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Impact of Therapeutic Interchange from Pravastatin to Lovastatin in a Veterans Affairs Medical Center

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Abstract

Objective: **To evaluate the impact of a therapeutic interchange from pravastatin to lovastatin on treatment outcomes, quality of life, patient satisfaction, and costs.**

Study Design: **A prospective cohort study of 170 patients switched from pravastatin to lovastatin from September 1997 through November 1997.**

Patients and Methods: **The therapeutic interchange program promoting lovastatin as the preferred agent went into effect June 2, 1997 after Merck & Co. was awarded the Veterans Health Administration national contract for 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors. Patients were switched to lovastatin by either their primary care physician during routine clinic visits or the pharmacist by mail. The following outcomes were measured before and after conversion to lovastatin: lipid values, liver function tests, National Cholesterol Education Program (NCEP) low-density cholesterol (LDL-C) goals achieved, quality of life (QOL) (measured by the Medical Outcomes Study 36-item short-form health survey [SF-36]), medication tolerance (measured with a global symptom survey), patient satisfaction, and cost-minimization analysis.**

Results: **Lipid values and liver function test results were similar for pravastatin and lovastatin treatment. Forty percent of patients achieved NCEP LDL-C goals before and after formulary conversion. There were no significant differences between pravastatin and lovastatin in QOL, medication tolerance, and patient satisfaction. The projected cost savings from this therapeutic interchange was approximately $211,000 annually.**

Conclusion: **Therapeutic interchange from pravastatin to lovastatin resulted in substantial cost savings. QOL, patient satisfaction, and achievement of NCEP LDL-C goals were maintained.**

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Expenditures for lipid-lowering agents are increasing and are a significant portion of the Veterans Health Administration (VHA) pharmaceutical budget. Over a 12-month period between October 1, 1996, and September 30, 1997, the VHA spent approximately $69.7 million for the procurement of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. Over a 1-year period between April 1, 1996, and March 31, 1997, the Long Beach Veterans Affairs Medical Center (LBVAMC) spent approximately $625,000 for HMG-CoA reductase inhibitors. The breakdown of formulary expenditures during this time was $536,000 for pravastatin and $89,000 for simvastatin. The VHA national contract for HMG-CoA reductase inhibitors was awarded June 2, 1997, to Merck & Co. for lovastatin and simvastatin (Table 1). Subsequently, the LBVAMC Pharmacy and Therapeutics (P&T) Committee designated lovastatin as their preferred agent and authorized therapeutic interchange of pravastatin to lovastatin, unless this was clinically contraindicated. Simvastatin prescribing remained restricted to patients who failed lovastatin therapy.

Lovastatin was designated the preferred HMG-CoA reductase inhibitor at the LBVAMC for several reasons. First, lovastatin and pravastatin are essentially equipotent on a milligram-per-milligram basis

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in reducing low-density lipoprotein cholesterol (LDL-C).[1-5] Thus, a switch to lovastatin would be less complex than switching to simvastatin, which is approximately twice as potent.[1-3] Second, lovastatin will be the first HMG-CoA reductase inhibitor to become available generically when the patent expires in June 2001. Finally, we consider cardiovascular event reduction a class effect of the HMG-CoA reductase inhibitors. This is based on coronary atheroma studies demonstrating a slowing of progression or actual regression of atherosclerotic lesions with intensive cholesterol lowering.[6] Coronary artery lesions have been shown to regress in patients treated with a cholesterol-lowering diet plus lovastatin.[7] Although the results of a primary prevention study, the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS),[8] were not available at the time lovastatin was designated as the preferred formulary agent, a reduction in cardiovascular events in patients treated with lovastatin was demonstrated in this trial.

Outcome measures are increasingly being used by healthcare organizations as a key indicator of healthcare quality.[9] Information on the outcomes of therapeutic interchange programs is limited. One study has evaluated the effect of replacing lovastatin with pravastatin on lipid values and costs,[10] but no studies to date have assessed quality of life, patient satisfaction, and healthcare utilization after a therapeutic interchange. We hypothesized that therapeutic interchange from pravastatin to lovastatin would reduce costs yet maintain the quality of treatment. The objectives of this study were to (1) measure therapeutic outcomes, (2) evaluate quality of life and patient satisfaction, and (3) assess the cost impact of a therapeutic interchange from pravastatin to lovastatin.

