MI are elderly, and our analysis demonstrated that the cost of β-blockers has a large impact on their cost-effectiveness. This suggests that policies currently under consideration, such as reducing the out-of-pocket cost of prescriptions and enabling the Medicare program to obtain federal price discounts and rebates, could substantially improve health and reduce costs.

Our analysis has several limitations. As with any simulation model, various assumptions had to be made to have a tractable analysis. Therefore, we used conservative assumptions for variables for which the model was sensitive that biased our findings against β-blockers. We also conducted extensive sensitivity analyses, which indicate our results are robust across a wide range of assumptions. Our study is also limited by available data. The benefits of β-blocker use are based on clinical trials, which may not reflect actual effectiveness in practice, particularly among women and racial/ethnic minorities. However, it is unlikely that different assumptions would have substantially changed our conclusions. The model has been shown to accurately predict actual CHD mortality[12] and our results are consistent with those of other analyses.[7,10,51]

In summary, our study quantifies the future epidemiological and economic impact of increasing β-blocker use to target rates using a validated model of CHD in the United States. We determined that increased use of β-blockers after MI would lead to impressive gains in health and potentially would be cost saving.

Author Contributions: Dr Phillips conceptualized the study, supervised all analyses, and wrote the manuscript.
Dr Shlipak participated in all aspects of the study, including conceptualization, analysis, and review of drafts.
Dr Coxson ran the analyses and participated in all aspects of the study.
Dr Goldman provided overall guidance, funding for data analyses, and participated in all aspects of the study.
Drs Heidenrich, Hunink, and Weinstein, Ms Goldman, and Mr Williams contributed to the study and reviewed drafts.

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TECHNICAL APPENDIX

We provide additional information on the model and analyses, as recommended by the US Panel on Cost-effectiveness in Health and Medicine.

β-BLOCKER USE RATES

The β-blocker use table below summarizes the assumptions that have been incorporated into the CHD Policy Model regarding past use and also the rates that form the basis of our primary projection model. The target population for our projection simulation consists of all patients who do not have absolute contraindications, increasing both use and eligibility to the fullest extent possible.

We assume that "new" β-blocker users (that is beyond the 44% baseline use) will have a significant withdrawal probability—12% for ideal candidates and 30% for nonideal candidates. The net use rates given in parentheses are used internally in our simulations to model the reduced benefit due to withdrawals.

Table 1. β-Blocker Use Rates

	X = % Use Ideal Patients	Y = % Use Extended Eligibility Patients	Z = % Use Contraindicated Patients	Overall Use Within a Post-MI Cohort r = 0.4 X + 0.52 Y + 0.08 Z [Effective Rate After Withdrawals = r–0.12 (x–xbase)–0.30 (y–ybase)]
1990-2000 Trends				
1990	40	27	0	30
1994/1995	49	33	0	37
2000	58	38	0	44
Cohort target projection simulation				
Zero β-blocker use	0	0	0	0
Current rate	58	38	0	44
Target	100 (95)	100 (81)	0	92 (80)

β-BLOCKER BENEFITS 1990-2000

The 1990-2000 β-blocker use trend is implemented as a trend in event rates (MI, arrest, and old CHD mortality). We estimated the relevant population fractions and event rate reductions as described below.

Survivors from the previous year's MIs represent roughly 10% of the total post-MI population (400 000 of 4 million) and that population decreases about 10% per year (see survival table below) due to deaths and "aging out of the model."

Table 2. Survival Fraction for a Cohort of New Individuals With MI Who Survived the Year

Years After MI	Fraction Alive
1	1.00
2	0.91
3	0.84
4	0.77
5	0.70
6	0.64

A finite difference equation was used to estimate the total fraction of the post-MI population who would be survivors of MIs in the past 3 years (for full β-blocker benefit) and the past 4 to 6 years (for small benefit). The additional users of β-blockers each year from 1990 to 2000 are (Year–1990) × 1.4% of this fraction, so that use increases from 30% in 1990 to 44% in 2000.

β-BLOCKER BENEFITS IN THE COHORT PROJECTION 2001-2020

The CHD Policy Model was modified for this project so that, beginning in 2001, only the cohort with MIs in the year 2000 is retained in the model. This narrows the population and also removes all uncertainty about the date of the benefit-defining MI. The model assumes that all patients had MIs at the end of 2000 and event rate reductions begin in 2001, which provides a conservative estimate of benefits. Event rates were adjusted up to represent 0% β-blocker use, and down to reflect 100% use.

