Clinical and Economic Outcomes of Conversion of Simvastatin to Lovastatin in a Group-Model Health Maintenance Organization

SARAH J. BILLUPS, PharmD, BCPS; SUSYN L. PLUSHNER, PharmD, BCPS; KARI L. OLSON, PharmD, BCPS; THOMAS J. KOEHLER, RPh, BCPS; and JANE KERZEE, PharmD, BCPS

ABSTRACT

OBJECTIVE: To (a) determine if converting patients on simvastatin to lovastatin affects whether they meet their low-density lipoprotein cholesterol (LDL-C) goals as defined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III) clinical practice guidelines and (b) assess the change in health care expenditures associated with such a conversion.

METHODS: Primary and secondary prevention patients receiving simvastatin 10 mg to 40 mg daily between September 1, 2001, and February 28, 2002, were offered lovastatin at a therapeutically equivalent dose. Fasting lipid profiles and alanine aminotransferase (ALT) levels were measured and recorded at least 6 weeks after starting lovastatin. A clinical pharmacy staff member, in collaboration with the subject’s primary care provider, subsequently adjusted lipid-lowering therapy as needed to attain target LDL-C goals, as determined by the ATP III clinical practice guidelines.

RESULTS: Of 5,286 patients converted to lovastatin and for whom follow-up laboratory tests were drawn, 5,046 (95.5%) were converted successfully, and 240 (4.5%) had to be converted back to simvastatin due to intolerance (N = 164, 3.1%) or failure to achieve LDL-C goal (N = 76, 1.4%). The proportion of patients with LDL-C at or less than their target goal increased from 75.9% before the intervention to 79.1% after conversion to lovastatin (P < 0.001). ALT levels did not change significantly. The mean ALT value, a proxy measure of safety before and after conversion for all patients, was 26.9 IU/L and 26.4 IU/L, respectively (P = 0.134). For the 2,235 patients converted fromLovastatin 80 mg to simvastatin 40 mg, the mean pre-ALT and post-ALT values were 26.9 IU/L and 26.5 IU/L (P = 0.498). The annualized cost savings due to the conversions, expressed across the entire membership of this health maintenance organization (HMO), was $4.14 per member per year (MMPY), with no change in ALT levels. Patient savings in reduced copayments in the conversion from brand simvastatin to generic lovastatin were an average of $145.29 (62%) per patient (95% confidence interval, $143-$149).

CONCLUSION: A clinical pharmacy-directed program designed to convert patients from simvastatin to lovastatin resulted in substantial expenditure reductions for this HMO and 62% copayment savings for members, without compromise in clinical outcomes as measured by lipid control (effectiveness) and ALT levels (safety). The proportion of patients at or less than their LDL-C goal increased coincident with the conversion from simvastatin to lovastatin.

KEYWORDS: Lovastatin, Simvastatin, Cost-minimization analysis, Clinical pharmacist, Therapeutic conversion

J Manag Care Pharm. 2005;11(8):681-86

Dyslipidemia is highly prevalent in the United States. As of 2002, nearly 107 million Americans over 20 years of age had blood cholesterol levels greater than 200 mg/dL.$^1$ When drug therapy is indicated, the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) are typically used as first-line therapy.$^2$ Statin expenditures approximated $12.5 billion in the United States in 2002. These expenditures will likely continue to increase as recommendations for initiating treatment expand to populations at high risk for cardiovascular disease (CVD), such as those with diabetes, peripheral arterial disease, and thromboembolic disease, and lipid goals become more aggressive.$^3,5$

Currently, there are 6 statins on the market in the United States, which differ somewhat in their lipid-lowering potency.$^6$ Of these, simvastatin, lovastatin, pravastatin, and atorvastatin have been evaluated in large clinical trials in patients with and without CVD and in patients with varying baseline cholesterol levels, and these trials have demonstrated reductions in morbidity and/or mortality.$^7-14$ Although the potency of these agents varies on a mg-per-mg basis, comparative studies have shown that their lipid-lowering effects are similar when given in equipotent doses.$^6,15,16,18$ A recent cohort study comparing clinical outcomes of patients using 1 of 5 different statins for secondary prevention found the statins to be equally effective at preventing acute myocardial infarction and death.$^{17}$ When efficacy is comparable, providers may consider cost when deciding which statin to offer as a covered benefit.

