

Drug and Medical Cost Effects of a Drug Formulary Change With Therapeutic Interchange for Statin Drugs in a Multistate Managed Medicaid Organization

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ABSTRACT

OBJECTIVE: Therapeutic interchange (TI) interventions are commonly used to manage pharmacy benefit costs. While several studies have considered the effect that TI interventions have on drug costs, most have not considered the effect they have on medical management costs. The purpose of the present study was to assess drug cost and drug therapy management costs of a TI intervention following a change in the drug formulary for 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin) drugs, including the conversion of atorvastatin from formulary to nonformulary status.

METHODS: A retrospective, quasi-experimental within-subjects design was used in this study. Administrative claims data were obtained from a select northeastern segment of a multistate Medicaid managed care organization (MCO). To be included in the study, patients had to meet the following criteria: (1) they must have had a minimum of 3 atorvastatin prescriptions during a 6-month enrollment phase, (2) they must have been continuously enrolled throughout the 900-day study period, and (3) they must have switched from atorvastatin to another statin between April 1, 2003, and July 31, 2003. The day of the switch from atorvastatin marked for each patient the end of the 12-month pre-TI period and the beginning of the 12-month post-TI period. Two separate dependent variables were developed: (1) statin drug costs (statin cost + dispensing fee) and (2) the costs paid by the MCO for the medical management of statin therapy, including office visit costs and the medical laboratory costs of measuring lipids and creatine kinase, and of checking liver functions. To estimate expenditures over 24 months, a panel analytic technique was used that allows each patient to serve as his or her own control. Multivariate models were used to assess the effects of the TI policy while controlling for age, gender, adjunctive dyslipidemia therapy, comorbidity, presence of a prior coronary artery event, statin compliance, cardiologist management, and disease severity.

RESULTS: Of the 3,636 patients who met the study inclusion criteria and were converted from atorvastatin to an alternate statin drug, 129 patients (3.5%) switched back to atorvastatin following the TI. The average statin cost per claim in the 12-month post-TI period was \$70.93, 9.5% less than the average cost in the 12-month pre-TI period (\$78.40). The average cost per patient per year (PPPY) for statin laboratory tests (lipid panels, creatine kinase tests, and liver function tests) increased by 31.5% to \$16.15 in the post-TI period compared with \$12.28 PPPY in the pre-TI period, and medical office visit costs increased by 44.9% to \$20.70 PPPY in the post-TI period compared with \$14.29 PPPY in the preperiod. These increased costs related to the medical management of statin therapy were overwhelmed by an 11.7% reduction in statin drug costs, from \$793.69 PPPY in the pre-TI period to \$701.01 PPPY in the post-TI period, resulting in a net 10.0% reduction for combined statin costs and related medical costs, from \$820.27 PPPY in the pre-TI period to \$737.87 in the post-TI period. After limiting the analysis to patients who did not convert from atorvastatin to pravastatin (which cost more than atorvastatin before the rebate) and controlling for the influence of potential confounders, statin expenditure decreased by 33% ($P < 0.001$). Multivariate models indicated no statistically significant differences in the costs related to the medical management of statin therapy after the TI compared with before the TI.

CONCLUSIONS: Total costs for medical management of dyslipidemia with statin therapy decreased following implementation of the TI intervention for atorvastatin

Using pharmaceutical expenditures have motivated pharmacy benefit managers (PBMs) and health plans to pursue various cost-control methods and interventions, including therapeutic interchange (TI). The practice of TI relies on the conversion of one drug to a different drug within the same therapeutic class to reduce the cost of drug therapy without compromising therapeutic efficacy or safety.¹ More than 50% of employers reported the use of TI in each of the years from 2000 to 2002,² and about 50% of Medicaid managed care organizations (MCOs) reported the use of TI in 2002 to 2004.³ The clinically similar effectiveness and side effect profiles of statins, coupled with their frequent use and high costs, make the statin class ideal for TI.⁴

Several studies have assessed the influence of a statin TI on economic and clinical outcomes from a health plan's perspective. Korman and Borysiuk examined the influence of a TI from lovastatin to pravastatin within a Veterans Affairs (VA) population

users. An 11.7% savings in statin drug cost, before consideration of manufacturer rebate revenues, became a net savings of 10.0% after inclusion of the medical costs associated with laboratory tests and physician office visits.

KEYWORDS: HMG-CoA reductase inhibitors (statins), Therapeutic interchange, Pharmacy expenditure, Ambulatory expenditure, Panel estimation

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using a pretest/posttest study design.⁵ They found that drug acquisition costs decreased by 21% (\$56,875 versus \$71,693) and that serum lipid levels did not change following the TI. Similarly, Patel et al. found a 21.9% decrease in drug acquisition costs during a 2-month period and no differences in the ability to achieve National Cholesterol Education Program goals following a TI from pravastatin to lovastatin.⁶ Fugit and Resch used a similar patient population and study design but limited the evaluation to individuals already at the low-density lipoprotein cholesterol (LDL-C) goal prior to the TI (simvastatin to lovastatin).⁷ In the study by Fugit and Resch, a pharmacist-managed hyperlipidemia clinic was utilized during the study period, making the percentage change in TI expenditure results difficult to interpret.

Ito et al. used a prospective pretest/posttest study design within a VA population to examine patients converted from pravastatin to simvastatin with a focus on achieving individual lipid goals.^{8,9} After considering costs directly related to the TI program (laboratory and personnel time, including physician, nursing, pharmacist, and technician time) and drug acquisition, TI costs totaled \$40,644 for the first year because of program implementation costs. This resulted in an increase of \$39.12 per patient per year (PPPY) following the TI although the actual drug cost decreased by \$0.23 per person. Furthermore, the TI program caused an additional 25% ($P < 0.001$) of patients to achieve LDL-C goal following the TI. Moisan et al. examined the influence of a TI from lovastatin or pravastatin to simvastatin or fluvastatin using a pretest/posttest study design.¹⁰ Based on health care service expenditure (laboratory and physician visits) and drug acquisition costs, the TI resulted in an average monthly savings of \$18.30 per patient. Moisan et al. also found that the proportion of patients meeting LDL-C goal increased by 18.2%.