Table 1. Acquisition Costs of HMG-CoA Reductase Inhibitors at the LBVAMC

HMG-CoA Reductase Inhibitor	Cost/Tablet ($)
Pravastatin	
10 mg	0.89
20 mg	0.89
40 mg	1.86
Lovastatin	
10 mg	0.41
20 mg	0.61
40 mg	1.01
Simvastatin	
10 mg	0.68
20 mg	1.25
40 mg	1.51

··· METHODS ···

Study Subjects

The therapeutic interchange from pravastatin to lovastatin was a phased-in formulary switch program, authorized by the P&T Committee at the LBVAMC and started June 2, 1997. Therapeutic interchange was not authorized for patients concomitantly receiving cyclosporine, erythromycin, gemfibrozil, itraconazole, or ketoconazole because of potentially clinically significant drug-drug interactions.[11,12] All healthcare providers were notified of the therapeutic interchange by educational electronic mail. Also, a "reminder message" to convert to lovastatin appeared on every prescription renewal form. Automatic conversion to lovastatin from pravastatin on a milligram-per-milligram basis (1:1 conversion) occurred when patients requested a refill for pravastatin through the outpatient pharmacy or when the physicians switched patients to lovastatin during routine clinic visits.

A prospective cohort analysis was conducted to evaluate the impact of therapeutic interchange from pravastatin to lovastatin at the LBVAMC. The study protocol was approved by the institutional review board of the LBVAMC. Patients with active prescriptions for pravastatin between September 1, 1997, and November 30, 1997, were eligible for inclusion. Patients in the study were switched to lovastatin either by their physician during routine clinic visits as described above or, for the remaining patients with active pravastatin prescription refills, by the pharmacist via letter explaining the formulary conversion process. The fill date for the new lovastatin prescription was scheduled for the next expected refill date for patients switched by the pharmacist.

Outcomes

Serum Lipids and Liver Function Tests. The following surrogate end points were measured before and after formulary interchange: total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and

alkaline phosphatase (ALP). The most recent laboratory values within the 6 months preceding the interchange were identified as pravastatin values. The time frame for lovastatin data collection was 6 weeks to 6 months after interchange. If more than one lipid panel measurement was available after the change to lovastatin, an average was used for comparison with pravastatin. Lipid levels and liver function tests were measured by standard enzymatic methods. LDL-C levels were calculated using the Friedewald formula[13] but were not estimated for patients who had TG levels of 400 mg/dL or higher. The laboratory participates with the Centers for Disease Control and Prevention Program for standardization of laboratory tests.

Therapeutic Outcomes. Therapeutic outcome measures included the percentage of patients achieving LDL-C National Cholesterol Education Program (NCEP) goals.[14] Electronic medical data (physician-generated problem list, outpatient clinic ICD-9 problem list, hospital discharge summary, and pharmacy prescription profile) were evaluated to determine coronary heart disease (CHD) risk factors and LDL-C goals. This database identified the following risk factors: age, HDL-C level less than 35 mg/dL, HDL-C higher than 60 mg/dL, and medical problems (diabetes mellitus, hypertension, evidence of CHD, evidence of peripheral vascular disease, or evidence of cerebral vascular disease). If fewer than 2 risk factors were identified, medical charts were reviewed to exclude current tobacco use and family history of premature CHD so that all patients were accurately classified.

Quality of Life. Quality of life (QOL) was assessed with the Medical Outcomes Study (MOS) 36-item short-form health survey (SF-36).[15] The SF-36 is a validated general health-related quality-of-life survey used commonly to evaluate medical outcomes. The SF-36 scores 8 individual QOL scales. The scores from these components are aggregated into the Physical Component Summary (PCS) scale and the Mental Health Component Summary (MCS) scale. The individual scales range from 0 to 100, whereas the summary scales have narrower possible ranges. Higher scores represent better QOL.

Medication Tolerance. Medication tolerance was assessed by use of a global symptom survey. The structural framework of the global symptom survey was based on the Hypertension/Lipid form 5.1 developed by the Health Outcomes Institute.[16] The global symptom survey targeted common adverse effects associated with HMG-CoA reductase inhibitors including gastrointestinal (GI), central nervous system (CNS), and muscle symptoms. Symptoms were scored according to frequency and intensity; higher scores represented greater frequency and intensity of symptoms.[17] The total possible points was 50 with the category breakdown as follows: GI = 20, CNS = 20, and muscle =10.