Kaiser Permanente of Colorado (KPCO) includes both simvastatin and lovastatin on its drug formulary since both have demonstrated lipid-lowering capability and clinical benefit.$^{10-12}$ Prior to January 2001, there was no preference for initiating statin therapy with either lovastatin or simvastatin. After January 2001, lovastatin became the only statin available on the U.S. market as a generic drug. As a result, the acquisition cost for group purchasing organizations was reduced, and lovastatin became the preferred drug of the statins.

Since the available evidence suggests thatLovastatin can achieve similar low-density lipoprotein cholesterol (LDL-C) reduction compared with simvastatin when given in equipotent doses,$^6,13,16$ this population-based study was conducted at KPCO among eligible patients with dyslipidemia to convert them from simvastatin to lovastatin in a safe, efficient manner, while maintaining lipid control. The purpose of this study was to evaluate both lipid and economic outcomes of this pharmacy-directed statin conversion project. Although medication conversions are not uncommon in health care settings, the large scale and
unique systems employed in this drug conversion differentiate this project from others. To assess the tolerability and efficacy of lovastatin 80 mg daily versus simvastatin 40 mg daily, we performed a subanalysis to supplement the limited data available for this lovastatin dose.\textsuperscript{17}

\textbf{Methods}

\textbf{Setting}

This retrospective study was conducted at KPCO, a group-model health maintenance organization (HMO) providing medical care to members at 16 medical facilities throughout the Denver/Boulder metropolitan area. Each facility is staffed by 1 to 3 primary care clinical pharmacy staff (PCCPS) members who collaborate with primary care providers to facilitate clinically appropriate, cost-effective use of medications and to care for patients with drug-related problems. KPCO patients with CVD, defined as the presence of acute myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention with or without stent placement, or unstable angina diagnosed and coded by a cardiologist, are enrolled in the Clinical Pharmacy Cardiac Risk Service (CPCRS), a clinical pharmacy-managed, physician-monitored service that assists physicians with the implementation and management of evidence-based treatment strategies. One aspect of this care is to monitor lipid-lowering therapy to achieve appropriate lipid targets as recommended by National Cholesterol Education Program Adult Panel Treatment Panel III (ATP III) clinical practice guidelines.\textsuperscript{2,19}

Both the PCCPS and CPCRS teams employ clinical pharmacists (BS or PharmD degree without residency training) and clinical pharmacy specialists (PharmD degree with specialized residency training). Members of these teams will be referred to here as clinical pharmacy services pharmacists (CPSPs). Approval to conduct this study was obtained from the KPCO Institutional Review Board.

\textbf{Subject Selection}

All active KPCO members of any age who received a prescription for simvastatin 10 mg to 40 mg daily between September 1, 2001, and February 28, 2002, were eligible for study inclusion. Patients were excluded if they were medically ineligible due to a previously documented intolerance or allergy to lovastatin, if their LDL-C was uncontrolled on simvastatin 40 mg, if they were on simvastatin 80 mg, or if it was deemed that the addition of nonstatin lipid-lowering therapy (e.g., fibrate, niacin) was more appropriate than converting to lovastatin to achieve lipid goals. In addition, patients were excluded if they received their prescriptions from non-KPCO pharmacies or if they or their primary care physician declined conversion. Potential study candidates followed in primary care were identified via KPCO administrative and pharmacy databases. A PCCPS pharmacist subsequently reviewed each patient’s chart to confirm eligibility. Any patient without a fasting lipid panel (FLP), including total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), and triglycerides or alanine aminotransferase (ALT), was considered for drug conversion. All eligible patients were contacted by phone or letter or in person at the pharmacy when they presented for a simvastatin refill and offered lovastatin at a clinically appropriate dose. Secondary prevention patients were already enrolled in the CPCRS at the time of the conversion project. Medication conversion for these patients was performed, if appropriate, upon receipt of results of each patient’s normally scheduled FLP.

