

Adherence to β -blocker Therapy Under Drug Cost-sharing in Patients With and Without Acute Myocardial Infarction

Sebastian Schneeweiss MD, ScD; Amanda R. Patrick, MS; Malcolm Maclure, ScD;
Colin R. Dormuth, ScD; and Robert J. Glynn, PhD, ScD

Spending for prescription drugs in the United States reached more than \$200 billion or 12% of all healthcare expenditures in 2004 and has been one of the fastest growing components of healthcare spending.^{1,2} Medicare Part D drug coverage will bring long-needed improvements in access to prescription drugs but is likely to increase these expenditures further.

In the first months of Part D, seniors were offered 1429 stand-alone drug plans³ that were regulated and overseen by the Centers for Medicare & Medicaid Services.⁴ These plans had many formularies with a wide range of patient cost sharing,³ few of which have been rigorously evaluated regarding their clinical and economic outcomes. Well-designed patient cost-sharing policies⁵⁻⁸ as well as coverage restrictions⁹ have been shown to produce net savings from the health plan's perspective¹⁰ without adversely affecting health outcomes. Other interventions that disregard clinical logic (eg, global physician budgets, prescription caps) can lead to unanticipated outcomes, including increased rates of hospitalization¹¹ and nursing home admissions.¹² The evidence is inconclusive for the common 3-tiered copayment systems.^{13,14} Generally these studies are criticized for their lack of generalizability because they were conducted in a wide range of patient populations and health systems. A direct comparison of several drug policies in a single system has not been published.

β -Adrenergic receptor blockers (β -blockers) are indicated for the treatment of hypertension^{15,16} and have been shown to be as efficacious as calcium channel blockers¹⁷ and angiotensin-converting enzyme inhibitors¹⁷⁻²⁰ in reducing blood pressure and cardiovascular risk. Oral β -blockers are further indicated for long-term use in all patients recovering from acute myocardial infarction (MI).^{21,22} Health plan performance measures like the Health Plan Employer Data and Information Set recommend β -blocker therapy after acute MI in patients who have no contraindications.²³ β -Blockers treat a largely asymptomatic condition (hypertension) and may lead to side effects including fatigue, erectile dysfunction, and dizziness. Not surprisingly, adherence to antihypertensive treatment was less than 50% in elderly patients after 1 year, and only 20% of patients were sufficiently compliant to obtain the therapeutic benefits observed in clinical trials.²⁴ Adherence was further reduced when β -blockers were combined with statin therapy.²⁵ The rate of initiation of β -blocker therapy after acute MI was found to be

Objective: To evaluate the effects of patient copayment and coinsurance policies on adherence to therapy with β -adrenergic blocking agents (β -blockers) and on the rate of initiation of β -blocker therapy after acute myocardial infarction (MI) in a population-based natural experiment.

Study Design: Three sequential cohorts included British Columbia residents age 66 years and older who initiated β -blocker therapy during time intervals with full drug coverage (2001), a \$10 or \$25 copayment (2002), and 25% coinsurance (2003-2004). We used linked data on all prescription drug dispensings, physician services, and hospitalizations. Follow-up of each cohort was 9 months after the policy changes.

Methods: We measured the proportion of subjects in each cohort who were adherent to β -blocker therapy over time, with adherence defined as having $\geq 80\%$ of days covered. We also measured the proportion of patients initiating β -blocker therapy after acute MI. Policy effects were evaluated using multivariable regression.

Results: Adherence to β -blocker therapy was marginally reduced as a consequence of the copayment policy (-1.3 percentage points, 95% confidence interval [CI] = -2.5, -0.04) or the coinsurance policy (-0.8 percentage points, 95% CI = -2.0, 0.3). The proportion of patients initiating β -blockers after hospitalization for acute MI remained steady at about 61% during the study period, similar to that observed in a control population of elderly Pennsylvania residents with full drug coverage.

Conclusions: Fixed patient copayment and coinsurance policies had little negative effect on adherence to relatively inexpensive β -blocker therapy, or initiation of β -blockers after acute MI.

(*Am J Manag Care.* 2007;13:445-452)

In this issue

Take-away Points / p451

www.ajmc.com

Full text and PDF

Web exclusive

Appendix

For author information and disclosures, see end of text.

less than 21% in a US Medicare population between 1987 and 1992.²⁶

Spending for β -blockers was \$2.1 billion among US seniors in 2001 according to an analysis of the Medical Expenditures Panel Survey.²⁷ However, despite the fact that the efficacy of β -blockers has been proven, they are used in too few patients and with disappointing adherence even in the absence of cost sharing, which makes them a problematic target for any cost-sharing policy.