Patient Satisfaction. The framework of the patient satisfaction questionnaire was based on a modified Consumer Assessment of Health Plans Survey (CAHPS) questionnaire.[18] The patient satisfaction categories were rated on a scale of 0 to 10, with 0 = worst possible and 10 = best possible. Patients rated satisfaction for the following categories: your personal doctor or nurse, the drugs you have been prescribed, your pharmacist, all your healthcare, and your VA health plan. The surveys were mailed before interchange and 3 months after interchange to the 118 patients switched by the pharmacist. Nonresponders were sent a second survey.

Economic Analysis. Cost-minimization analysis (CMA)[19] was performed to study the economic impact of implementing a formulary switch policy, with the assumption that the 2 drugs were therapeutically equivalent. Projected cost avoidance was determined by calculating the reduction in the average cost per HMG-CoA reductase inhibitor prescription after the change to lovastatin.

Adverse Events. Adverse events were evaluated by using the Naranjo nomogram[20] to determine causality between the medication and the adverse outcome. The nomogram utilizes a probability scale for adverse drug reactions based on a series of 10 scored questions that evaluate the relationship between an adverse event and the suspected drug. The 4 classification categories of the adverse drug reaction include the following: doubtful reaction (likely related to factors other than a drug), possible reaction (followed a temporal sequence after a drug, possibly followed a recognized pattern to the suspected drug, and could be explained by characteristics of the patient's disease), probable reaction (could not reasonably be explained by other causes), and definite reaction (confirmed by dechallenge and rechallenge of the suspected drug).[20]

Healthcare Resource Utilization. Utilization of healthcare resources was evaluated to determine whether any problem related to the formulary switch resulted in more hospital visits or hospitalization. The number of and reason for emergency department and walk-in clinic visits 6 months before

Table 2. Baseline Characteristics of Study Patients

Variable	Value
No. of patients	170
Age (mean ± SD)	68.8 ± 8.8
Men: Women	165:5
CHD risk factors, no. (%)	
Hypertension	128 (75.7)
Diabetes	50 (29.6)
HDL-C < 35 mg/dL	30 (18.5)
HDL-C ≥ 60 mg/dL	21 (13.0)
CHD risk assessment, no. (%)*	
Low risk (< 2 RFs, LDL-C goal < 160 mg/dL)	7 (4.1)
Moderate risk (≥ 2 RFs, LDL-C goal < 130 mg/dL)	61 (35.9)
High risk (established AVD, LDL-C goal ≤ 100 mg/dL)	102 (60.0)
Concomitant cholesterol medications, no.	
Colestipol	2
Gemfibrozil	0
Fish oil	1
Niacin	4

CHD = coronary heart disease; HDL-C = high-density lipoprotein cholesterol; RFs = risk factors; LDL-C = low-density lipoprotein cholesterol; AVD = atherosclerotic vascular disease (coronary heart disease, cerebral vascular disease, and/or peripheral vascular disease).
*Classification of LDL-C goals is based on reference 14.

Table 3. Lipid Values at Baseline and after Therapeutic Interchange

Variable	n	Pravastatin (mg/dL) (Mean ± SD)	Lovastatin (mg/dL) (Mean ± SD)	*P* Value*
Total cholesterol	108	197.8 ± 38.5	195.3 ± 34.8	0.4312
LDL cholesterol	86	118.0 ± 31.0	116.8 ± 29.1	0.7062
HDL cholesterol	96	43.6 ± 10.9	46.0 ± 13.5	0.0037
Triglycerides	96	168.3 ± 110.9	173.5 ± 107.0	0.5396

LDL = low-density lipoprotein; HDL = high-density lipoprotein.
*Paired *t*-test.

Table 4. Liver Function Values at Baseline and after Therapeutic Interchange

Variable	n	Pravastatin (Mean ± SD)	Lovastatin (Mean ± SD)	*P* Value*
AST, U/L	93	23.2 ± 14.8	25.1 ± 19.6	0.4226
ALT, U/L	76	20.8 ± 12.5	23.1 ± 14.8	0.1515
ALP, U/L	68	85.4 ± 22.7	85.8 ± 25.5	0.7723

AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase.
*Paired *t*-test.

and 6 months after formulary interchange to lovastatin were compared.