\textbf{Simvastatin-Lovastatin Conversion Project}

Conversion guidelines were established based upon published literature comparing equivalent lipid-lowering doses of lovastatin and simvastatin.\textsuperscript{5,15,16} Most patients receiving simvastatin 10 mg, 20 mg, or 40 mg daily were converted to lovastatin 20 mg, 40 mg, or 80 mg daily, respectively. However, patients above or substantially below their LDL-C goal at the time of the conversion were converted to an adjusted dose if deemed appropriate by a CPSP and the subject’s primary care physician. All patients were required to return to the laboratory for repeat FLP and ALT measurements at least 6 weeks after starting lovastatin. Based upon the follow-up FLP results, a CPSP adjusted the lovastatin dose if needed to attain the target LDL-C goal. If the LDL-C goal was not attainable on lovastatin or if a subject did not tolerate lovastatin, the subject was switched back to simvastatin, and/or an alternative medication (e.g., fibrate, niacin) was initiated. All therapeutic interventions were made according to ATP III clinical practice guidelines for cholesterol management\textsuperscript{2} and were approved by the patients’ primary care providers. Patients or providers could refuse to change or request reconversion from lovastatin to simvastatin for any reason at any time.

\textbf{Outcome Measures}

The primary outcome for the study was the proportion of patients achieving their LDL-C goals after conversion to lovastatin (final) compared with their LDL-C results while on simvastatin (baseline). LDL-C goal was defined as $<100$ mg/dL, $<130$ mg/dL, and $<160$ mg/dL for patients with CVD, without CVD but with 2 or more cardiac risk factors, and without CVD and 1 or fewer cardiac risk factors based upon ATP III guidelines.\textsuperscript{2} The baseline LDL-C was the most recent LDL-C obtained while using simvastatin, but within 12 months of conversion to lovastatin. Final LDL-C was the LDL-C obtained from the first FLP performed at least 6 weeks after starting lovastatin. A conversion was considered successful if the patient converted tolovastatin, remained on the drug without reporting an adverse event for at least 6 months, and a final FLP was drawn.
Secondary outcomes of the study were (1) the proportion of patients achieving their non–HDL-C (total cholesterol minus HDL-C) goal preconversion versus postconversion, (2) the change in mean LDL-C and non–HDL-C values preconversion and postconversion, (3) the proportion of patients who switched back to simvastatin due to intolerance or inability to achieve target LDL-C goals on lovastatin (therapeutic failure), (4) changes in drug acquisition and laboratory costs over 12 months (cost-minimization analysis), and (5) change in mean ALT levels (a surrogate measure of safety). In order to assess the therapeutic effects of conversion to lovastatin 80 mg from simvastatin 40 mg daily, we performed a subanalysis evaluating these outcomes for patients who underwent this conversion.

To assess whether differences in non–HDL-C or LDL-C control were attributable to differences in statin adherence, we performed a post hoc analysis on a sample of the patients converted from simvastatin to lovastatin. Adherence to simvastatin was calculated as a proportion of the quantity of tablets dispensed during the 12 months prior to the conversion date (a minimum of 3 refills in this time was required) divided by the number of days between the earliest simvastatin fill date during this time and the first prescription fill for lovastatin. The same method was used to calculate lovastatin adherence during the 12 months after the conversion date. To achieve 90% power to detect a 5% absolute difference in adherence rate with an alpha of 0.05, we needed 97 patients.

We performed cost-minimization analysis from the perspective of the payer to assess expenditure changes after the conversion project. Statin costs were calculated using representative group purchasing costs. This analysis took into account the number of tablets dispensed per 2-month supply (the standard KPCO quantity dispensed), including cases where patients used half tablets of simvastatin. The resultant cost savings were converted to per-member-per-year (PMPY) savings to provide a better measure of the cost impact to the organization. The FLP and ALT costs included test performance, phlebotomy costs, and a factor for the time a clinician spent evaluating the results. Follow-up laboratory tests performed after medication conversion were assumed to be an additional cost. Baseline laboratory costs were not included as these were considered part of usual care. One-way sensitivity analyses were performed by varying the costs of medications and laboratory tests between 50% and 150%.

To measure cost savings from our patients’ perspective, we calculated the average change in patient copays paid per year by subtracting the copay each patient would have paid for their lovastatin prescriptions over 1 year from what they would have paid for their simvastatin prescriptions over the same period.

**Statistical Analysis**

Descriptive statistics were utilized for the demographic data. McNemar’s test was utilized to test for differences in the proportions of patients achieving LDL-C and non–HDL-C goals before and after the intervention. The paired t test was utilized to examine mean changes in LDL-C, non–HDL-C, and ALT laboratory values preconversion and postconversion.

