

Growth in Use of Lipid-lowering Therapies: Are We Targeting the Right Patients?

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Background: Prescription drug spending has been rising at >10% per year, with volume of use (rather than price) being the primary driver for that growth. Concern exists that industry marketing has led to increased use of medications by patients with marginal indications.

Objective: To determine whether the increase in the number of patients receiving lipid-lowering therapy represents a shift away from treatment of patients at highest cardiovascular (CV) risk towards patients in lower risk categories.

Study Design and Methods: Cardiovascular risk criteria adapted from guidelines were applied to an administrative database of medical and pharmaceutical claims for 1997 and 1999 that included managed care plan enrollees in 22 states. Patients were assigned to 1 of 7 categories representing CV risk based on documentation of CV disease/risk factors, with category 1 and 2 indicating the highest risk group (secondary prevention). The odds of the treated population being in the highest risk during 1997 versus 1999 were calculated, adjusting for age and sex.

Results: Patients treated with lipid medications in the study population increased from 5% in 1997 to 8% in 1999. During the same period, the percentage of treated patients in categories 1 through 6 rose from 17% to 21%. The odds of the treated population being in the highest risk group did not differ significantly between the 2 years (odds ratio (OR) = 0.99; 95% confidence interval, (CI) 0.96-1.01; $P = .40$).

Conclusions: Despite an increase in the percentage of patients receiving lipid-lowering therapy from 1997 to 1999, treatment rates rose modestly across all categories. Greater overall use did not appear to be associated with a shift in use towards patients with less CV risk.

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whether this increased use is among patients with the greatest medical need.

To explore this issue, we examined whether the increased use of lipid-lowering medication has occurred among high-risk individuals or whether the recent increase represents a shift toward treatment of low-risk patients. Although the results observed from 1 therapeutic area cannot be generalized to other areas, information about lipid treatment can begin to provide insights into this issue.

Lipid drugs represent 1 of the highest areas of drug spending in the United States, with \$12 billion spent on these therapies in 1999.⁵ In recently published work, Dubois et al,³ showed that an important factor contributing to this level of drug spending (and the rapid rate of increase over time) was an increase in the prevalence of treatment; 54% more patients used lipid-lowering drugs in 1997 versus 1995. In the current study, we explored whether growth in the number of prescriptions for lipid medications represented treatment of high- or low-risk patients as defined by documentation of cardiovascular (CV) disease or risk factors adapted from national cholesterol guidelines.

METHODS

Data Source and Patient Selection

A retrospective cohort of individuals with medical and pharmaceutical claims incurred during calendar years 1997 and 1999 was selected from approxi-

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Spending on prescription drugs has grown rapidly in the past few years. Annual prescription expenditures now exceed \$90 billion, with continued growth anticipated.^{1,2} Recent studies have examined the causes behind this growth and have shown that changes in volume exceeded changes in price as the key factor.³⁻⁵ As the volume of use of certain pharmaceuticals rises, a question of concern is

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mately 1.2 million continuously eligible annual covered lives in Protocare Sciences' managed care database. These data included managed care enrollees residing in 22 states, primarily in the Midwest and South. We considered for inclusion patients aged 25 years or older with health maintenance organization, preferred provider organization, administrative services only, or Medicare coverage who were fully eligible to receive medical and pharmacy benefits for either complete calendar year. Individuals with Medicare supplemental plans were disqualified because the data for this type of policy were incomplete. Eligibility in both years was not required. Patients contributing data to the study in 1999 may or may not have been the same as those who contributed data in 1997.

Patients needed to have pharmacy claims for a lipid-lowering medication to be included in the treated cohorts. To choose drugs for inclusion in the analysis, outpatient pharmacy claims containing National Drug Codes were grouped using a modified version of the Uniform Classification System into qualified therapeutic categories. Treated patients were required to have at least 1 claim for a medication in 1 of the following categories: HMG-CoA reductase inhibitors or statins (32130–32139), fibrates (32120–32125), bile acid sequestrants (32110, 32155), omega-3 fatty acid preparations (32140), and other lipoprotein reducers, niacin/nicotinic acid, and probucol (32150, 32151, and 32153, respectively). Relevant diagnoses were not required.