Statistical Analysis

Blood lipid values, liver function test results, SF-36 results, global symptom scores, patient satisfaction results, and number of hospital visits comparing pravastatin treatment versus lovastatin treatment were analyzed by Student's paired *t*-test. Achievement of NCEP LDL-C goals before and after switch was analyzed by χ^2 test. The level of statistical significance was set at $\alpha = 0.05$.

··· RESULTS ···

Patient Characteristics

As of June 2, 1997, 2501 patients had active pravastatin prescriptions. This study included a cohort of 170 patients with active perscriptions for pravastatin between 9/1/97 and 11/30/97. Baseline characteristics are summarized in Table 2. Fifty-two patients were switched to lovastatin by their physician during routine clinic visits, and 118 patients by the pharmacist via mail. Patients were primarily elderly male veterans. Other CHD risk factors were commonly present including hypertension (76%) and diabetes mellitus (30%). The majority of patients were in either the moderate-risk category (36%) or high-risk category (60%). Seven (4%) patients received other concomitant cholesterol-lowering agents, and these patients remained on the same doses after being switched to lovastatin. One patient was started on gemfibrozil after the interchange to lovastatin. Of the 170 patients on pravastatin, 34 (20%) were prescribed 10 mg/day; 95 (56%), 20 mg/day; 3 (2%), 30 mg/day; and 38 (22%), 40 mg/day.

Serum Lipids and Liver Function Tests

Mean lipid values at baseline and after therapeutic interchange to lovastatin are summarized in Table 3. There were no differences between pravastatin and lovastatin in TC, LDL-C, and TGs. A significant difference was observed for HDL-C between pravastatin (mean, 43.6 mg/dL) and lovastatin (46.0 mg/dL) (P = 0.0037). No significant differences were observed in mean levels of the hepatic enzymes AST, ALT, and ALP (Table 4).

NCEP LDL-C Goals

The percentage of patients achieving NCEP LDL-C goals is summarized in Figure 1. Evaluable data were available for 86 patients to determine whether NCEP goals were achieved with pravastatin and maintained after interchange to lovastatin. No significant differences were observed between pravastatin and lovastatin in the ability to achieve all levels of NCEP LDL-C goals. The NCEP LDL-C goals achieved with pravastatin and lovastatin, respectively, were as follows: all levels combined, 40% and 40%; LDL-C < 100 mg/dL, 35% and 29%; LDL-C < 130 mg/dL, 44% and 53%; and LDL-C < 160 mg/dL, 80% and 80%.

Quality of Life, Medication Tolerance, and Patient Satisfaction

The QOL results measured by the SF-36 survey are summarized in Table 5. Of 118 patients switched to lovastatin by the pharmacist, 52 (44%) completed a survey both before and after the interchange. No significant differences were observed in QOL for any of the dimensions comparing pravastatin to lovastatin. The results of the global symptom survey for medication tolerance are summarized in Table 6. Again, there were no significant differences in the total symptom score and symptoms known to be associated with HMG-CoA reductase inhibitor adverse effects (GI, CNS, and muscle). Patient satisfaction ratings are summarized in Table 7. Patient satisfaction ratings were high for all categories, averaging scores greater than 8. No significant differences were