Hilleman et al. used a pretest/posttest study design to assess the influence of a TI from pravastatin or simvastatin to atorvastatin in patients with coronary artery disease. This study was conducted in a university-affiliated hospital and outpatient clinics and limited its economic analysis to drug acquisition costs.¹¹ Conversion to atorvastatin resulted in a savings of \$558 PPPY.

Billups et al. examined both the clinical and economic outcomes associated with a pharmacy-intensive conversion program in which patients were switched from doses of simvastatin up to 40 mg per day to equipotent doses of lovastatin within a group-model health maintenance organization (HMO).¹² They found that the proportion of patients at LDL-C goal increased from 75.9 to 79.1% ($P < 0.001$), and the mean alanine aminotransferase (ALT) levels, a measure of safety, were 26.9 IU/L before and 26.4 IU/L after the conversion ($P = 0.134$). After considering drug costs and appropriate monitoring costs, they found that the total cost for statin therapy decreased by \$1.6 million, or \$4.14 per member per year (PMPY), across the entire HMO membership of nearly 400,000.

Cheetham et al. also documented the clinical effectiveness of converting patients from simvastatin to lovastatin using equipotent doses.¹³ Their results indicated a statistically significant reduction in LDL-C: 110.9 mg/dl during the preconversion phase compared with 108.4 mg/dl during the postconversion phase ($P < 0.001$).

Taylor et al. and Grace et al. used decision analysis models to examine the influence of a TI from atorvastatin, fluvastatin, or pravastatin to either cerivastatin or simvastatin in a patient group from the Walter Reed Army Medical Center.^{14,15} Both of these studies used the same decision analytic model to determine the potential cost savings associated with TI. Interestingly, these were the only 2 of a few studies to consider additional costs related to TI, such as additional medical visits and laboratory tests. Model uncertainties included adverse events (minor and serious), physical complaints, and medication tolerance. The authors assumed that any physical complaints/adverse events would generate 1 to 2 physician visits and laboratory-related costs. All probabilities and costs (drug, laboratory, and physician) were calculated from the study population. After considering the conversion cost, including medication, laboratory monitoring, adverse events, and personnel costs, the researchers found a \$115 per-patient savings in the first year following the TI.

Although numerous studies have examined the economic influence of a statin TI, a few limitations compromise the usefulness of the results of prior studies. All of the studies employed a simple pretest/posttest study design without a control group. Additionally, no multivariate statistical analyses were used to address potential confounding variables such as disease severity, which is often predictive of the intensity of health resource utilization and costs. Lastly, only a few studies included additional resource utilization costs associated with the statin TI; yet even these did not control for confounding variables. Given the limitations in previous work, this study will examine the economic outcomes, including statin acquisition costs and select health care utilization costs, induced by a statin TI. Furthermore, this study enhances the methodological and statistical robustness of prior studies by utilizing a panel analytic technique allowing the individual to serve as his or her own control and permitting consideration of an explicit time component during the study period. The present study was conducted from the perspective of a third-party Medicaid payer.

Methods

This study was conducted using data from the northeastern market segment of a Medicaid MCO with approximately 330,000 beneficiaries. This study was reviewed and approved by the University of South Carolina Institutional Review Board.

Description of the TI Intervention

Significant rebate incentives contributed to the decision by the

pharmacy and therapeutics committee of the Medicaid MCO to change the formulary status of atorvastatin from preferred drug to nonformulary and to implement a TI intervention to convert atorvastatin patients to other statins. The confidentiality of rebate contract prices preclude the presentation of cost data specific to these contracts; therefore, the cost data presented in this study understate the actual value (after rebate revenues) to the MCO of this TI intervention.

Implementation of the drug formulary change occurred in multiple phases. Beginning in April 2003, all physicians under contract with the managed Medicaid provider were notified by letter that atorvastatin would become a nonformulary drug on July 1, 2003, and that all patients on atorvastatin would need to be converted to an alternate formulary statin (simvastatin, lovastatin, pravastatin, or fluvastatin) since the health plan would no longer reimburse for atorvastatin. No treatment guidelines were developed to encourage use of a specific statin as a therapeutic alternative to atorvastatin or to ensure equipotent doses of the alternative statin. Thus, the choice and dose of the alternate statin were determined entirely by each patient's prescriber.

In May 2003, physicians prescribing and pharmacies dispensing atorvastatin to health plan beneficiaries were sent a letter reminding them of the formulary change with the specific names of patients who were taking atorvastatin. In collaboration with the state's regulatory agency, patients were also sent letters explaining that they would be converted to another statin in the upcoming months.

On July 1, 2003, the health plan modified the drug claim adjudication system so that when a patient presented with either a new prescription or refill request for atorvastatin, the claim would be rejected with a nonformulary message to the pharmacist. As a consequence of this rejection, pharmacists were required to contact the prescribing physician to change the prescription to a formulary statin. For a patient to remain on atorvastatin and have his or her prescription reimbursed by the health plan, the prescribing physician was required to submit a prior authorization request explaining the rationale for keeping the patient on atorvastatin. For a patient to remain on atorvastatin after implementation of the drug formulary conversion, 2 conditions were necessary: (1) the physician was required to indicate that the patient was previously not successful using any of the multiple formulary statins, and (2) the PBM could document prior statin use. There were no other statin formulary changes during the time of this study.