Classification and Analysis

The patient's CV risk was classified from evidence of documented CV disease or risk factors for each patient, using a hierarchical assignment based on presence of CV disease or risk factors adapted from the National Cholesterol Education Program (NCEP) Adult Treatment Panel III guidelines.⁶ The NCEP guidelines define 3 major categories of risk: 1) those with coronary heart disease (CHD) or CHD risk equivalent, 2) those with multiple CV risk factors, and 3) those with fewer than 2 risk factors. We expanded the 3 NCEP categories into 7 categories of lipid therapy use based on documentation of CV disease or risk factors adapted from the NCEP guidelines. We expanded the number of categories for several reasons. First, administrative claims data have inherent inaccuracies in labeling patients with a disease when they do not have the disease and in not labeling patients when in fact the disease is actually present. The diagnosis of myocardial infarction may have greater reliability of representing a patient with actual CV disease than a diagnosis of angina. Second, more subtle changes in use may be able to be detected over time when the analysis has more categories (ie, greater granularity).

We divided the NCEP's first category (patients with CHD, risk equivalent to CHD, and diabetes) into 3 categories. These categories included patients (1) who had experienced a specific event such as a myocardial infarction or revascularization (eg, coronary artery bypass graft surgery, coronary angioplasty), (2) with other manifestations of atherosclerotic

Table. Health Plan Populations With Documented Cardiovascular Disease or Risk Factors by Category

Category	1997	1999
Category 1: Patients who have had cardiac events and/or coronary interventional procedures	6908 (3%)	11 953 (4%)
Category 2: Patients with cardiovascular disease (eg, angina pectoris, cerebrovascular disease, peripheral vascular disease)	44 317 (20%)	65 086 (22%)
Category 3: Patients with diabetes	33 803 (15%)	44 858 (15%)
Category 4: Patients with 2 or more risk factors (ie, hypertension, tobacco use, obesity) or age risk factor* plus 1 risk factor	73 642 (33%)	103 462 (34%)
Category 5: Patients with 1 risk factor (ie, hypertension, tobacco use, obesity) or age risk factor*	57 438 (26%)	65 621 (22%)
Category 6: Patients with only hypercholesterolemia/ hyperlipidemia diagnosis	8772 (4%)	9367 (3%)
Total: All patients with evidence of documented cardiovascular risk factors or cardiovascular disease	224 880 (100%)	300 347 (100%)

Values are number (percentage).

*Men aged 45 years or older; women aged 55 years or older.

DRUG UTILIZATION

disease (eg, angina, peripheral vascular disease), and (3) with diabetes mellitus. We also grouped patients with multiple risk factors into a moderate-risk category. Patients with just a single risk factor (eg, hypertension, obesity, smoking, age >55 years in men or >65 years in women) and those treated for only hypercholesterolemia were assigned a lower risk primary prevention category. We assigned patients to a category based on the occurrence of relevant *International Classification of Diseases, 9th Revision* diagnoses and procedures, Current Procedural Terminology/Health Care Procedure Coding System procedures, or marker medications in the medical and pharmacy claims data.

Administrative data for each of the study years were evaluated separately for the purpose of this study. A flag indicating category was set for each patient based on the qualifying diagnoses, procedures, or medications. Age and sex criteria were also used for the assignment of categories 4 and 5. Patients who could not be assigned to any category (1-6, listed in **Table**) were assigned to category 7. In cases in which patients qualified for multiple categories, they were assigned to the lowest numbered (highest-risk) category. Because pretreatment cholesterol levels were not available for this population and the NCEP guidelines cannot be applied directly to administrative data, these factors alone were used for assignment in this analysis. Untreated patients with evidence of CV disease or risk factors (categories 1-6) were also identified to calculate treatment rates. Data were not subsequently collapsed to the 3 major NCEP categories. Because the ability of claims data to make such assignments varies by diagnosis, the authors thought that providing information for each of these categories would better inform the reader.

The initial descriptive analysis compared the distribution of patients on lipid therapy by risk category for the years 1997 and 1999. For the multivariate analysis of the treated population, category 1 and category 2 were combined to form a highest-risk (secondary prevention) category. Logistic regression analysis was used to model the odds of being in the highest-risk categories (categories 1 and 2) versus all other categories (categories 3-7), adjusting for age, sex, and year of the observation (1997 vs 1999). Because observations in 1997 and 1999 were clustered rather than independent, the generalized estimating equation method was used to calculate the parameter estimates to account for this dependency.