Figure 1. Percentage of Patients Achieving NCEP LDL-C Goals

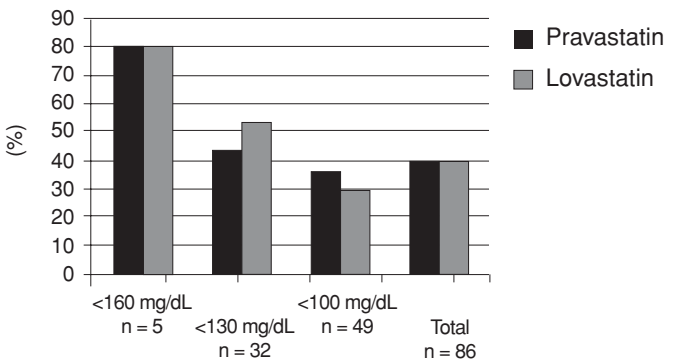


Table 5. Quality of LIfe at Baseline and After Therapeutic Interchange*

Scale	n	Pravastatin (Mean ± SD)	Lovastatin (Mean ± SD)	*P* Value†
MCS	48	48.2 ± 11.0	48.1 ± 12.4	0.9131
Social functioning	51	70.4 ± 28.2	64.8 ± 34.1	0.2369
Role—emotional	51	67.6 ± 30.5	62.6 ± 32.3	0.2915
Vitality	51	49.9 ± 19.6	49.8 ± 25.1	0.9718
Mental health	52	67.6 ± 21.3	67.7 ± 21.9	0.9536
PCS	49	37.0 ± 10.5	35.7 ± 10.4	0.2639
Physical functioning	52	55.1 ± 28.6	48.9 ± 28.1	0.0766
Role—physical	52	53.9 ± 30.7	50.6 ± 30.3	0.4721
Bodily pain	52	53.4 ± 25.5	49.1 ± 24.6	0.1254
General health	50	44.0 ± 21.9	47.8 ± 23.6	0.1512

MCS = Mental Health Component Summary; PCS = Physical Component Summary
*Quality of life is as measured with the SF-36.
†Paired *t*-test.

noted in any of the satisfaction categories comparing pravastatin to lovastatin.

Adverse Drug Events and Healthcare Resource Utilization

Adverse events occurred in 2 (1.2%) patients after conversion to lovastatin. One patient experienced moderate-intensity headaches with lovastatin that required discontinuation and reversion to pravastatin. In 1 patient who received lovastatin, AST and ALT levels increased to 3 times the upper limit of normal. However, this patient had a history of elevated AST and ALT (more than 2 times the upper limit of normal) while taking pravastatin. On the basis of the Naranjo criteria for causality of drug-induced adverse events,[20] it was probable that this patient experienced lovastatin-induced hepatotoxicity. No differences were noted in the number of emergency room (0.162 vs 0.162, P = 1.0) or walk-in visits (0.180 vs 0.168, P = 0.7864) 6 months before and 6 months after conversion to lovastatin, respectively.

Table 6. Medication Tolerance at Baseline and after Therapeutic Interchange*

n = 52	Pravastatin (Mean score)	Lovastatin (Mean score)	*P* Value†
Total symptom score	37.0	37.0	0.9468
GI symptoms	13.5	14.7	0.2070
CNS symptoms	15.3	15.6	0.6407
Muscle symptoms	7.8	7.9	0.8226

GI = gastrointestinal; CNS = central nervous system.
*Medication tolerance was measured with a global symptom survey (see Methods for details). Total possible points = 50; GI = 20, CNS = 20, Muscle = 10.
†Paired *t*-test.

Table 7. Patient Satisfaction Ratings at Baseline and after Therapeutic Interchange*

Variable	n	Pravastatin (Mean)	Lovastatin (Mean)	*P* Value†
Personal doctor or nurse	45	8.0	8.1	0.7194
Drugs you have been prescribed	48	8.4	8.4	0.9569
Your pharmacist	49	8.7	8.9	0.4435
All your healthcare	48	8.3	8.4	0.6775
Your VA health plan	48	8.6	8.7	0.8272

*Patient satisfaction was measured with a modified CAHPS questionnaire (see Methods for details).
†Paired *t*-test.

Cost-Minimization Analysis

Figure 2 shows the number of prescriptions filled per quarter for pravastatin, lovastatin, and simvastatin from April 1997 through March 1998. A comparison of the number of prescriptions for April 1997 versus March 1998 showed that pravastatin prescriptions decreased (from 973 in April 1997 to 26 in March 1998), whereas the number of prescriptions increased for both lovastatin (from 0 in April 1997 to 1042 in March 1998) and simvastatin (from 125 in April 1997 to 185 in March 1998). Overall prescription of HMG-CoA reductase inhibitors has increased at the LBVAMC. In an effort to substantially reduce the number of pravastatin prescriptions dispensed, patients concomitantly receiving gemfibrozil were switched to simvastatin at 50% of the pravastatin dose. The number of simvastatin prescriptions increased approximately twofold from the last quarter of 1997 to the first quarter of 1998. The number of prescriptions dispensed and HMG-CoA reductase

inhibitor costs per quarter are shown in Figure 3. Despite an increasing number of prescriptions dispensed, costs were contained through the implementation of national contract pricing and therapeutic interchange. The average cost per HMG-CoA reductase inhibitor is shown in Figure 4. This represents a cost reduction of 21.9% per prescription when the average cost per prescription for 2 months before the interchange ($76.84) is compared with the most recent 2-month average ($59.98). By multiplying this difference by the number of prescriptions filled for lovastatin (1042 prescriptions) in March 1998, the projected savings from this conversion program is $17,568 per month or $210,816 annually. The prescription quantity (number of days' supply per fill) did not change during the study period. The percentage of 90-day fills compared with 30-day fills were 86.0% and 14.0%, respectively, in April 1997 versus 85.6% and 14.4%, respectively, in March 1998.