A quasi-experimental design was used to evaluate the medical management costs and pharmacy costs following a statin TI. Since the TI process used by the Medicaid MCO did not permit identification of a control group, a panel estimation technique was used, which is a more robust methodology than a traditional pretest/posttest cohort because the panel estimation method allows each patient to serve as his or her own control;

thus, the design has a within-subjects control group. Furthermore, the panel estimation method explicitly considers multiple measurements of both the dependent variable and confounders throughout the study's time frame.¹⁶ (See Statistical Methods section.)

Patients were followed for a total of 900 days, which included a 180-day enrollment preperiod, a 360-day pre-TI period, and a 360-day post-TI period. Within the two 360-day measurement periods, 4 quarterly panels (3 months each) were created for a total of 8 quarterly panels for the entire study period. Based on the clinical literature and prior statin TI studies, the 2-year study period is appropriate to examine the economic expenditures related to the TI.

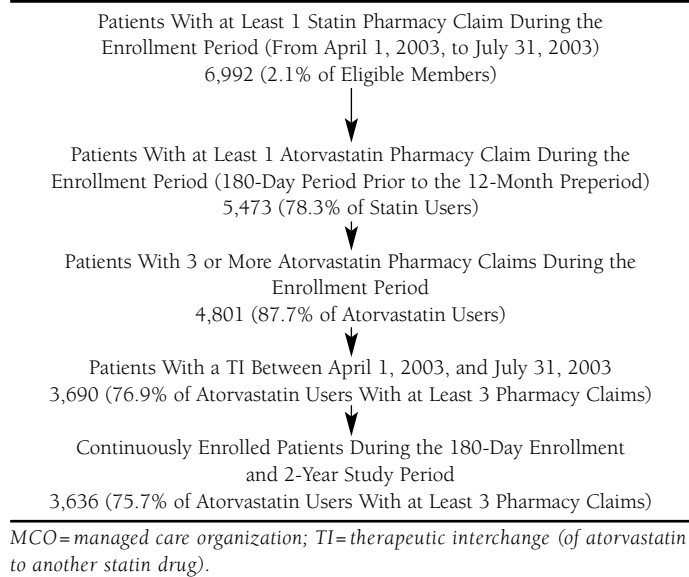
This study evaluated administrative claims to determine patients who switched from atorvastatin during a 4-month (April 1, 2003, to July 31, 2003) time frame. Since not all patients converted on the same calendar day, the TI date determined the study time frame for each subject. The 360-day pre-TI period (panels 1-4) began 360 days before the TI conversion date and ended the day before the conversion date. Likewise, the 360-day post-TI period (panels 5-8) began the day of the TI and ended 360 days thereafter. Thus, the date of the first nonatorvastatin statin claim was defined as day 1 of panel 5 and day 1 of the 360-day post-TI period. The day prior to the first nonatorvastatin claim was defined as day 180 of panel 4 and day 360 of the pre-TI period.

To be included in the study, a minimum of 3 atorvastatin claims per patient was required during the 180-day enrollment period. This criterion was intended to ensure that only patients stabilized on statin therapy were included in the study. New statin users were excluded as they had the potential to artificially inflate the pre-TI expenditure, given the laboratory monitoring associated with initial prescribing and monitoring. To ensure that patients who went through the TI had a minimum of 1 year of data following the TI and were continuously enrolled throughout the study period, the switch from atorvastatin to another statin must have occurred between April 1, 2004, and July 31, 2004.

The 3 main dependent variables were statin drug cost, statin therapy medical management cost, and combined statin drug and medical management cost. To ensure an even comparison of costs across the 2-year study time frame, post-TI costs were discounted by 5% to account for price inflation. Statin drug costs comprised the statin ingredient cost plus a dispensing fee. These costs were summed every 3 months. Statin rebate information was not available; thus, statin cost estimates in the present study overstate actual MCO statin drug costs after consideration of rebate revenues. As a result, several 1-way sensitivity analyses were performed using an upper-bound rebate percentage of 40% and a lower-bound of 15% for the statins. Since the actual rebate percentages are unknown, these lower- and upper-bound estimates are an educated guess of a reasonable range of

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FIGURE 1 Enrollment Criteria and Sample Size—
Medicaid MCO



discounts to entice a TI. Additionally, a break-even analysis was conducted to determine the rebate percentage necessary to result in savings or at least no loss to the health plan after accounting for all costs related to the management of hyperlipidemia.

Statin therapy medical management costs include only those costs directly attributable to the management of statin therapy, including laboratory and physician office encounters. Laboratory encounter costs were associated with the following Current Procedural Terminology (CPT) codes: LDL-C (83721), very-low-density lipoprotein cholesterol (83719), high-density lipoprotein cholesterol (83718), total cholesterol (80061, 82465), creatine kinase (82550), and liver function tests (80053, 80076, 84460, 84450, 84455, 84465). Similarly, office encounter expenditure were based on the costs associated with the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes: hypercholesterolemia (272.0), hyperlipidemia (272.2, 272.4), arteriosclerotic heart disease (414.0), myopathy (359.4), and rhabdomyolysis (728.88). All of the costs attributable to the aforementioned ICD-9-CM and CPT codes were summed every quarter throughout the study time frame. To derive a value that approximates the true cost of statin therapy, we added the statin cost estimates to the statin therapy medical management cost estimates. The capitation of physician services limited the ability to measure the full extent of the TI on ambulatory expenditure. To address this issue, an average cost was derived from non-capitated claims for each of the CPT codes and ICD-9-CM codes mentioned above. These values were then imputed for equivalent capitated encounters.

