



Outcomes Assessment

Hyperlipidemia

Prepared for Kansas Medical Assistance Program in August, 2008

EXECUTIVE SUMMARY

Purpose of Intervention	The purpose of this intervention is to identify opportunities for improving coronary heart disease (CHD) prevention with lifestyle modifications and lipid lowering drug therapies following NCEP guidelines.
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Intervention	Intervention Type	Population-based mailing
	Intervention Mailing Date	October 2007
	Pre-intervention Period (Baseline)	April 2007 – September 2007
	Post-intervention Period (Post)	November 2007 – April 2008
	Number of Letters Mailed	554
	Number of Targeted Physicians	554
	Number of Targeted Patients	2,005
	Adjusted Targeted Patients	1,112

Changes in Clinical Indicators

Clinical Indicators	Target		
	Baseline	Apr-08	% C change
Underutilization	834	501	-39.9%
Medication Non-Compliance	123	43	-24.5%
Increased Risk of ADE	79	41	-48.1%
Drug-Drug Interactions	78	59	-24.4%
Total	1,114	644	-42.2%

Savings Calculation

Intervention-Related Drug Therapy	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	\$25.73
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	\$22.22
Estimated Savings Per Patient Per Month	\$3.51
Total Number of Targeted Patients	1,112
6-Month Total Savings	\$23,432.45



BACKGROUND

Coronary heart disease (CHD) is the leading cause of death in the US afflicting more than 13 million patients, thus it imposes a major burden on society in terms of morbidity, mortality and economic costs. According to the 2005 Heart and Stroke Statistics, the total (direct and indirect) costs of care for CHD in 2005 is estimated to be \$142 billion. Of the total direct costs, hospital and nursing home costs account for \$49.9 billion and drugs/other medical durables for \$9.0 billion.¹

Elevated cholesterol is a known risk factor for CHD. Lowering cholesterol slows the progression of coronary artery lesions and decreases coronary event rates.² Recent clinical trials have demonstrated reductions in morbidity and mortality with LDL lowering therapy in particular with HMG-CoA reductase (statins) inhibitors.^{3,4,5,6,7,8,9,10} The National Cholesterol Education Program (NCEP) was formed in 1985 and subsequently released the first cholesterol treatment guidelines in 1988. The NCEP is an effort to increase awareness of the dangers of high cholesterol levels and the benefits of reducing cholesterol levels. The treatment guidelines provided by the NCEP aid clinicians in making decisions regarding cholesterol monitoring and therapy initiation thereby reducing the risk of CHD. The expert panel from this program released its most recent report, the NCEP-Adult Treatment Panel (ATP) III, in May 2001. The ATP III provides new guidelines for assessment of CHD risk and continues to emphasize LDL cholesterol as the primary target of therapy.

A 2004 update to the NCEP clinical practice guidelines suggests a more aggressive therapeutic option (LDL cholesterol < 70 mg/dL) for patients at very high risk for CHD based on recent clinical trials. Factors that place patients at very high risk include:¹¹

- The presence of established CVD plus (1) multiple major risk factors (especially diabetes)
- Severe and poorly controlled risk factors (especially continued cigarette smoking)
- Multiple risk factors of the metabolic syndrome (especially high triglycerides ≥ 200 mg/dL plus non-HDL-C ≥ 130 mg/dL with low HDL-C of ≤ 40 mg/dL), and
- On the basis of PROVE IT, patients with acute coronary syndromes

Despite the information from recent trials and the NCEP guidelines, hyperlipidemia is often untreated or undertreated. National estimates indicate that only 35% of primary prevention patients needing therapy are receiving it.¹² In 2002, 61% of patients enrolled in commercial managed care plans and hospitalized for heart attack, bypass surgery or angioplasty were

¹ American Heart Association. Heart Disease and Stroke Statistics – 2005 Update. Dallas, Tex: American Heart Association; 2005.