PharmaCare, the province-funded drug insurance plan in British Columbia, provided full prescription drug coverage for all elderly persons before January 2002. In January 2002, a prescription copayment policy for elderly residents of Can\$25 (Can\$10 for low-income seniors) was implemented. In May 2003, the seniors' copayment was replaced with a 25% coinsurance payment plus an income-based deductible policy. Linking deductible cost-sharing levels to income was intended to prevent low-income patients from underutilizing essential drugs.^{28,29}

This natural experiment among all elderly British Columbia residents provided the opportunity to evaluate the consequences of 2 subsequent patient cost-sharing interventions on adherence to β -blocker therapy among patients who initiated this therapy and on the initiation of β -blocker therapy after acute MI in a large, stable population of older adults.

seniors initiating β -blocker therapy within 6 months before January 2001, a *copayment cohort* of seniors initiating β -blocker therapy within 6 months before the copayment policy in January 2002, and a *coinsurance cohort* initiating β -blocker therapy within 6 months before the coinsurance policy in May 2003 (Figure 1). To be eligible for any of the 3 cohorts, patients had to be beneficiaries of the provincial healthcare system during the respective 6-month periods. Initiation was defined as filling a first β -blocker prescription during the 6-month cohort entry period without having filled a β -blocker prescription in the 6 months before the initiation date. We required evidence of hypertension as indicated by a diagnosis of hypertension (*International Classification of Diseases, Ninth Revision [ICD-9] codes 401.x-404.x*) recorded during an office visit or as a hospital discharge diagnosis during the 6 months before initiation date. Follow-up included up to 6 months during the cohort entry phase, depending on when patients initiated β -blocker use, and an additional 9 months after the policy changes or the respective dates in the control group (Figure 1).

All patients were identified in the linked healthcare utilization databases of the publicly funded healthcare system of British Columbia. Pharmacists enter medication names, dose, and dispensed quantity for all prescribed drugs into a single database via a province-wide network that ensures minimal underreporting and misclassification.³⁰ This recording is independent of the payer and includes out-of-pocket purchases of prescription medications. The Ministry of Health maintains linkable data on all physician services and hospitalizations for all persons age 65 years and older. Up to 25 diagnoses for hospital discharges and 1 diagnosis for each medical service are recorded, with good specificity and completeness.³¹

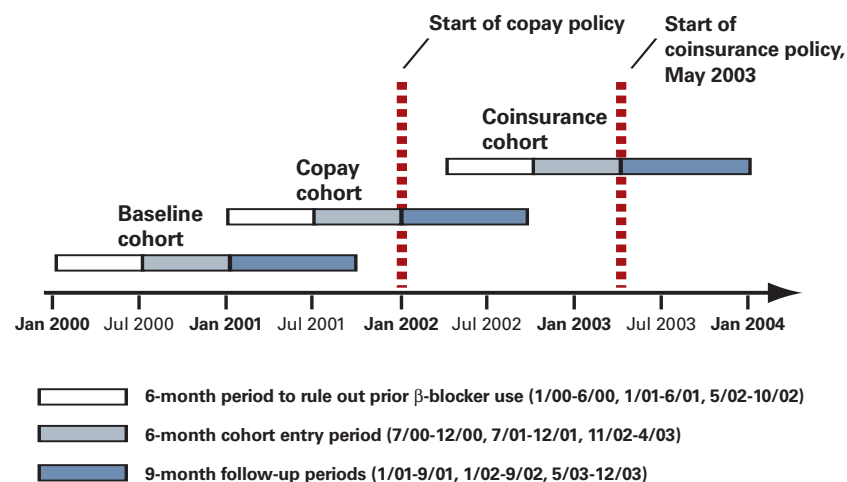
To assess the effects of the policy changes on rates of β -blocker initiation after MI, we identified all patients who were hospitalized with an acute MI between January 2000 and December 2004, a period spanning the baseline and policy periods. Myocardial infarctions were identified based on the presence of an ICD-9 diagnosis code of 410.x as a primary diagnosis and a length of hospitalization between 3 and 180 days; this definition has been found to be highly accurate (positive predictive value, 95%).³² Patients also were required to survive at least 60 days after hospital discharge. The outcome of interest was β -blocker initiation within

METHODS

Patients

To evaluate the effects of the copayment and coinsurance policies on β -blocker adherence rates among new users of β -blockers, we selected 3 cohorts, including a *baseline cohort* of

■ **Figure 1.** Design of a Multicohort Evaluation of β -Blocker Adherence After the Start of 2 Cost-sharing Policies



Adherence to β -blocker Therapy Under Drug Cost-sharing

60 days of discharge. We created identically defined cohorts of elderly patients with a hospitalization for acute MI in Pennsylvania and used their β -blocker initiation rates to control for any temporal trends that might exist in β -blocker prescribing post-MI. These patients were Medicare beneficiaries and enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly, a state-funded prescription benefit program for low-income seniors with constant \$6 copayment drug coverage throughout the study period.