··· DISCUSSION ···

The practice of therapeutic interchange has become common throughout the United States. The

Figure 2. Number of Prescriptions Filled Per Quarter from April 1997 through March 1998 at the LBVAMC

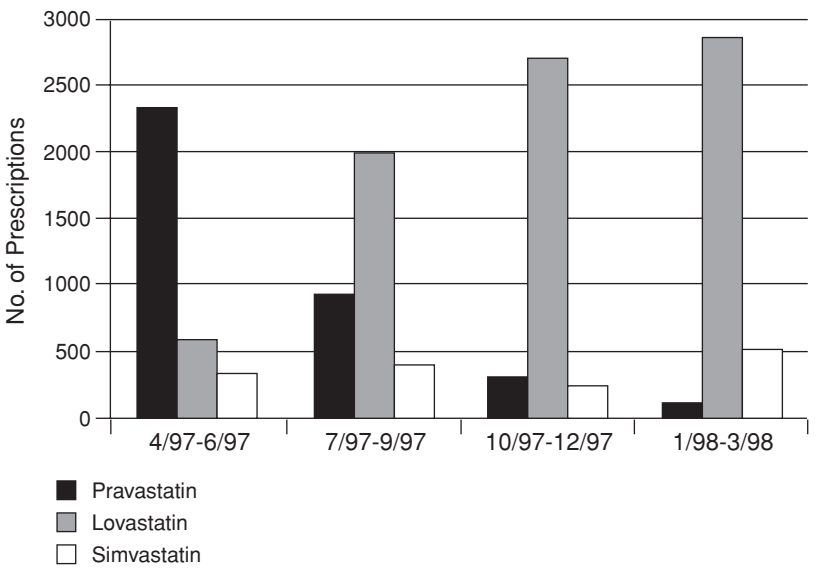
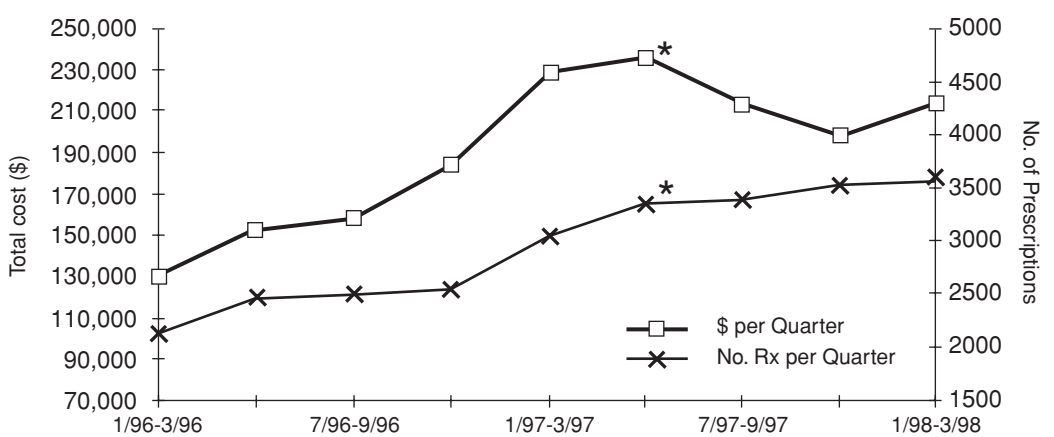


Figure 3. Total HMG-CoA Reductase Inhibitor Costs Per Quarter at LBVAMC from January 1996 through March 1998