² National Cholesterol Education Program. Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-2497

³ Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia: West of Scotland Coronary Prevention Study Group. N Engl J Med 1995; 333: 1301-1307

⁴ Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS-Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 1998; 279: 1615-1622.

⁵ Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-1389.

⁶ Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels: Cholesterol and Recurrent Events Trial Investigators. N Engl J Med 1996; 335: 1001-1009.

⁷ The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339: 1349-1357.

⁸ Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of Cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomized placebo-controlled trial. Lancet 2002; 360:7-22.

⁹ Sever PS, Dahlöf B, Poulter NR, et al., for the ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower than average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicenter randomized controlled trial. Lancet 2003; 361: 1149-1158.

¹⁰ The Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in Myocardial Infarction 22 Investigators, Cannon CP, Eugene Braunwald E, McCabe CH, et al. Comparison of intensive and moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med 2004; 350.

¹¹ NCEP Report. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. Circulation 2004; 110:227-239

¹² Hoerger TJ, et al. Treatment patterns and distribution of low-density lipoprotein lowering: a managed care perspective. Am J Man Care 1998;4:65-74



treated to an LDL cholesterol goal of less than 130 mg/dL. This proportion represented an increase from 45% from 1999. If all practices performed at the 90th percentile level (72%), 6,500 deaths could be avoided each year. The 2001 NCEP ATP III guidelines recommend a more aggressive goal of less than 100 mg/dL. With this in mind, the treatment rates are likely much worse than suggested.¹

When targeting patients at greatest risk for having a CHD event, lipid lowering therapy has been shown to be cost effective. The average costs of a coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty (PTCA) in 2002 were \$60,853 and \$28,558, respectively.² Studies have shown that if cholesterol levels can be lowered in high risk patients, the costs to treat CHD complications can potentially be avoided.¹³

¹³ McKenney JM, Knosian B. Economic benefits of aggressive lipid lowering: a managed care perspective. *Am J Man Care* 1998;4:65-74.



METHODOLOGY

Changes in intervention-related pharmacy dollars paid, pharmacy dollars paid per patient per month (PPPM), and number of pharmacy claims were examined. This intervention identified providers whose patients were affected by underutilization, medication non-compliance, increased risk of adverse drug effects, and drug-drug interactions. To assess the impact of the intervention, pharmacy drug claims were reviewed from November 2007 through April 2008.

Clinical Criteria: Criteria, rationale, and text message(s) to providers are listed below. All physicians with at least one recipient "hitting" on criteria received letters.

- Underutilization

The underutilization of therapy indicator identifies patients with a history of CHD or CHD risk equivalents as determined by diagnoses, procedures or drug use, or with risk factors placing them at moderate to high risk for developing CHD.

Rationale: Clinical studies have shown the benefits of lipid lowering agents, particularly HMG-CoA reductase inhibitors, in patients with coronary heart disease, as well as patients with borderline cholesterol levels and no clinically evident disease. As stated above, there are large groups of patients who are either not treated or under treated.

Sample Provider Paragraph:

Potential underutilization of lipid lowering therapy (primary prevention): According to submitted diagnosis and/or pharmacy claim data, it appears that your patient has 2 or more risk factors (i.e., age, hypertension, smoking history) for CHD and is not receiving pharmacological lipid lowering therapy. According to the National Cholesterol Education Program (NCEP) guidelines, patients with a history of 2 or more risk factors should maintain LDL cholesterol \leq 130mg/dL. Please review your records to determine if a lipid panel has been checked recently (i.e., in the past year) and evaluate the potential need for lipid lowering therapy (diet and pharmacological).

- Medication Non-Compliance

Patients receiving lipid lowering therapy who received less than 60 days supply of the drug during a 90-day period of time.