Study Population

There was a 1% decline in the total study population aged 25 years or older with continuous medical

and pharmacy benefit eligibility who had complete administrative claims data available for analysis (825 360 vs 814 031 for 1997 vs 1999). The proportion of patients with documented CV disease or risk factors increased from 27.2% in 1997 to 36.9% in 1999.

The Table shows the percent of members in the health plan population with documented CV disease and risk factors (categories 1-6) in 1997 and 1999 by risk category. Approximately one quarter of the patients had evidence of coronary or CV disease (categories 1 and 2).

RESULTS

Treatment Rates

Overall, the total population treated with lipid medications rose from 5% in 1997 to 8% in 1999, while patients with documentation of CV disease or risk factors on lipid medications rose from 17% to 21% during this time period (**Figure 1**). Analysis of treatment rates by CV risk category (not shown) indicated that the proportion of patients on lipid-lowering therapy who had cardiac events or vascular disease was 39% (category 1) and 24% (category 2) in 1997 (combined 26%). The corresponding lipid treatment rates for patients who had diabetes, multiple risk factors, only a single risk factor, or a diagnosis of hyperlipidemia (categories 3-6) ranged from 14% to 16% (combined 14%), less than half the lipid treatment rate for category 1. By 1999, while the treatment rates for those with cardiac events or vascular disease had increased to 43% (category 1) and 28% (category 2) (combined 30%), the rates for categories 3 through 6 continued to remain much lower, ranging from 17% to 20% (combined 18%).

Treated Population

While the number of patients in categories 1 to 6 climbed 34% (224 880 to 300 347) from 1997 to 1999, the number of treated patients rose 67% from 39 487 to 65 945. Among the treated population, 10 163 patients had observations in both 1997 and 1999, whereas 29 394 and 55 782 patients had only 1 observation in either 1997 or 1999, respectively.

In each of the study years, men and women comprised a fairly equal percentage of the treated population (50.6% vs 49.4% for men and women in 1997; 49.7% vs 50.3%, respectively, in 1999). The mean age of treated patients in the 1997 and 1999 populations was 60.9 and 63.0 years, respectively, whereas the mean age for the overall health plan populations was 48.4 and 51.5 years, respectively.

Although the treatment rates for diabetes, hypertension, and other risk factors were substantially lower compared with treatment rates for CV disease in both years of the study, the prevalence of these conditions among patients treated with lipid-lowering therapy was relatively high. **Figure 2** shows the distribution of CV risk categories among treated patients in 1997 and 1999. Despite the increase in the size of the treated population (which may be due at least partially to changes in the enrolled population), the percent distribution of patients by risk category was remarkably similar in 1997 and 1999. In each year, approximately 95% of all patients studied had some documented objective level of risk. Approximately one third had lipid-lowering therapy for coronary heart or atherosclerotic disease (categories 1 and 2). Most of the remainder had lipid-lowering therapy for other reasons. Of these, 14% had diabetes (category 3), and 26% to 27% had multiple risk factors (Category 4). Only one fifth had 1 identified risk factor. Approximately 6% had either documented hypercholesterolemia or no documented reason for treatment. Overall, about three quarters of patients were documented to have moderate to high risk (categories 1-4).

Confirming the impression from **Figure 1** that the distribution of categories among treated patients was similar between 1997 and 1999, the multivariate model indicated that the odds of the treated population being in the highest risk group (categories 1 and 2) compared with all other categories (categories 3-7) did not differ significantly between the 2 years (excluding patients with observations for both years, odds ratio [OR] = 0.99; 95% confidence interval [CI], 0.96-1.01; *P* = .40). Patients with observations for both study years were significantly more likely to be in the highest risk group in 1999 compared with 1997 (OR = 1.07; 95% CI, 1.01-1.12; *P* = .0002).