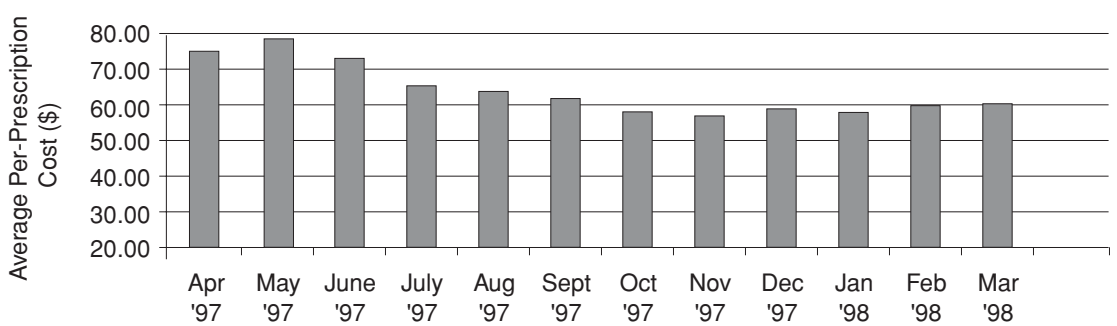
*Therapeutic interchange program implemented June 2, 1997.

American Medical Association defined therapeutic interchange as authorized exchange of a therapeutic alternative in accordance with previously established and approved written guidelines or protocols within a formulary system.[21] The formulary system is routinely used by hospitals and managed care organizations to select preferred products, providers, and suppliers to decrease costs and help control drug utilization, yet maintain quality of treatment.[22,23] Maintaining quality of treatment should not be limited to evaluation of safety and efficacy of drug therapy. Outcome measures such as healthcare utilization, health-related QOL, and patient satisfaction also need to be considered in determining the success of therapeutic interchange programs.

Lovastatin and pravastatin are equally effective in lowering LDL-C on a milligram-per-milligram basis.[1-5] Korman et al[10] evaluated the effect of therapeutic interchange from lovastatin to pravastatin on serum lipids and costs in a veterans population. In their study, the conversion to pravastatin was at 50% of the lovastatin dose in milligrams (ie, lovastatin 40 mg to pravastatin 20 mg). The authors concluded that replacement of lovastatin with pravastatin was associated with a 21% cost reduction and no significant change in mean serum lipid concentrations. The mean LDL-C values for lovastatin and pravastatin were 156 ± 38 mg/dL and 176 ± 40 mg/dL, respectively, and the mean TC values for lovastatin and pravastatin were 224 ± 39 mg/dL and 226 ± 39 mg/dL, respectively. Although a statistical difference was not seen in mean LDL-C and TC concentrations, a scrutiny of the data suggests that using one half the dose of pravastatin was not therapeutically equivalent in lowering LDL-C. Our study demonstrates that therapeutic interchange from pravastatin to lovastatin (118.0 ± 31.0 mg/dL and 116.8 ± 29.1 mg/dL, respectively), on a milligram-per-milligram basis, resulted in similar LDL-C values. The statistically significant difference observed for HDL-C comparing pravastatin to lovastatin (mean 43.6 mg/dL versus 46.0 mg/dL, respectively) was unexpected. Whether this statistically significant increase in HDL-C is clinically relevant cannot be determined. Factors that may raise HDL-C, such as increasing aerobic activity and alcohol consumption, were not assessed in our study. The reported average effects on HDL-C for pravastatin (+7% to +12% [10 mg to 40 mg per day]) and lovastatin (+6% to +10% [20 mg to 80 mg per day]) are similar.[1,24]

NCEP guidelines are used by the LBVAMC Lipid Clinic to define therapeutic goals for patients with hypercholesterolemia. This study evaluated a cohort of patients treated by their primary care providers. Forty percent of patients achieved LDL-C goals with pravastatin treatment, and 40% reached goal after conversion to lovastatin. The Lipid Treatment Assessment Project (L-TAP)[25] evaluated 901 primary care providers who frequently prescribe lipid-lowering medications. Of 5601 patients treated for hypercholesterolemia, the overall percentage of patients achieving NCEP goals was 38%, and for secondary prevention patients, 18%. In comparison with L-TAP, achievement of overall LDL-C goals is comparable in our study, whereas achievement of LDL-C goals for secondary prevention patients is greater (29%) at the LBVAMC. The L-TAP study also illustrates the difficulty in lowering LDL-C levels to less than 100 mg/dL, despite the use of powerful

Figure 4. HMG-CoA Reductase Inhibitor Average Cost Per Prescription from April 1997 to March 1998



cholesterol-lowering agents. We recognize that 29% achievement in LDL-C goal for secondary prevention patients is not ideal. In an effort to maximize therapy and achieve better results in treating dyslipidemia, patients may need to be switched to a higher potency agent such as simvastatin or be referred to the LBVAMC Lipid Clinic.