Study End Points

Adherence was calculated for each calendar month as the proportion of patients days categorized as adherent. First the proportion of days covered (PDC)³³ was calculated for each patient by dividing the number of days on which the patient had a β -blocker supply available by the number of cohort membership days the patient contributed in that calendar month. Based on their PDC, patients were then classified as adherent in that month if their PDC was larger than 0.80, a somewhat arbitrary but widely used threshold.³⁴⁻³⁶

The numerator of the PDC measure was calculated by creating a β -blocker supply diary for each patient day by stringing together consecutive β -blocker dispensings based on dispensing dates and reported “days supply.”³⁷ When a dispensing occurred before the previous prescription should have run out, utilization of the new prescription was assumed to begin the day after the end of the old prescription and days supply were accumulated. If a dispensing caused a patient’s accumulated supply to exceed 180 days, accumulated supply was truncated at 180 days. Discontinuation was defined as failing to fill a new β -blocker prescription within 90 days of exhausting a previous prescription. The discontinuation date was the end of the previous prescription.

The denominator of the PDC measure was the number of days the patient contributed in that calendar month. Residents who left the province or died were censored from the denominator on their date of death or at the end of their enrollment in the British Columbia Medical Services Plan.

Patient Characteristics

A number of patient characteristics were assessed at cohort entry for members of each of the 3 cohorts. These included age, sex, adjusted family income status (Can\$16 000, \geq Can\$16 000 to \leq Can\$22 000, and $>$ Can\$22 000 as defined by premium subsidy levels),³⁸ number of days with a physician visit, number of acute hospitalizations, number of different diagnoses at the 3-digit ICD code root level, Charlson comorbidity index,³⁹ history of MI, congestive heart failure (hospitalization with ICD-9 code 425 or 428 plus a prescription for

a loop diuretic or digoxin), angina (visit with ICD-9 code 411 or 413 or a nitrate prescription), revascularization procedure, diabetes (visit with ICD-9 code 250 or 357 plus 2 insulin or oral antiglycemic prescriptions), peripheral vascular disease (visit with ICD-9 code 440), and cerebrovascular disease (visit with ICD-9 codes 433, 434, or 436). For the adherence analysis, the covariate assessment period was 12 months. For the β -blocker initiation analysis post-MI, it was 6 months, and the presence or absence of hypertension was assessed as a baseline covariate. Income status was imputed based on Medical Service Plan subsidy level, which is a good proxy for family adjusted income, although it tends to slightly underestimate the proportion of elderly in low-income strata.³⁸

Statistical Analyses

Policy Effects on β -Blocker Adherence. Time trends of monthly adherence proportions were plotted for all 3 cohorts and aligned at the first day of the cohort entry period to achieve comparability of trends. We used segmented linear regression to estimate sudden changes in slopes or levels of the monthly probability of patients being nonadherent, ranging from 0 to 1. To estimate changes in level and slope attributable to the policy, we used regression models that included a constant term, a linear time trend (months 0-5), a binary indicator for a 3-month transition period (months 6-8), a binary indicator for the postpolicy period starting at month 9, and linear time trends for the transition and postpolicy periods.⁴⁰ The 3-month transition period was evaluated because the median prescription length, 90 days, suggested that policy effects might be delayed; however, it was later dropped because we could not observe any significant effect of the transition phase. Policy effects were determined as interaction terms between policy indicators and the level and slope parameters. This analysis leads by design to an underestimation of the decline in adherence during the cohort entry period because of the varying time of cohort entry; however, it does provide valid and most efficient estimates of the policy effects on adherence. We used a longitudinal repeated measures design and adjusted standard errors using generalized estimating equations,⁴¹ assuming an autocorrelated covariance structure with a 1-month lag period,⁴² and assumed normally distributed errors. This linear model estimated absolute percent change, which we thought was the most clinically meaningful effect measure. The normal approximation of a binomial error distribution in a regression model may lead to slightly larger standard errors. (All models are described in detail in the [Appendix](#) and can be viewed at www.ajmc.com).

■ CLINICAL ■

Policy Effects on β -blocker Initiation After Acute MI. We used a segmented linear regression analysis to model the proportion of β -blocker initiations after MI among those patients without pre-MI β -blocker exposure as a function of the copayment and coinsurance policies, adjusted for the confounders listed above and the Pennsylvania control population. Multiplicative interaction terms between the indicator term for the British Columbia policy interventions and region indicators (British Columbia vs Pennsylvania) can be inter-

preted as a time-trend adjusted estimate of the proportions of β -blocker initiators after MI.

Ethics Approval

The human subjects review boards of the Brigham and Women's Hospital and the University of Victoria approved the study. Data use agreements were in place with the Ministry of Health in British Columbia and the Centers for Medicare & Medicaid Services.