The multivariate models addressed potential confounding through the use of several independent variables. Age and gender were controlled, but race was unavailable. Level of comorbidity was measured using the latest version of the chronic disease score.¹⁷ To determine the level of coronary artery disease burden, a disease staging procedure based on work by the Medstat Group was used.¹⁸ The scale ranges from 0 to 4, where 0 indicates no complications and stage 4 indicates death. To address patients' medication-taking behavior, the maximum gap in statin therapy was computed and used as a proxy to predict an individual's compliance behavior, such as scheduling and meeting appointments. The maximum gap in therapy captures the largest theoretical period of time an individual is without a therapy. A dichotomous variable was used to indicate individuals who had visited cardiologists since these individuals may require more intensive management than those managed by primary care physicians. Furthermore, a variable to indicate patients on certain medications that may influence the intensity of ambulatory services was included in the model. For example, concomitant multiple lipid-lowering agents and medications that interact with statins or increase serum lipid levels may be associated with greater overall resource use. A dichotomous variable was included to indicate unstable patients who switched statin therapy before or after TI since switching statin therapy may result in additional physician visits. As cardiac events may substantially increase expenditure, a dichotomous variable was created using ICD-9-CM and CPT codes to capture major cardiac events such as acute myocardial infarction, other acute and subacute forms of ischemic heart disease, angioplasty, coronary artery bypass graft, or placement of a coronary stent.

Statistical Methods

Basic descriptive statistics were used to describe the study population. Paired *t* tests were conducted to determine if significant differences in expenditure existed between the pre-TI and post-TI periods. Panel estimation regression modeling was used to control for potential confounding and to permit each patient to serve as his or her own control. A unique advantage of panel estimation is that it permits estimation of unobserved effects influencing the dependent variable, such as patient characteristics (e.g., smoking status, family medical history) not captured in the data.

A basic panel analytic model uses the following equation: $Y_{it} = \alpha_i + \beta_1 X_{1it} + \beta_2 X_{2it} + e_i + u_{it}$, where *i* is the subject; *t* is the time component; *Y* is the dependent variable; and *Y_{it}* is a linear function of the intercept α_i , the parameter estimates β_1 , the independent variables *X_{it}* (some of which may be time-varying while others may be time-invariant), the time-invariant individual specific unobserved error term *e_i* (also called the unobserved effect), and the time-variant error component *u_{it}*. More specifically, *e_i* is an unobserved patient effect that represents all factors influencing expenditure that do not change over time, such as family history.

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Both error terms (e_i and u_{it}) are assumed to be independent and normally distributed with 0 mean and constant variance. All multivariate models were examined for multicollinearity. Both SAS version 8.2 and Stata version 8 were utilized for descriptive and multivariate statistics.^{19,20} An α level of 0.05 was used for all multivariate models.

Results

The final study population consisted of 3,636 patients who were continuously enrolled throughout the entire study (pre-TI and post-TI) period (Figure 1). Of the 3,636 atorvastatin patients involved in the TI intervention, 3.5% (129) converted back to atorvastatin during the 12-month post-TI period. The majority of study participants were female, 67.4% (2,454), with an average age of 63 (SD, 12.7). Interestingly, 97.5% of the final study population had experienced a major cardiac event. As a result of the TI, 78.4% (2,851) of the study population converted to either lovastatin or pravastatin (Table 1).

The mean cost per claim for a statin lab increased from \$6.94 (SD, 16.8) to \$8.06 (SD, 11.5), while the average office visit claim (related to statin therapy) increased from \$40.29 (SD, 602.80) to \$42.21 (SD, 618.7). A combination of an increase in ambulatory service utilization and an average cost per claim (unadjusted) contributed to a 38.6% increase in statin therapy medical management cost per person (\$26.58 PPPY vs. \$36.86 PPPY; $P < 0.001$), a 31.5% increase in statin therapeutic and adverse-event laboratory monitoring costs per person (\$12.28 PPPY vs. \$16.15 PPPY; $P < 0.001$), and a 44.9% increase in statin office visit expenditure per person (\$14.29 PPPY vs. \$20.70 PPPY; $P < 0.001$) (Table 2). These increased expenditures are primarily the result of an increase in the average cost/claim. When limited to expenditures related to the medical management of statin therapy, the multivariate models did not indicate an increase in expenditure after controlling for potential confounding variables (Table 3).

The total number of statin prescriptions dispensed for these 3,636 patients was 2.3% less in the post-TI intervention period than in the pre-TI period (35,935 vs. 36,807 statin claims), 0.82 claims PPPM (SD, 0.31) in the post-TI period versus 0.84 claims PPPM (SD, 0.24) in the pre-TI period. This result is consistent with the maximum-gap-in-therapy compliance measure, which increased from 30.4 days (SD, 44.2) to 63.1 days (SD, 86.2) following the TI program.

Among statin claims, atorvastatin claims accounted for 99.8% (36,748) of all statins dispensed in the pre-TI period (Table 4). In the post-TI period, atorvastatin claims accounted for only 1.4% (509) of all statin claims. The prior authorization process permitted individuals to switch back to atorvastatin if they reportedly were not successful using any of the other statins, thus explaining the 509 atorvastatin claims during the post-TI period. The mean statin cost per claim declined by 9.5%, from \$78.40 to \$70.93 ($P < 0.001$), and resulted in a

TABLE 1 Distribution of Statin Therapeutic Interchange Outcomes (From Atorvastatin)

Atorvastatin Switched to:	No. of Patients	% of Total
Pravastatin (Pravachol)	1,353	37.2
Lovastatin (generic)	1,010	27.8
Fluvastatin (Lescol XL)	433	11.9
Lovastatin (Altocor)*	410	11.2
Fluvastatin (Lescol)	329	9.0
Lovastatin plus niacin (Advicor)	78	2.1
Simvastatin (Zocor)	23	0.6
Total	3,636	100

* Branded generic.