CHD AND β-BLOCKER TREATMENT COSTS

We assume the cost of β-blocker treatment to be $432 (in 2000 dollars) per person per year as indicated in the article. Total costs in each year are calculated using the following formula:

Total Cost (2001) = $\$432 \times (F + 0.5 \times W) \times BB100\ pop(2001)$

Total Cost (Year) = $\$432 \times F \times BB100$ population(year) for year = 2002 to 2020, where F is the β-blocker use fraction (Table 1 above) excluding withdrawal fraction (W); and BB100 population(year) is the total cohort population for the simulation with 100% β-blocker use.

YEAR 2001 COHORT OF MI SURVIVORS

We used the 1986 version of the CHD Policy Model including trends to 1990, modified to follow the cohort of people who have an MI in the year 2000. In 2001, the cohort consists of 405 643 persons distributed as follows:

Cohort Population Distribution by State (Beginning of Year)

Age Range, y	Angina, M/F	Revascularization, M/F	MI		Arrest, M/F	Revascularization + MI	
			Male	Female		Male	Female
35-44	0	0	20 320	5433	0	1686	133
45-54	0	0	45 818	15 067	0	10 548	1955
55-64	0	0	45 239	21 079	0	17 079	4723
65-74	0	0	43 062	30 171	0	21 425	7830
75-84	0	0	42 774	42 270	0	14 423	6735

Age Range, y	Revascularization + Arrest, M/F	MI + Arrest		Revascularization + MI + Arrest	
		Male	Female	Male	Female
35-44	0	419	101	43	3
45-54	0	1035	346	364	70
55-64	0	982	445	632	183
65-74	0	754	471	640	245
75-84	0	352	371	263	134

Total Cohort Population by Age Range

Age Range, y	Male	Female
35-44	22 469	5672
45-54	57 768	17 439
55-64	63 934	26 433
65-74	65 883	38 719
75-84	57 814	49 512

Verification that cohort selection is complete:

Data Summary	
MIs in 2000	552 000
Cohort in 2001	406 000
Difference = Death and "aging out"	146 000

Accounting for the difference:

MI-only deaths	55 000
MI + revascularization deaths	12 000
Non-CHD deaths	9000
Chronic CHD deaths	8000
85-year-olds	8000
Arrest + MI deaths	65 000
Total	**157 000**

CUMULATIVE ANALYSIS OF SUCCESSIVE COHORTS OF FIRST MI

The cohort in 2001 consists of 296 613 survivors of a first MI, with the following age and sex distribution:

Age Range, y	Male	Female
35-44	21 160	5306
45-54	48 534	14 870
55-64	46 273	20 414
65-74	41 642	27 530
75-84	36 368	34 516

Twenty successive cohorts are simulated: 1 for each year from 2001 to 2020. Then the outcomes are summed over this period to assess the impact of changing β-blocker use on an ongoing basis beginning in 2000.

ELDERLY AND NONELDERLY β-BLOCKER RATES

These simulations separately follow the elderly (≥65 years) and the nonelderly (35-64 years) of the year 2000 cohort. Numbers in parentheses are used internally in our simulations to model the reduced benefit due to withdrawals.

Table 3. β-Blocker Use Rates in the Elderly

Projection Simulations	X = % Use Ideal Patients	Y = % Use Extended Eligibility Patients	Z = % Use Contraindicated Patients	Overall Use Within a Post-MI Cohort = 0.31 X + 0.61 Y + 0.08 Z
Zero	0	0	0	0
Current	58	38	0	41
Target	100 (95)	100 (81)	0	92 (79)

Table 4. β-Blocker Use Rates in the Nonelderly

Projection Simulations	X = % Use Ideal Patients	Y = % Use Extended Eligibility Patients	Z = % Use Contraindicated Patients	Overall Use* Within a Post-MI Cohort = 0.6 X + 0.32 Y + 0.08 Z
Zero				
Current	58	38	0	47
Target	100 (95)	100 (81)	0	92 (83)

*The 60% estimates are from Brand et al.[28]