■ **Table.** Baseline Characteristics for 3 Cohorts of Subjects With a Hypertension Diagnosis Who Initiated β -blocker Therapy*

Characteristic	Cohort 1 (Baseline)	Cohort 2 (\$10-\$25 Copayment)	Cohort 3 (25% Coinsurance)	P Values of χ^2 Test
No. of subjects	4079	4105	5009	
Age, y				
Mean (SD)	74.4 (6.5)	74.4 (6.5)	74.6 (6.7)	
65-70	1339 (32.8)	1364 (33.2)	1617 (32.3)	0.52
71-75	1113 (27.3)	1082 (26.4)	1334 (26.6)	
76-80	872 (21.4)	904 (22.0)	1064 (21.2)	
81+	755 (18.5)	755 (18.4)	994 (19.8)	
Female sex	2500 (61.2)	2470 (60.1)	2916 (58.7)	0.02
Annual income (Can\$)				
>22 000	2472 (60.7)	2493 (60.9)	3199 (63.9)	0.01
>16 000-22 000	455 (11.2)	448 (10.9)	488 (9.8)	
≤16 000	1148 (28.2)	1155 (28.2)	1316 (26.3)	
Use of additional antihypertensive agents	804 (19.7)	818 (19.9)	924 (18.5)	0.15
No. of physician visit days				
0-7	581 (14.2)	547 (13.3)	739 (14.8)	0.15
≥8	3498 (85.8)	3558 (86.7)	4270 (85.3)	
Hospitalization	1131 (27.7)	1116 (27.2)	1306 (26.1)	0.19
No. of different diagnoses				
0-5	925 (22.7)	914 (22.3)	1190 (23.8)	0.21
≥6	3154 (77.3)	3191 (77.7)	3819 (76.2)	
Charlson Comorbidity Index				
0-3	3821 (93.7)	3802 (92.6)	4652 (92.9)	0.14
≥4	258 (6.3)	303 (7.4)	357 (7.1)	
Prior MI	329 (8.1)	305 (7.4)	365 (7.3)	0.35
Prior CHF	31.7 (5.1)	184 (4.5)	259 (5.2)	0.29
Prior angina	720 (17.7)	694 (16.9)	861 (17.2)	0.67
Prior revascularization	143 (3.5)	164 (4)	215 (4.3)	0.16
Diabetes	326 (8.0)	364 (8.9)	489 (9.8)	0.01
Peripheral vascular disease	107 (2.6)	107 (2.6)	157 (3.1)	0.22
Cerebrovascular disease	152 (3.7)	159 (3.9)	196 (3.9)	0.89

*Values are number (%) except where specified. SD indicates standard deviation; MI, myocardial infarction; CHF, congestive heart failure.

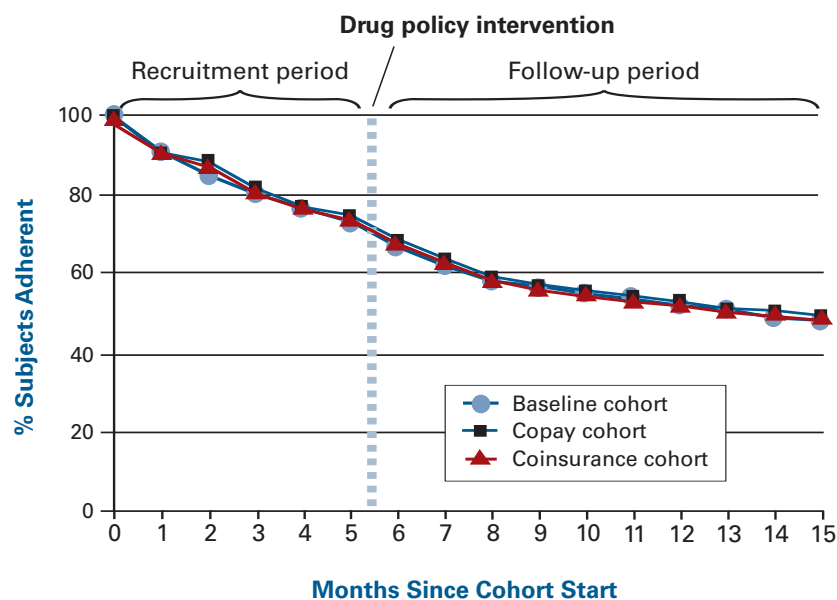
RESULTS

The number of new starters increased over time from 4079 (baseline), to 4105 (copayment cohort), to 5009 (coinsurance cohort) (Table). There was very little change in the distribution of patient characteristics except for a slight increase in diabetes rates over time, a decrease in the percentage of women, and a slight upward shift in income distribution. About 5% of cohort members were censored due to death or loss of eligibility for the provincial healthcare system.

Patients identified with acute MIs during the study period (9118) were older (78 ± 7.2 years) than the group of all β -blocker initiators. They had the following frequencies of pre-existing conditions: diabetes (7.4%), hypertension (26.7%), angina (12.6%), congestive heart failure (5.7%), peripheral vascular disease (1.9%), cerebrovascular disease (2.2%), prior MI (7%), and prior revascularization (1.5%). The Pennsylvania control population (6080) was older than the British Columbia acute MI population (82 ± 7.3 years) and had more comorbidities, including diabetes (14.3%), hypertension (50%), congestive heart failure (9.9%), peripheral vascular disease (10.1%), cerebrovascular disease (12.1%), and prior MI (16.6%). Rates of angina (13%), and prior revascularization (1%) did not differ from those in the British Columbia population.