11.5% decrease, from \$66.14 PPPM (SD, 20.12) in the pre-TI period to \$58.41 PPPM (SD, 35.68) after the TI (Table 4).

Pravastatin had the largest percentage (38.3%) of statin claims in the post-TI period even though pravastatin was more than 3 times more expensive than generic lovastatin, the cheapest statin, and 40% more expensive, before rebate, than atorvastatin (Table 4). The absence of rebate contract information makes this switch from atorvastatin to pravastatin appear to be irrational for this Medicaid MCO. As a consequence of the high utilization and high price of pravastatin following the TI relative to the price of atorvastatin during the pre-TI period, no cost differences were found between the 2 periods after controlling for confounders (Table 3). The calculated average cost per claim for pravastatin does not reflect the discount resulting from the contract rebates, so pravastatin patients were excluded from the multivariate analysis. When the model was limited to patients who were not converted to pravastatin, the statin costs decreased by 33% ($P < 0.001$) after controlling for explanatory variables (Table 4). Discussions with the pharmacy benefit administrators revealed that, in fact, the cost for pravastatin was significantly less than atorvastatin after rebates were considered.

Total statin expenditure (unadjusted for potential confounders) but discounted at a 5% rate) decreased by 10.0%, from \$820.27 PPPY in the pre-TI period to \$737.87 PPPY in the post-TI period ($P < 0.001$, Table 2). This change is driven primarily by an 11.7% decrease in statin expenditure per person, which underscores the high drug cost of statins as compared with the medical costs for office visits and laboratory tests necessary to ensure safe and effective use of statin pharmacotherapy. Similar to the statin expenditure multivariate models, the total statin expenditure multivariate models did not indicate a statistically significant difference following the TI (Table 3). However, when the models were limited to those individuals who did not convert to pravastatin, TI resulted in a 33% ($P < 0.001$) decrease in total expenditure, which is consistent

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TABLE 2 Mean Ambulatory Costs* Per Patient Per Year Attributable to Statin Therapy Management During Pre-TI and Post-TI Periods

Variable Mean [SD]	12-month Pre-TI Period (\$ [SD])†	12-month Post-TI Period (\$ [SD])†	% Change	P Value‡
Statin labs§	12.28 [34.80]	16.15 [35.87]	31.5	<0.001
Office visits	14.29 [80.31]	20.70 [107.14]	44.8	0.001
Total medical¶	26.58 [91.00]	36.86 [119.76]	38.6	<0.001
Statin drug cost#	793.69 [241.46]	701.01 [428.16]	-11.7	<0.001
Total cost**	820.27 [261.27]	737.87 [447.80]	-10.0	<0.001

* All costs were discounted using a 5% rate.

† The pre-TI period commenced 12 months before the switch from atorvastatin during the conversion period from April 1, 2003, to July 31, 2003, and the 12-month post-TI period for each patient commenced with the day of conversion to atorvastatin.

‡ Paired t test.

§ These encounter costs are strictly related to statin therapy management including CPT codes indicating laboratory encounters for cholesterol levels (LDL-C, VLDL-C, HDL-C, and total cholesterol) and LFTs. Thus, costs associated with each of these CPT codes were considered.

|| These encounter costs are strictly related to statin therapy management including ICD-9-CM codes for the following conditions: hypercholesterolemia, hyperlipidemia, arteriosclerotic heart disease, creatine kinase, myopathy, and rhabdomyolysis. Thus, costs associated with each of these ICD-9-CM codes were considered.

¶ Total medical expenditure related to statin therapy for the health plan was \$96,646 during the pre-TI period and \$134,026 during the post-TI period.

Statin drug cost for the health plan was \$2,885,860 during the pre-TI period and \$2,548,898 during the post-TI period.

** Total statin-related expenditure for the health plan was \$2,982,506 during the pre-TI period and \$2,682,925 during the post-TI period.

CPT=Current Procedural Terminology; HDL-C=high-density lipoprotein cholesterol; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; LDL-C=low-density lipoprotein cholesterol; LFT=liver function test; TI=therapeutic interchange; VLDL-C=very-low-density lipoprotein cholesterol.

with the statin expenditure models.

Sensitivity Analysis

Based on the total statin expenditure related to the TI before (medical management expenditure, \$96,646; statin drug cost, \$2,885,860) and after (medical management expenditure, \$134,026; statin drug cost, \$2,548,898), statin costs would only need to decrease by 1.2% in order to account for the additional costs related to the medical management of statin therapy following the TI. When a 15% discount rate was applied to the post-TI statins, the multivariate models (including pravachol patients) resulted in an 18% ($P < 0.001$) decrease in total expenditure. When a discount rate of 40% was applied, the estimated total expenditure decrease (when pravachol patients were included) increased to 50% ($P < 0.001$).

Discussion

Results of this study show that total medical management and statin drug costs decreased following a statin TI intervention. The decrease in total statin cost was driven primarily by the estimated 11.7% reduction in statin drug acquisition cost (unadjusted for potential confounders), which represented 97% of the total expenditure (medical management and statin cost) in the pre-TI period and 97% in the post-TI period. These findings were validated using multivariate models after adjusting for study design artifacts (including the exclusion of patients converting to pravachol) and sensitivity analyses. These results highlight the high acquisition cost of statins relative to the

reimbursement claims for laboratory costs and physician encounters necessary for the appropriate management of patients on statin therapy.