Rationale: Compliance with prescribed maintenance drug regimens is paramount to successful patient outcomes. More than \$100 billion is spent yearly for problems related to noncompliance. Over half of written prescriptions are taken incorrectly.¹⁴

Sample Provider Paragraph:

Your patient may be non-compliant with the identified chronic antilipemic therapy. From prescription data, it appears that your patient received <60 days of maintenance therapy in a 90 day period. Please review this information to determine the best course of action for your patient.

¹⁴ Berg JS et al. Medication compliance: a healthcare problem. *Ann Pharmacother* 1993;27(supp19): S1-S24.



- Increased Risk of Adverse Drug Events

The increased risk of adverse drug event indicator identifies patients receiving nicotinic acid with a history of diabetes, gout or peptic ulcer disease, a HMG CoA inhibitor with a history of liver dysfunction, myopathy or current pregnancy, or fibrate with a history of hepatic or renal dysfunction, primary biliary cirrhosis or current pregnancy.

Rationale: Patients with potential drug-disease interactions are at an increased risk of having an adverse drug event.

Sample Provider Paragraph:

Increased risk of adverse effect: Niacin use in gout patients. According to submitted diagnosis and/or pharmacy claim data, it appears that your patient has gout and recently received niacin. Niacin can cause hyperuricemia which can worsen gout. Please consider if an alternative antilipemic agent is appropriate or monitor for signs and symptoms of hyperuricemia.

- Drug-Drug Interactions

This indicator identifies patients receiving a lipid lowering medication and concomitantly receiving an interacting drug.

Rationale: Patients with potential drug-drug interactions are at increased risk of having an adverse drug event. There may be coordination of care issues if more than one prescriber is involved.

Sample Provider Paragraph:

Lovastatin - Warfarin: Lovastatin may increase the hypoprothrombinemic effect of warfarin. Please consider an alternative or monitor the prothrombin time (PT) or international normalized ratio (INR) when the combination is prescribed, especially when changes in lovastatin therapy are made.

Definitions:

Adjusted Target Patients – All patients of physicians who were included in the intervention, who had pharmacy claims and were active plan members throughout the post-intervention time period. Additionally, when outcomes are performed, these patients' pre-intervention (baseline) hits are re-evaluated to make certain that the status of clinical indicators haven't changed for each patient due to late pharmacy and medical claims.

Intervention Related Drugs – Antilipemics, nefazodone, calcium channel blockers, danazol, macrolides, telithromycin, and azoles.

RESULTS

Characteristics

Table 1 describes the patient population included in the population-based intervention based upon mean age, gender, number of providers, average number of prescriptions per patient per month, and utilization of intervention-related drugs at baseline. As can be seen from the table, the target group was seeing 3.7 providers, receiving 6.7 prescriptions per month, and utilizing 1.5 intervention-related drugs during the baseline period.

Table 1: Patient Characteristics

	Target (N=1,112)
Mean Age	54.2
Percentage Male	38.1%
Percentage Female	61.9%
Number of Providers	3.7
Average Number of Prescriptions PPPM*	6.7
Utilization of Intervention-Related Drugs**	
Average Number of Drugs***	1.5
Average Number of Claims	6.4
Average Days Supply	189.3
Average Amount Paid	\$367.65

* Number of prescriptions per patient per month (PPPM) is the average for the 6 month baseline period

** Based on 6 months of baseline claims data

*** A distinct drug is defined by using a coding system similar to the Hierarchical Ingredient Code List (HICL) in that distinct drugs are identified at the ingredient level.

Underutilization

Table 2 exhibits the incidence of patients identified as underutilizing lipid lowering therapy and antilipemic therapy. Overall, a reduction in underutilization clinical indicators of 39.9% was achieved during the post-intervention period.