Among β -blocker initiators there was a sharp reduction in adherence in the 6-month cohort entry periods in all 3 cohorts (-6.3% per month, $P < .0001$). This decline stabilized after 9 months (Figure 2), with the rate of decrease in adherence falling to $\sim 1\%$ per month in all 3 cohorts. The drop in adherence level at the third month after the policy changes was slightly greater in the copayment cohort (-1.3 percentage points; 95% confidence interval [CI] = $-2.5, -0.04$) than in the baseline cohort after adjusting for patient characteristics. There was no difference between the coinsurance and baseline cohorts (-0.08 percentage points; 95% CI = $-2.0, 0.3$). Low-income subjects had lower adherence levels than higher-income subjects in all 3 cohorts (-2.6 percentage points; 95% CI = $-4.6, -0.6$). This trend was neither improved nor exacerbated by the policy changes. Similarly, the tendency for subjects with a prior MI or revascularization to be more adherent

■ **Figure 2.** Monthly β -blocker Adherence for the Baseline, Copayment, and Coinsurance Cohorts*



*Adherence was nondifferential across the baseline and copayment and coinsurance cohorts after the respective policy changes at month 6, suggesting the absence of a policy effect. Adherence was measured as the proportion of patients with $\geq 80\%$ of days covered during each month. Unadjusted proportions were plotted. For descriptions of the cohorts, see the Table.

(6.2 percentage points; 95% CI = 3.5, 9.4) was not affected by the policy changes.

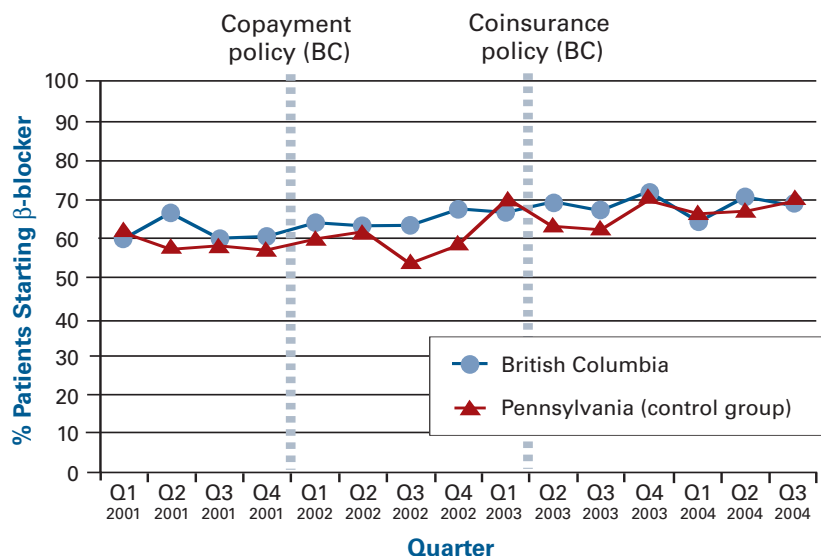
The proportion of new initiations of β -blocker therapy after acute MI remained constant over time at about 61% in both British Columbia and Pennsylvania (Figure 3). This trend was not interrupted by the 2 policy changes in British Columbia after adjusting for the Pennsylvania time trend.

DISCUSSION

β -Blockers are effective drugs to treat hypertension and reduce the risk for MI, cardiac mortality, and stroke.^{43,44} However, adherence with β -blocker therapy has been consistently found to be far from optimal, even in populations with full drug insurance coverage.^{24,26} It was speculated that patient copayments may worsen this already unfavorable situation.

This evaluation of a population-based natural experiment with older adults found that adherence to newly initiated β -blocker therapy was only minimally compromised by a fixed copayment policy and a subsequent coinsurance policy. Although a 1% drop in adherence seems negligible, it was shown that reducing the population average blood pressure by only 2 mm Hg may have a large population impact in terms of the number of avoided cardiovascular events because of the

■ **Figure 3.** Time Trend of β -blocker Initiation Rates Among Subjects Who Had a Myocardial Infarction in British Columbia*



*The time trend among subjects in British Columbia (BC) is presented with a control time trend of β -blocker initiation in Pennsylvania, a region that was not affected by policy changes. As seen in the graph, neither the level nor the rate of change in β -blocker initiation in BC was affected by the policy changes.

high prevalence of hypertension in elderly patients.⁴⁵ Initiation of β -blocker therapy after acute MI was not affected by these cost-sharing policies and increased at a rate comparable to that observed in a control population with uninterrupted full drug coverage.