Preliminary analyses produced varying estimates due to the distribution of statins to which patients were converted. First, it was determined that almost 40% of the study population was converted to a statin that was 40% more expensive (pravastatin) than atorvastatin. This pharmacy cost was offset by the other 60% of the patient population who were converted to statins that were between 12.1% (fluvastatin) and 57% (lovastatin) less expensive than atorvastatin. As a result, the multivariate models differed when the population was limited to those converted to pravastatin and those converted to another less-expensive statin. The multivariate model including all statin users indicated no difference in statin expenditure after the TI. This finding can be attributed directly to the higher drug cost of pravastatin relative to atorvastatin. In contrast, the multivariate models limited to nonpravastatin patients found that statin expenditure decreased by 33% following the conversion, which can be attributed to a lower drug cost relative to atorvastatin. This decrease in statin expenditure is driven primarily by the lower cost per statin claim resulting from the statin TI and secondarily by a 2.3% decrease in the number of statin claims following the TI.

As stated in the Methods section, statin rebates were not considered, which resulted in an overestimate of the actual cost paid by the MCO. Due to the confidentiality of rebate contracts, it is difficult to assess the true cost difference or magnitude of

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TABLE 3 Regression Model^a for Related Medical and Statin (Drug) Costs^b

Variable ^c Coefficient (Standard Error)	Statin Therapy Medical Management Costs	Statin Costs	Total Statin Expenditure Without Pravachol Patients ^p	Total Statin Expenditure	Statin Costs Without Pravachol Patients ^p
TI ^d	-0.015 (0.015)	-0.10 (0.015)	-0.33* (0.18)	-0.026 (0.015)	-0.33* (0.018)
Age ^e	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o
Gender ^f	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o	Dropped out of model ^o
Adjunctive ^g	0.14* (0.030)	0.99* (0.029)	0.95* (0.035)	1.05* (0.028)	1.00* (0.034)
Comorbidity ^h	0.041* (0.0094)	-0.13* (0.0091)	-0.13* (0.011)	-0.11* (0.0089)	-0.10 (0.010)
Coronary event ⁱ	0.040 (0.055)	-0.019 (0.053)	-0.015 (0.063)	0.021 (0.052)	0.022 (0.055)
Gap ^j	-0.00041* (0.00014)	-0.013* (0.00013)	-0.012* (0.00015)	-0.012* (0.00013)	-0.011* (0.00015)
Cardiologist ^k	0.74* (0.022)	0.061* (0.021)	0.056* (0.026)	0.16* (0.021)	0.18* (0.025)
Disease severity ^l	0.20* (0.018)	-0.023 (0.017)	-0.021* (0.021)	-0.00091 (0.017)	-0.00085 (0.0011)
Switches ^m	0.19* (0.039)	0.61* (0.038)	0.74* (0.043)	0.575* (0.037)	0.69* (0.043)
SHC ⁿ	0.38* (0.025)	-0.074* (0.024)	-0.076* (0.030)	-0.050* (0.024)	-0.057* (0.029)
R-squared	0.0916	0.454	0.505	0.4375	0.4844
Model significance	F = 251*	F = 1,627*	F = 1,339*	F = 1,554*	F = 1,621*

* P < 0.05.

a Fixed-effects model was based on a significant Hausman test.

b All costs were discounted at a 5% rate.

c Dependant variable is log of statin expenditure.

d TI=1 for the post-TI period; TI=0 for the pre-TI period: positive values reflect increased expenditure, and negative values reflect decreased expenditure.

e Age is a continuous variable.

f Male=1; female=0.

g Adjunctive therapy=1 for the presence of an adjunctive medication; adjunctive therapy=0 without the presence of an adjunctive medication.

h Range 0-29; a higher value indicates a greater number of comorbidities.

i Cardiac event=1 for patients who experienced a myocardial infarction, acute ischemic heart disease, angioplasty, CABG, or stent placement during study; cardiac event=0 for patients who did not experience a cardiac event during the study period.

j Maximum gap in therapy is a continuous variable.

k Cardiologist=1 for patients with a medical claim for a cardiologist during the study period; cardiologist=0 for patients who did not have a medical claim for a cardiologist during the study period.

l Disease severity is an ordinal scale with a higher value indicating a more-severe disease severity.

m Switches=1 for patients who either switched statin doses or statin therapy during the study period; Switches=0 for patients who did not switch statin doses or statin therapy during the study period.

n Secondary heart care prevention=1 for patients who were secondary heart care patients; secondary heart care prevention=0 for patients who were primary heart care patients.

o Because it was a fixed-effects model, variables that do not change over time are dropped from the model.

p Without rebate information, this switch from atorvastatin to pravastatin would appear to be an irrational choice for the Medicaid managed care organization. The calculated average cost per claim of pravastatin does not reflect the deep discount resulting from the contract rebates, so pravastatin patients were excluded from the multivariate analysis.

CABG=coronary artery bypass graft; SHC=secondary heart care; TI=therapeutic interchange.

change among the different statin drugs in the post-TI period as compared with the pre-TI period. This situation is further confounded by the fact that almost 40% of the patients were converted to pravastatin, which was about 40% more expensive than atorvastatin in direct drug cost before rebates. However, the break-even analysis shows that even a minimal reduction in statin acquisition costs of 1.2% or more would result in total expenditure savings. These expenditure reductions are consistent with other published studies, which have shown a statin expenditure reduction of between 10% and 58%.^{6,8,14,15}

This was the first study to explicitly assess the medical

management expenditure associated with statin therapy following a TI intervention. However, findings from other related studies are consistent with these estimates. Moisan et al. separated ambulatory costs from the total costs associated with the TI and found that the average cost for a medical encounter related to cholesterol management was \$16.46 (1997 Canadian estimates).¹⁰ This figure is much lower than the average ambulatory cost per statin management claim (\$36.20 and \$37.40 per claim in 2004) found in the present study. A couple of factors besides medical inflation between 1997 and 2004 may explain the difference. The Moisan et al. study was conducted in Ontario