Table 2: Changes in Underutilization

Underutilization	Target		
	Baseline	Apr-08	% Change
Lipid lowering therapy [primary prevention]	517	342	-33.8%
Lipid lowering therapy [2nd prevention]	278	159	-42.8%
Antilipemic Therapy (primary prevention)	6	0	-100.0%
Antilipemic Therapy (secondary prevention)	33	0	-100.0%
Total	834	501	-39.9%



Medication Non-Compliance

Table 3 exhibits the changes in the number of patients identified as being non-compliant with their drug therapy. The intervention saw a sizable reduction in the antilipemics indicator. Overall, a reduction of 65.0% was achieved during the post-intervention period.

Table 3: Changes in Medication Non-Compliance

Medication Non-Compliance	Target		
	Baseline	Apr-08	% Change
Antilipemics	123	43	-65.0%
Total	123	43	-65.0%

Increased Risk of ADE

The changes in the number of patients flagged for being at an increased risk of adverse drug events are displayed in Table 4. Overall, there was a 48.1% reduction in the number of target patients.

Table 4: Changes in Risk of ADE

Increased Risk of ADE	Target		
	Baseline	Apr-08	% Change
Statin and Renal Insuff	45	23	-48.9%
Fibrate & Renal Dysfunction	17	11	-35.3%
HMG & Liver Dysfunction	12	5	-58.3%
HMG & Myopathy	2	1	-50.0%
Niacin & Hx Hepatic Impairment	2	1	-50.0%
Fibrates & Hepatic Dysfunction	1	0	-100.0%
Total	79	41	-48.1%

Drug-Drug Interactions

Table 5 exhibits the incidence of patients identified as being at risk for potential drug-drug interactions. Overall, a reduction in drug-drug interaction clinical indicators of 24.4% was achieved during the post-intervention period.

Table 5: Changes in Drug-Drug Interactions

Drug-Drug Interactions	Target		
	Baseline	Apr-08	% Change
HMG COA Reductase Inhibitors-CCB	63	50	-20.6%
Gemfibrozil-Warfarin	5	4	-20.0%
HMG-Fenofibrate, >1 MD	4	2	-50.0%
Fenofibrate-Warfarin	4	2	-50.0%
HMG-Macrolides	1	1	0.0%
HMG-Niacin, >1 MD	1	0	-100.0%
Total	78	59	-24.4%



BUSINESS ANALYSIS

The overall savings for the intervention is calculated in Table 6. Per patient per month (PPPM) drug amount paid for intervention-related drugs was calculated for the target group for the six-month baseline and six-month post-intervention periods. The post-period PPPM amount paid for the target group was subtracted from the baseline PPPM amount paid to obtain the estimated PPPM savings. The PPPM savings was then multiplied by the number of intervention months and number of target patients.

As a result of the intervention, the estimated per patient per month paid amount for intervention-related drugs decreased \$3.51 for the target group. This yields an overall estimated savings of \$23,432 in amount paid for intervention-related drugs during the six-month post-intervention period.

Table 6: Intervention-Related Drug Savings

Intervention-Related Drug Therapy	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	\$25.73
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	\$22.22
Estimated Savings Per Patient Per Month	\$3.51
Total Number of Targeted Patients	1,112
6-Month Total Savings	\$23,432.45



LIMITATIONS

A control group was not utilized for this intervention. This limited the comparisons that could be performed in the analysis. Therefore, instead of being able to compare an intervention group with a non-intervention group, the analysis is essentially limited to changes in the intervention group before and after intervention.

The time frame of 6 months may not capture the full extent of the impact of the intervention. Providers may be required some time before they can change their patient's drug regimens. Additionally, if this study included only users of chronic medications, this may have more accurately reflected the pharmacy cost changes in both groups.

CONCLUSIONS

This intervention focused on improving prescribing practices and reducing the overall cost of care. Overall, the intervention was successful in reducing the total number of clinical indicators for target patients by 42.2%.

In terms of financial outcomes, the amount paid for total drugs decreased \$5.04 in the post-intervention period. This yielded an overall estimated savings of \$23,432 in intervention-related drug expenditures during the six-month post-intervention period.