**Results**

A total of 7,637 patients receiving simvastatin were identified (Figure 1). Of these, 2,087 (27.3%) were excluded: 943 (12.3%) were medically ineligible (e.g., taking 80 mg simvastatin per day or had a history of intolerance to lovastatin), 543 (7.1%) refused to be converted, 491 (6.4%) were noncontinuous members, and 110 (1.4%) were unable to be contacted as outlined in Figure 1. The mean age of the 5,550 patients converted was 67 ± 10.8 years, 59% were male, and 53% were secondary prevention patients. The majority of patients (90.9%, n = 5,046) were successfully converted to lovastatin and had follow-up laboratory tests drawn, while 4.3% (n = 240) switched back to simvastatin. Of those converted successfully, 91.3% (n = 4,607) were converted to a lovastatin dose of equivalent potency to their baseline simvastatin dose.

Greater proportions of patients achieved LDL-C (P < 0.001) and non–HDL-C (P = 0.047) goals postconversion (final) compared with preconversion (baseline) (Figure 2). The largest change in control rate was seen in the primary prevention group. This likely reflects that this population had less intensive monitoring at baseline compared with secondary prevention patients who were enrolled in CPCRS. There were no significant changes or elevations in ALT values (Table 1).

Among all patients with preconversion and postconversion laboratory values, mean laboratory values (mean, 95% confidence interval [CI]) decreased as follows: LDL-C (-1.7, -1 to -2.4 mg/dL, P < 0.001); non–HDL-C (-3.2, -2.4 to -4 mg/dL, P < 0.001). Among patients converted to lovastatin 80 mg from simvastatin 40 mg, non–HDL-C decreased by -3.7 mg/dL, (-2.4 to -4, P < 0.001), but the mean LDL-C change (-1.3, -0.3 to -2.3 mg/dL, P = 0.058) was not significant.

We sampled 254 patients to assess statin adherence. Twelve were eliminated because they had fewer than 3 medication fills of either simvastatin or lovastatin during the evaluation period. The adherence rates forLovastatin and simvastatin in the remaining 242 patients were 93.8% (±14.7%) and 96.0% (±15.9%), respectively (P = 0.065).

The annualized statin cost savings from the conversion to Lovastatin from simvastatin approximated $1.6 million, or $4.14 PMPY (Table 2). Reduced expenditure change persisted when drug or laboratory costs were varied from 50% to 150%.

We also evaluated expenditure changes from the patients’ perspective. The average annual savings per patient in reduced copayment after changing from brand simvastatin to generic Lovastatin was $145.29 (95% CI, $142.68-$147.90; P < 0.001) or 62%.
A goal of therapeutic conversion programs is to reduce overall health care costs without compromising therapeutic efficacy or patient safety. Our study demonstrated that this goal is achievable among a large number of patients, utilizing a pharmacist-directed conversion intervention. In our population of more than 5,000 patients, the proportion achieving LDL-C and non–HDL-C goals postconversion was higher than preconversion, although the clinical significance of the small improvement in quality is likely negligible. In the subgroup of patients converted to lovastatin 80 mg daily from simvastatin 40 mg, the proportion achieving non–HDL-C goals was also higher postconversion, indicating that simvastatin 40 mg does not have superior lipid-lowering effects compared with lovastatin 80 mg in actual clinical practice. The safety of lovastatin compared with simvastatin was supported by our findings that only 4.3% of patients switched back to simvastatin due to intolerance, and ALTs did not change.

Previous smaller studies have shown similar safety and efficacy results after statin conversion programs. Fugit and Resch evaluated lipids and safety measures after the conversion of 157 patients with (60.5%) and without CVD to lovastatin 10 or 20 mg daily from simvastatin 5 or 10 mg daily, respectively, by a pharmacist-managed hyperlipidemia clinic. After conversion, the percentage of patients at LDL-C goal was not significantly changed. Patel and colleagues converted 170 patients from pravastatin to lovastatin by implementing a therapeutic interchange program in a Veterans Affairs medical center. They found no significant difference in the percentage of patients at LDL-C goal (40% on pravastatin and lovastatin), and no significant differences in LDL-C values (118.0 mg/dL on pravastatin, 116.8 mg/dL onLovastatin). In contrast to our study, both of these previous studies had much smaller patient populations and therefore may not have been powered to detect a change. They also employed more labor-intensive patient management strategies, while our program utilized letters in many cases to notify patients of the medication change. Taylor and colleagues evaluated lipid control rates and safety in 942 patients converted from various statins to cerivastatin. They reported increased LDL-C control rates (64.8% to 74.5%, P <0.001) and adverse events requiring drug discontinuation in 3% of patients, including 5 (0.6%) with myositis.