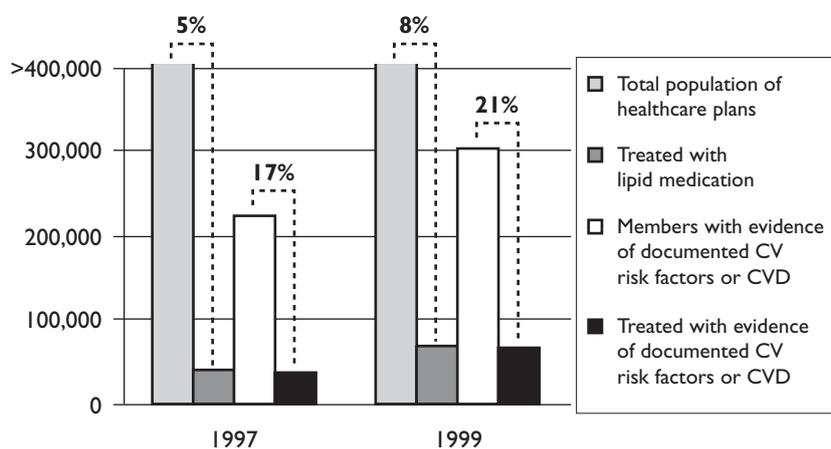
DISCUSSION

The patterns of use of lipid-lowering treatment during 1997 and 1999 observed in this

study suggested that use of this treatment was largely targeted at patients in the high-risk categories, and the use appeared to be consistent with evidence-based guidelines. Despite an increase in the number of treated patients, the distribution of risk categories among treated patients did not change during this period. To our knowledge, no prior study has applied specific criteria to evaluate growth in drug use.

Several limitations should be noted. The administrative database lacked the patients' pretreatment cholesterol values. However, the databases had information about diagnoses and relevant CV procedures. Where these databases had incomplete information, we may have missed evidence of CHD or its risk factors for selected patients, biasing the results toward lower apparent risk. It is possible that some of the patients with only hypercholesterolemia, hyperlipidemia, or no documented reason for therapy actually carried markers in claims outside the timeframe studied or in their nonelectronic medical records. Similarly, we did not know whether the treated patients in the lowest risk categories previously tried and failed other lipid-lowering measures (eg, diet and exercise.) An alternative bias would have occurred toward higher risk in the event of a coding error and the patient did not actually have the condition listed on the claim form.

Figure 1. Total Population of Health Plans, Numbers With Evidence of Documented Cardiovascular Disease or Risk Factors, and Numbers Treated in 1997 and 1999



Total population of health plans: in 1997, n = 825 360; in 1999, n = 814 031. Lipid treatment rates for total population and members with evidence of documented cardiovascular (CV) risk factors or cardiovascular disease (CVD) in 1997 and 1999 are also shown.

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Biases inherent in the data would probably exist in both 1997 and 1999, and thus should not greatly impact our results. Finally, the health plans' enrolled population itself appears to have changed during this period.

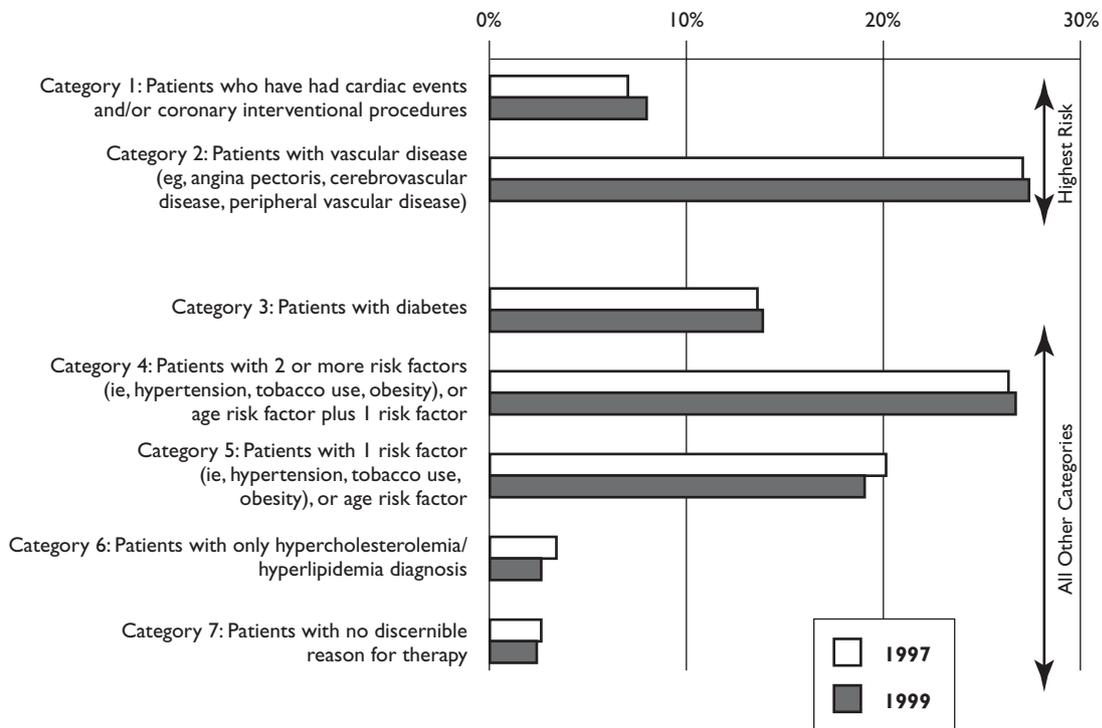
The primary focus of the study was to understand the CV risk profile of treated patients, not to determine the absolute number of patients meeting criteria for therapy. Further analyses to examine this and other relevant questions were suggested during the manuscript review process. These could not be addressed since we did not have current access to the dataset because of changes in data management procedures at Protocare Sciences (the transition to Health Insurance Portability and Accountability Act compliance required the elimination of noncompliant data).