A subgroup analysis in low-income patients and patients with prior MI or revascularization showed that the cost-sharing policies did not further compromise the generally decreasing adherence to β -blockers over time. These findings are in contrast to earlier findings that any cost-sharing policies will reduce drug use.⁵⁻¹⁴ This discrepancy may be explained by the availability of low-cost β -blockers in British Columbia. The median spending, including insurance and out-of-pocket spending, for a 90-day β -blocker supply in our study was \$29 under full coverage, and \$22 and \$23 under cost sharing, indicating that patients switched to lower-cost β -blockers. Adherence to statins, a much more expensive medication group treating a largely asymptomatic condition, was much more affected by patient cost sharing.⁴⁶ Price elasticity for drugs was shown earlier to be relatively low,^{47,48} particularly for drugs used to treat chronic cardiovascular conditions as opposed to drugs used for fast symptom relief.⁴⁹ If ingredient costs are low, it can be expected that patients will continue using β -blockers, despite a slightly increased out-of-pocket contribution.

Time trend analyses or repeated cohort designs are considered valid study designs to study short-term effects of drug pol-

icy changes by adjusting for most time-invariant confounders.^{50,51} A potential threat to validity in such designs when studying longer-term effects is the presence of underlying utilization time trends independent of the policy interventions, which is why we adjusted for time trends in secondary-prevention use of β -blockers and compared any potential changes in trend with similar changes in a comparable population who did not have drug cost sharing.

Another concern is other interventions that took place at the time of the study intervention. We found a continuous increase in patients with recorded diabetes even before initiation of the disease management program that was adjusted for in our analysis. β -blocker stockpiling also could not have distorted our result because we accounted for the quantity dispensed when we calculated adherence and discontinuation.

In conclusion, fixed patient copayment and coinsurance policies had little negative effect on adherence to relatively inexpensive β -blocker therapy or the initiation of β -blockers after acute MI.

Acknowledgments

We appreciate the contributions by Sean Burnett, MA, and Greg Carney, BSc, at PFLA Corporation, Victoria, for their expert advice and support in linking individual databases and Claire Canning for analytic support.

Author Affiliations: From the Division of Pharmacoepidemiology and Pharmacoeconomics (SS, ARP, CRD, RJG) and the Division of Preventive Medicine (RJG), Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Mass; the Department of Epidemiology (SS, MM, CRD) and the Department of Biostatistics (RJG), Harvard School of Public Health, Boston; the Department of Health Information Sciences, University of Victoria, British Columbia, Canada (MM); and the Therapeutics Initiative, University of British Columbia, Vancouver, Canada (CRD).

Funding Sources: The study was funded by grants to Dr Schneeweiss from the National Institute on Aging (grant R01-AG021950) and the Agency for Healthcare Research and Quality (grant 2-RO1-HS10881), Department of Health and Human Services, Rockville, Md. Dr Maclure is a Senior Scholar at the Michael Smith Foundation. Dr Dormuth is the recipient of a Canadian Institute of Health Research dissertation grant.

Author Disclosure: Dr Schneeweiss reports serving on the advisory board for Aheris, Inc. Dr Glynn reports receiving grants from Astra-Zeneca, Bristol-Myers Squibb, and Novartis.

The authors (ARP, MM, CRD) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter discussed in this manuscript.

Authorship Information: Concept and design (SS, ARP); acquisition of data (SS, MM, CRD); analysis and interpretation of data (SS, MM, RJG, ARP); drafting of the manuscript (SS, ARP); critical revision of the manuscript for important intellectual content (SS, MM, CRD, RJG, ARP); statistical analysis (SS, RJG, ARP); obtaining funding (SS); administra-

tive, technical, or logistic support (SS, MM, CRD); supervision (SS).

Address correspondence to: Sebastian Schneeweiss, MD, ScD, Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 1620 Tremont St (Ste 3030), Boston, MA 02120. E-mail: schneeweiss@post.harvard.edu.