After conversion, 79.1% of all 5,046 patients who came in for follow-up laboratory tests achieved their LDL-C goals. This is a substantially higher lipid control rate than that described in other studies. A multicenter survey designed to evaluate lipid control in 4,888 primary- and secondary-prevention patients receiving lipid-lowering therapy...
found an LDL-C control rate of just 38.6%.22 Nationally, LDL-C control rates in patients with CVD (LDL-C goal <100 mg/dL) have been reported to be 47.6%.23 In contrast, 76.7% of our CVD patients had an LDL-C below goal, which is likely due to the close follow-up these patients receive with the CPCRS.

To date, there have been no reports published of therapeutic conversion programs specifically evaluating the conversion to lovastatin 80 mg daily from simvastatin 40 mg. In one comparative dose efficacy trial, lovastatin 40 mg twice daily (i.e., 80 mg per day) (n = 11) lowered LDL-C 48% versus a decrease of 41% by simvastatin 40 mg once daily (n = 61, the P value was not reported).24 Illingworth and colleagues reported a nonsignificant LDL-C decrease of 35% for lovastatin 80 mg versus 39% for simvastatin 40 mg daily in 24 patients participating in this cross-over study.25 Our study was not designed to directly compare the extent of LDL-C lowering for lovastatin versus simvastatin; however, the results of our subanalysis suggest similar efficacy of both agents on LDL-C and non-HDL-C without an increase in adverse effects.

The net cost savings from this statin conversion intervention, expressed across the entire membership of this HMO, was $4.14 PMPY after accounting for the additional laboratory costs. Our expenditure reduction was significant even though most of our patient population used half tablets of simvastatin at baseline, a strategy that has already been shown to reduce costs while maintaining lipid control.26 While drug-acquisition line, a strategy that has already been shown to reduce costs in adverse effects.

**TABLE 1** Laboratory Results for Patients With a Follow-up Fasting Lipid Profile Converted to Lovastatin

<table>
<thead>
<tr>
<th>Laboratory Measure</th>
<th>Preconversion Value</th>
<th>Postconversion Value</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean LDL-C mg/dL</td>
<td>97.5 (96.8-98.2)†</td>
<td>95.8 (95.1-96.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean non–HDL-C mg/dL</td>
<td>135.9 (130.5-136.8)</td>
<td>132.7 (131.9-133.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ALT IU/L</td>
<td>26.9 (26.4-27.4)</td>
<td>26.4 (26.0-26.8)</td>
<td>0.134</td>
</tr>
</tbody>
</table>

**TABLE 2** Cost-Minimization Analysis for All Patients Converted to Lovastatin From Simvastatin (N = 5,046)

<table>
<thead>
<tr>
<th>Primary Analysis*</th>
<th>Per-Member-Per-Year Expenditure Change ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross antihyperlipidemic drug costs†</td>
<td>(4.41)</td>
</tr>
<tr>
<td>Additional FLP and ALT lab costs ($20.25 each)‡</td>
<td>0.27</td>
</tr>
<tr>
<td>Net drug cost savings</td>
<td>(4.14)</td>
</tr>
</tbody>
</table>

**Limitations**

A limitation of this study may be that not all patients were converted to an equivalent lovastatin dose from simvastatin. In 8.7% of cases, a CPSP recommended modifying the statin dose. However, our primary purpose was not to evaluate dose equivalency but rather to evaluate the conversion process and the proportion of patients who would remain at or reach their LDL-C goal through the conversion. We considered any FLP within 12 months prior to the conversion as “baseline” rather than obtaining a more recent lipid profile on all patients. While there may have been a number of patients who were not at their LDL-C goal immediately prior to the conversion, we were still able to demonstrate that a significant number of patients can reach or remain at their LDL-C goal after conversion to a less potent, less expensive statin if dosed appropriately.

The results of our study cannot be extrapolated to patients who have dyslipemias not controlled on the maximum dose of simvastatin since these patients were excluded from our study. The cost savings observed in this study may not be fully
reproducible in health care organizations that do not utilize lovastatin or are not structured to obtain group purchasing discounts on statin medications.

**Conclusion**

Our study provides evidence that a clinical pharmacy-directed program that converts dyslipidemia patients to generic lovastatin from brand simvastatin can result in reduced expenditures for both the health plan and for the patient while maintaining or improving lipid control and without increasing risk to the patient.

**REFERENCES**