The available data could not provide the impetus for the significant growth in treatment of hyperlipidemia during the study period. However, concurrent public and private efforts aimed at physicians and consumers were related to the increased diagnosis

and treatment of hyperlipidemia. Physician-directed initiatives have included pharmaceutical industry marketing, continuing medical education programs, and promotion of the NCEP guidelines. Consumer-directed initiatives have included direct-to-consumer advertisements sponsored by various pharmaceutical companies and patient education programs sponsored by many managed care organizations. Additionally, public health and managed care initiatives (eg, National Committee for Quality Assurance; Health Plan Employer Data and Information Set) have focused attention on heart disease and cholesterol screening. Magazines and newspapers regularly contain articles on these topics. Whatever the relative contribution of each of these efforts, the observed distribution of CV risk among the treated population remained similar between 1997 and 1999.

These efforts were largely motivated by evidence in the published medical literature that many patients who could benefit from therapy had not been receiving evidence-based standards of care.⁷⁻¹⁰

Figure 2. Distribution of Cardiovascular Risk Categories Among Lipid-Treated Patients in 1997 (n = 39 487) and 1999 (n = 65 945)



Patients with markers in multiple categories are assigned to the highest ranked (lowest-numbered) category.

A retrospective outpatient chart audit of 48 586 patients with CHD from 140 medical practices in the United States, for example, showed that only 44% had annual low-density lipoprotein (LDL) cholesterol testing, only 25% reached LDL cholesterol goal, and only 39% of patients were treated with lipid medications (which is similar to the treatment rates for CHD patients in our study).⁸ Another study quantified the treatment gap in patients hospitalized for coronary disease in the United States and found that only 24% had reached the LDL cholesterol level goal (ie, <100 mg/dL) by 6 months after discharge.⁷ Thus, both of these published reports showed that an inadequately treated pool of patients existed during the time of the current study. In a much smaller study (n = 544 for secondary prevention, n = 1080 for primary prevention), investigators at a single academic institution reported evidence of statin overuse.¹⁰ However, their reported treatment rates for CHD (27%) were lower than rates reported for the National Registry of Myocardial Infarction 3 study (31%, n = 138 001), in which the authors concluded that lipid levels were being significantly undertreated.⁹

Treated patients in our study consisted mainly of patients with evidence of CHD or with clinically related risk factors, among whom treatment with lipid-lowering medications may be potentially cost effective or perhaps even cost saving.¹¹⁻¹⁴ The increase in prescriptions for lipid medications observed in this study was consistent with national guidelines and societal goals for healthcare.

Whether the increase in treatment with other drug classes over time is similarly consistent with guidelines and healthcare priorities requires additional study. Whether these results can be generalized to other managed care settings also requires further study. We note, however, that despite the recent growth of the number of patients treated with lipid medications, a substantial proportion of patients continue to remain untreated or undertreated who could benefit from therapy as advocated by the national guidelines.⁶

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