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TABLE 4 Mean Statin Expenditure* Per Claim During Pre-TI and Post-TI Periods

Statin	12-Month Pre-TI Period†			12-Month Post-TI Period‡		
	Formulary Status	No. of Claims (%)	Mean Cost per Claim (\$) [SD]	Formulary Status	No. of Claims (%)	Mean Cost Per Claim (\$) [SD]
Lovastatin‡ (Altacor)	NF	3 (0)	50.60 [4.68]	F	685 (1.9)	57.15 [7.52]
Lovastatin plus niacin (Advicor)	NF	0 (0)	–	F	4,115 (11.4)	57.60 [18.11]
Rosuvastatin (Crestor)	NF	0 (0)	–	F	6 (0)	50.22 [28.74]
Fluvastatin (Lescol)	NF	1 (0)	28.10 [-]	F	3,005 (8.3)	50.54 [4.63]
Fluvastatin (Lescol XL)	NF	9 (0.02)	58.75 [11.37]	F	4,167 (11.5)	64.53 [4.61]
Atorvastatin (Lipitor)	F	36,748 (99.8)	73.40 [17.88]	NF	509§ (1.4)	74.72 [33.93]
Lovastatin (generic)	NF	2 (0)	23.19 [23.71]	F	9,630 (26.7)	31.29 [12.41]
Pravastatin (Pravachol)	NF	34 (0.09)	91.14 [28.66]	F	13,770 (38.3)	104.88 [21.55]
Simvastatin (Zocor)	NF	10 (0.02)	15.50 [3.79]	F	48 (0.13)	24.29 [20.71]
Total drug cost PPPM (\$)			66.14 [20.12]			58.41 [35.68]
Rxs PPPM			0.84 [0.24]			0.82 [0.31]
Total/average	–	36,807	\$78.40 [19.09]	–	35,935	\$70.93 [35.20]

* All costs were discounted at a 5% rate.

† The pre-TI period commenced 12-months before the switch, and the 12-month post-TI period commenced the day of conversion to a non-atorvastatin prescription between April 1, 2003, and July 31, 2003.

‡ Branded generic.

§ The prior authorization process permits individuals to switch back to atorvastatin if they were not successful using any of the other statins, thus explaining the 509 atorvastatin claims during the post-TI period.

|| P < 0.001; analysis was limited to the mean total statin expenditure pre-TI period versus post-TI period and not the individual statins.

F=formulary; NF=nonformulary; PPPM=per patient per month; TI=therapeutic interchange.

and thus may not be representative of a managed Medicaid study population in the United States. Furthermore, the patient population and associated costs were derived from the Canadian armed forces.

Except for the Billups et al. study, external validation of these study results is difficult since no previous statin TI study has adequately assessed both related medical costs and pharmacy costs of a drug formulary change for statins and the associated TI intervention.¹² Billups et al. found an overall PMPY decrease in antihyperlipidemic drug costs and a slight increase in additional laboratory costs resulting from the statin TI, although no statistical tests were conducted. Despite study limitations, Moisan et al. was one of the few papers that considered physician, laboratory, and drug expenditure.¹⁰ They found that the average monthly cost savings were \$6.56 per patient. In contrast, the present study estimated \$6.86 (based

on descriptive statistics) in cost savings per statin patient per month, which is remarkably similar to that found in Moisan et al. Taylor et al. and Grace et al. used decision analysis to estimate the cost associated with converting patients at the Walter Reed Army Medical Center from atorvastatin, fluvastatin, or pravastatin to either cerivastatin or simvastatin.^{14,15}

Similar to the present study, the studies of Grace et al. and Taylor et al. included ambulatory expenditure (both laboratory and general statin management cost), pharmacy cost, and personnel cost. After the first year, savings of \$115 per patient were realized. This is consistent with the findings of the present study in which the unadjusted data show a mean statin cost savings of \$92.68 PPPY following the TI intervention, which became net savings of \$82.40 PPPY after the addition of medical management costs associated with statin drug therapy. This cost difference of \$82.40 versus \$115 may be attributed to

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a greater reduction in drug acquisition cost by Grace et al. and Taylor et al. as compared with the 11.7% reduction found in the present study.

Limitations

Foremost among the several limitations of this study was the selective method of determining the administrative claim records to include in the study. Patients had to have demonstrated continued use of atorvastatin. Therefore, the effects of this TI policy on all affected Medicaid recipients or the overall statin budget for this multistate Medicaid MCO are not evaluated.

Second, the pharmacy claims database only captured pharmacy claims that were adjudicated by the PBM. Thus, prescription claims that were either paid in full by the patient or paid under dual pharmacy benefits coverage were not captured. No data are available to determine the frequency of these events. However, unlike patients within private employer-sponsored health plans, these Medicaid patients are required to meet household income levels that would limit their ability and willingness to pay out of pocket for their prescription medication.

Third, the confidentiality of manufacturer rebate contracts precludes assessment of total actual MCO cost savings associated with drug TI interventions. As observed in the present study, the higher cost of pravastatin compared with atorvastatin seems counterproductive to MCO cost management in the absence of information about drug manufacturer rebate revenues.

Fourth, this study did not measure humanistic service outcomes. While no adverse patient effects, including dissatisfaction, were anticipated from this TI intervention, this category of outcome should be measured in future studies.

Fifth, the enrollment criteria restricted the patient population to a group of patients who were demonstrated atorvastatin users, thus limiting external validity. Additional research is needed to identify the influence of a statin TI intervention on individuals not stabilized on statin therapy. As a result, the conclusions of this study are conditional on a select patient population.