REFERENCES

1. **Heffler S, Smith S, Keehan S, Clemens MK, Won G, Zezza M.** Health spending projections through 2013. *Health Aff (Millwood)*. 2004; Suppl Web Exclusives:W4-79-W4-93.
2. **Strunk BC, Ginsburg PB.** Tracking health care costs: trends turn downward in 2003. *Health Aff (Millwood)*. 2004; Suppl Web Exclusives:W4-354-W4-362.
3. **Hoadley J, Hargrave E, Cubanski J, Neuman T.** *An In-Depth Examination of Formularies and Other Features of Medicare Drug Plans*. Washington, DC: The Henry J Kaiser Family Foundation; April 2006.
4. **Centers for Medicare & Medicaid Services.** Medicare program; Medicare prescription drug benefit; proposed rule. August 2004. Available at: http://search.cms.hhs.gov/search?q=CMS4068P&btnG.x=21&btnG.y=6&site=default_collection&output=xml_no_dtd&client=my_frontend&proxystylesheet=my_frontend&oe=UTF-8. Accessed September 4, 2004.
5. **Schneeweiss S, Walker AM, Glynn RJ, Maclure M, Dormuth C, Soumerai SB.** Outcomes of reference pricing for angiotensin-converting enzyme inhibitors. *N Engl J Med*. 2002;346:822-829.
6. **Grootendorst PV, Dolovich LR, O'Brien BJ, Holbrook AM, Levy AR.** Impact of reference-based pricing of nitrates on the use and costs of anti-anginal drugs. *CMAJ*. 2001;165:1011-1019.
7. **Schneeweiss S, Soumerai SB, Maclure M, Dormuth C, Walker AM, Glynn RJ.** Clinical and economic consequences of reference pricing for dihydropyridine calcium channel blockers. *Clin Pharmacol Ther*. 2003;74:388-400.
8. **Marshall JK, Grootendorst PV, O'Brien BJ, Dolovich LR, Holbrook AM, Levy AR.** Impact of reference-based pricing for histamine-2 receptor antagonists and restricted access for proton pump inhibitors in British Columbia. *CMAJ*. 2002;166:1655-1662.
9. **Schneeweiss S, Maclure M, Carleton BC, Glynn RJ, Avorn J.** Clinical and economic consequences of a formulary restriction of nebulized respiratory drugs in adults: direct comparison of randomized and observational evaluations. *BMJ*. 2004;328:560-564.
10. **Schneeweiss S, Dormuth C, Grootendorst P, Soumerai S, Maclure M.** Net health plan savings from reference drug pricing for angiotensin-converting enzyme inhibitors in elderly British Columbia residents. *Med Care*. 2004;42:653-660.
11. **Schöffski O.** Consequences of implementing a drug budget for office based physicians in Germany. *Pharmacoeconomics*. 1996; 10(suppl 2):37-47.
12. **Soumerai SB, Ross-Degnan D, Avorn J, McLaughlin T, Choodnovsky I.** Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med*. 1991;325:1072-1077.
13. **Motheral B, Fairman KA.** Effect of a three-tier prescription copay on pharmaceutical and other medical utilization. *Med Care*. 2001;39: 1293-1304.
14. **Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG.** The effect of incentive-based formularies on prescription-drug utilization and spending. *N Engl J Med*. 2003;349:2224-2232.
15. **Gibbons RJ, Chatterjee K, Daley J, et al.** ACC/AHA/ACP-ASI. Guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol*. 1999;33:2092-2197.
16. **Recommendations of the Second Joint Task Force of European and Other Societies on Coronary Prevention.** Prevention of coronary heart disease in clinical practice. *Eur Heart J*. 1998;19:1434-1503.
17. **Blood Pressure Lowering Treatment Trialists' Collaboration.** Effects of ACE inhibitors, calcium antagonists, and other blood pressure lowering drugs: results of prospectively designed overviews of randomized trials. *Lancet*. 2000;355:1955-1964.
18. **Hansson L, Lindholm LH, Niskanen L, et al.** Effect of angiotensin-

Take-away Points

We evaluated the consequences of patient co-payment and co-insurance policies on the adherence to β -blocker therapy and on the rate of initiation of β -blocker therapy after acute myocardial infarction (MI) in a population-based natural experiment.

- We confirmed that adherence to β -blocker therapy is decreasing quickly after initiation and the proportion of patients starting β -blockers is still less than optimal after an acute MI.
- Fixed patient co-payment and co-insurance policies had little negative effect on adherence to relatively inexpensive β -blocker therapy, or the initiation of β -blockers after acute MI.

converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial. *Lancet*. 1999;353:611-616.