HMG-CoA reductase inhibitors are remarkably safe drugs. Approximately 1% to 3% of patients in clinical trials are forced to withdraw from treatment because of a perceived or real adverse effect associated with the drugs. The most common side effects associated with HMG-CoA reductase inhibitor therapy are GI intolerance and headache, which occur in 2% to 7% of patients. Hepatotoxicity and myopathy are uncommon but worrisome side effects associated with HMG-CoA reductase inhibitors. We did not compare creatine phosphokinase (CPK) levels because CPK is not routinely measured at our facility. Hepatotoxicity, as evidenced by increases in aminotransferase levels to greater than 3 times the upper limit of normal, occurs in fewer than 1% of patients receiving starting doses and in up to 2% of patients receiving maximum doses.[24] In our study, 1 patient displayed elevated aminotransferase levels that were 3 times the upper limit of normal and that were probably associated with lovastatin. Drug-induced adverse effects or medication tolerance, as perceived by the patients, were not different between pravastatin and lovastatin, based on the global symptom survey results.

Holdford and Smith[9] reviewed published pharmaceutical studies to examine the extent to which pharmaceutical research demonstrates the impact of pharmaceutical services and programs on healthcare outcomes. They found that patient satisfaction and health-related QOL components were not included in most pharmaceutical outcome studies. In an attempt to explore these outcomes, we incorporated the SF-36, global symptom survey, and patient satisfaction questionnaire into our methodology. To interpret the clinical significance of our QOL results, a comparison with the US population norm is useful.[26] The US population means for both the MCS and PCS scales are 50.0 ± 10.0. Our population of veterans scored similarly on the MCS scale but scored much lower on the PCS scale. However, if we compare our study results with norm-based mean scores for men over 65 years (MCS = 52.51 ± 9.78 and PCS = 41.95 ± 11.95), our results are more closely matched on the PCS scale. A direct comparison study[27] assessed QOL in men with primary hypercholesterolemia after 12 weeks' treatment with lovastatin 40 mg or pravastatin 40 mg. The Nottingham Health Profile was used, and no significant differences were found between the 2 groups in health-related QOL, a finding similar to that in our study. The results from all 3 surveys indicate that therapeutic interchange does not adversely affect health-related QOL, medication tolerance, and patient satisfaction. The patients' perception of these 3 outcome measures was not influenced by the formulary conversion.

Cost-minimization analysis compares the cost difference between alternative therapies that are known or assumed to result in identical outcomes.[19,28] CMA is criticized because the assumption of equal outcomes seems unlikely in many cases.[28] We looked at healthcare resource utilization to determine if this therapeutic conversion program resulted in increased hospital visits or hospitalizations that would negate the cost reduction seen with switching to lovastatin. Healthcare utilization remained unchanged after implementation of the therapeutic interchange. Although there are added costs for conversion to lovastatin by the pharmacist, such as time spent canceling old prescriptions and mailing surveys, this was not an appreciable contribution and subsequently was not included in the cost analysis.

Our study captures the real-life implementation and impact of a therapeutic interchange program. Several limitations do exist when conducting a study of this type. One limitation is that we did not include an equally matched control group. This was not feasible because the P&T Committee authorized conversion to lovastatin for all patients with active pravastatin prescriptions. Misclassification of patients based on NCEP goals may have occurred because family history and current tobacco use might not be recorded in the medical record. Because this was not a controlled trial, we could not ensure that all patients would complete the surveys before and after conversion to lovastatin; therefore, a possibility of introducing patient survey response bias may exist. Although the population in this study consisted primarily of male veterans, these patients are comparable to others over the age of 65 years with comorbid conditions. The data from our study may, therefore, be applicable to other healthcare organizations with similar patients.

The P&T Committee approved lovastatin as the preferred HMG-CoA reductase inhibitor because of mandatory national VHA contracts. This study demonstrates that the therapeutic interchange of lovastatin for pravastatin resulted in equivalent cholesterol lowering and significant cost savings yet

maintained health-related QOL, patient satisfaction, and achievement of NCEP target LDL-C goals.

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