Sixth, the personnel time and administrative costs associated with the implementation of the TI intervention were not assessed since few administrative resources were required. However, there was an unknown cost for the plan administrator for contracting with a third party to generate and send letters to the pharmacies, physicians, and patients. On the other hand, the cost of pharmacy personnel at the managed Medicaid plan for reviewing prior authorizations is primarily a fixed cost and would not be expected to add to the administrative cost of this TI intervention; this may not be a relatively fixed cost for other MCOs. Finally, the personnel and administrative costs incurred by community pharmacies in calling physicians to convert patients from atorvastatin to other statins were also not measured. There were, of course, community pharmacy costs and some PBM and health plan administrative costs incurred that

would reduce the total system costs savings associated with this TI intervention.

Conclusions

Total expenditures for drug costs and the costs of medical management of hyperlipidemia with statin drug therapy decreased by 10% before consideration of rebate revenues, following the implementation of a TI intervention to convert atorvastatin patients to other statin therapy. The savings in drug costs overwhelmed the increase in medical management costs related to statin therapy. Total costs after consideration of rebate revenues would exceed the 10% cost savings found with this TI intervention in a managed Medicaid MCO. Future research on TI interventions might include clinical effectiveness, safety, and humanistic service outcomes in addition to the drug and medical management costs assessed in the present study.

DISCLOSURES

No outside funding supported this study. Author Brian Meissner served as principal author of the study. Study concept and design were contributed by Meissner and authors Michael Dickson, Judy Shinogle, C.E. Reeder, and Viran Senevirante. Data collection was the work of Senevirante and author Dea Belazi; data interpretation was primarily the work of Meissner and Shinogle, with input from the coauthors. Writing of the manuscript was primarily the work of Meissner and Dickson, with input from Reeder and Senevirante; its revision was primarily the work of Meissner, with input from Reeder, Dickson, and Belazi. The authors disclose no potential bias or conflict of interest relating to this article.

REFERENCES

1. American College of Clinical Pharmacy, Clinical Practice Affairs Committee. Guidelines for therapeutic interchange, ACCP position statement. *Pharmacotherapy*. 1993;13(2):253-56.
2. *The Prescription Drug Benefit Cost and Plan Design Survey Report*. 2003 ed. Tempe, AZ: Pharmacy Benefit Management Institute; 2003.
3. *Novartis Pharmacy Benefit Report: Facts and Figures*. 2005 ed. Wayne, NJ: Emron; 2005:21.
4. National Institute for Health and Clinical Excellence. Statins for the prevention of cardiovascular events. Technology appraisal 94. January 2006. Available at: <http://www.nice.org.uk/page.aspx?o=TA094guidance>. Accessed April 22, 2006.
5. Korman L, Borysiuk L. Replacing lovastatin with pravastatin: effect on serum lipids and costs. *Am J Health Syst Pharm*. 1995;52:1078-92.
6. Patel JR, Gray DR, Pierce R, Jafari M. Impact of therapeutic interchange from pravastatin to lovastatin in a Veterans Affairs medical center. *Am J Manag Care*. 1999;5:465-74.
7. Fugit RV, Resch ND. Conversion of patients from simvastatin to lovastatin in an outpatient pharmacy clinic. *Am J Health Syst Pharm*. 2000;57:1703-08.
8. Ito KM, Stolley SN, Morreale AP, et al. Rationale, design, and baseline results of the pravastatin-to-simvastatin conversion lipid optimization program (PSCOP). *Am J Health Syst Pharm*. 1999;56:1107-13.
9. Ito MK, Lin JC, Morreale AP, et al. Effect of pravastatin-to-simvastatin conversion on low-density-lipoprotein cholesterol. *Am J Health Syst Pharm*. 2001;58:1734-39.
10. Moisan J, Vaillancourt R, Gregoire JP, et al. Preferred hydroxymethylglutaryl enzyme A reductase inhibitors: treatment-modification program and outcomes. *Am J Health Syst Pharm*. 1999;56:1437-41.

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11. Hilleman DE, Qurdeman RL, Lenz TL. Therapeutic change of HMG-CoA reductase inhibitors in patients with coronary artery disease. *Pharmacotherapy*. 2001;21(4):410-15.
12. Billups SJ, Plushner SL, Olson KL, Koehler TJ, Kerzee J. Clinical and economic outcomes of conversion of simvastatin to lovastatin in a group-model health maintenance organization. *J Manag Care Pharm*. 2005;11(8):681-86.
13. Cheetham TC, Chan J, Benson V, Richmond C, Levin E, Campen D. Successful conversion of patients with hypercholesterolemia from a brand name to a generic cholesterol-lowering drug. *Am J Manag Care*. 2005;11:546-52.
14. Taylor AJ, Grace K, Swiecki J, et al. Lipid-lowering efficacy, safety and costs of a large-scale therapeutic statin formulary conversion program. *Pharmacotherapy*. 2001;21(9):1130-39.
15. Grace KA, Swiecki J, Hyatt R, et al. Implementation of a therapeutic-interchange clinic for HMG-CoA reductase inhibitors. *Am J Health Syst Pharm*. 2002;59:1077-82.
16. Wooldridge JM. *Introductory Econometrics: A Modern Approach*. 2nd ed. Mason, OH: South-Western College Publishing/Thomson Learning; 2003.
17. Clark DO, VonKorff M, Sunders K, et al. A chronic disease score with empirically derived weights. *Med Care*. 1995;33:783-95.
18. The Medstat Group. *Disease Staging Clinical Criteria (Version 17)*. 4th ed. Ann Arbor, MI: Thomson/Medstat; 1999.
19. SAS version 8.2. Cary, NC: SAS Institute, Inc.; 2002.
20. Stata version 8. College Station, TX: Stata Corporation; 2003.