19. **Hansson L, Lindholm LH, Ekblom T, et al.** Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity in the Swedish Trial in Old Patients with Hypertension-2 Study. *Lancet*. 1999;354:1751-1756.
20. **Tight blood pressure control and risk of macrovascular and microvascular complications in type-2 diabetes: UKPDS-38 (UK Prospective Diabetes Study Group).** *BMJ*. 1998;317:703-713.
21. **Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction) ACC/AHA.** Guidelines for the management of patients with acute myocardial infarction American College of Cardiology. September 1999. Available at: <http://www.acc.org>.
22. **Priori SG, Aliot E, Blomstrom-Lundqvist C, et al.** Task Force on Sudden Cardiac Death of the European Society of Cardiology. *Eur Heart J*. 2001;22:1374-1450.
23. **National Committee for Quality Assurance.** Beta blocker treatment after heart attack. Available at: http://www.ncqa.org/somc2001/BETA_BL/SOMC_2001_BBH.html. Accessed December 2, 2006.
24. **Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J.** The effects of initial drug choice and comorbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. *Am J Hypertens*. 1997;10:697-704.
25. **Chapman RH, Benner JS, Petrilla AA, et al.** Predictors of adherence with antihypertensive and lipid-lowering therapy. *Arch Intern Med*. 2005;165:1147-1152.
26. **Soumerai SB, McLaughlin TJ, Spiegelman D, et al.** Adverse outcomes of underuse of beta-blockers in elderly survivors of acute myocardial infarction. *JAMA*. 1997;277:115-121.
27. **Moeller JF, Miller GE, Banthin JS.** Looking inside the nation's medicine cabinet: trends in outpatient drug spending by Medicare beneficiaries, 1997 and 2001. *Health Aff (Millwood)*. 2004;23:217-225.
28. **Marmot M.** The influence of income on health: views of an epidemiologist. *Health Aff (Millwood)*. 2002;21:31-46.
29. **Deaton A.** Policy implications of the gradient of health and wealth. *Health Aff (Millwood)*. 2002;22:13-30.
30. **British Columbia Ministry of Health.** PharmaNet. Available at: <http://www.health.gov.bc.ca/pharmane/pharmanet/netindex.html>. Accessed September 4, 2004.
31. **Williams JI, Young W.** *Inventory of Studies on the Accuracy of Canadian Health Administrative Databases*. Toronto, Ontario, Canada: Institute for Clinical Evaluative Sciences (ICES); December 1996. Technical report.
32. **Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH.** The accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value based on review of hospital records. *Am Heart J*. 2004;148:99-104.
33. **Steiner JF, Prochazka AV.** The assessment of refill compliance using pharmacy records: methods, validity, and applications. *J Clin Epidemiol*. 1997;50:105-116.
34. **Andrade SE, Kahler KH, Frech F, Chan KA.** Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiol Drug Saf*. 2006;15:565-574.

■ CLINICAL ■

- 35. The Coronary Drug Project.** Influence of adherence to treatment and response of cholesterol on mortality in the coronary drug project. *N Engl J Med.* 1980;303:1038-1041.
- 36. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J.** Long-term persistence in use of statin therapy in elderly patients. *JAMA.* 2002;288:455-461.
- 37. Dormuth CR, Glynn RJ, Neumann P, Maclure M, Brookhart A, Schneeweiss S.** Impact of income-based deductibles with coinsurance compared to copay and full coverage policies on the utilization of inhaled medications by elderly patients with COPD or asthma. *Clin Ther.* 2006;28:964-978.
- 38. Warburton RN.** Takeup of income-tested health-care premium subsidies: evidence and remedies for British Columbia. *Can Tax J.* 2005; 53:1-28.
- 39. Charlson ME, Pompei P, Ales KL, MacKenzie CR.** A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-383.
- 40. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D.** Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther.* 2002;27:299-309.
- 41. Liang K-Y, Zeger SL.** Longitudinal data analysis using generalized linear models. *Biometrika.* 1986;73:13-22.
- 42. Fitzmaurice GM, Laird NM, Ware JH.** *Applied Longitudinal Analysis.* Hoboken, NJ: Wiley; 2004.
- 43. Yusuf S, Lessem J, Pet J, et al.** Primary and secondary prevention of myocardial infarction and strokes. An update of randomly allocated controlled trials. *J Hypertens.* 1993;11(suppl 4):S61-S73.
- 44. Freemantle N, Cleland J, Young P, Mason J, Harrison J.** Beta blockade after myocardial infarction. Systematic review and meta regression analysis. *BMJ.* 1999;318:1730-1737.
- 45. Cook NR, Cohen J, Hebert PR, Taylor JO, Hennekens CH.** Implications of small reductions in diastolic blood pressure for primary prevention. *Arch Intern Med.* 1995;155:701-709.
- 46. Schneeweiss S, Patrick A, Maclure M, Dormuth C, Glynn RJ.** Adherence to statin therapy under drug cost-sharing in patients with and without acute MI: a population-based natural experiment. *Circulation.* 2007;115:2128-2135.
- 47. Landsman PB, Yu W, Liu X, Teutsch SM, Berger ML.** Impact of 3-tier pharmacy benefit design and increased consumer cost-sharing on drug utilization. *Am J Manag Care.* 2005;11:621-628.
- 48. Contoyannis P, Hurley J, Grootendorst P, Jeon SH, Tamblyn R.** Estimating the price elasticity of expenditure for prescription drugs in the presence of non-linear price schedules: an illustration from Quebec, Canada. *Health Econ.* 2005;14:909-923.
- 49. Goldman DP, Joyce GF, Escarce JJ, et al.** Pharmacy benefits and the use of drugs by the chronically ill. *JAMA.* 2004;291:2344-2350.
- 50. Soumerai SB, Ross-Degnan D, Fortess EE, Abelson J.** A critical analysis of studies of state drug reimbursement policies: research in need of discipline. *Milbank Q.* 1993;71:217-252.
- 51. Schneeweiss S, Maclure M, Soumerai SB, Walker AM, Glynn RJ.** Quasi-experimental longitudinal designs to evaluate drug benefit policy changes with low policy compliance. *J Clin Epidemiol.* 2002; 55:833-841. ■