Physician Extenders for Cost-Effective Management of Hypercholesterolemia

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OBJECTIVE: **Treatment of elevated cholesterol levels reduces morbidity and mortality from coronary heart disease in high-risk patients, but can be costly. The purpose of this study was to determine whether physician extenders emphasizing diet modification and, when necessary, effective and inexpensive drug algorithms can provide more cost-effective therapy than conventional care.**

DESIGN: **Randomized controlled trial.**

SETTING: **A Department of Veterans Affairs Medical Center.**

PATIENTS: **Two hundred forty-seven veterans with type IIa hypercholesterolemia.**

INTERVENTIONS: **Patients assigned to either a cholesterol treatment program (CTP) or usual health care provided by general internists (UHC). CTP included intensive dietary therapy administered by a registered dietitian utilizing individual and group counseling and drug therapy initiated by physician extenders for those failing to achieve goal low-density lipoprotein (LDL) levels with diet alone. A drug selection algorithm for CTP subjects utilized niacin as initial therapy followed by bile acid sequestrants and lovastatin. Subjects were followed prospectively for 2 years.**

MEASUREMENTS: **Primary outcome measurements were effectiveness of therapy defined as reductions in LDL cholesterol (LDL-C), and whether goal LDL-C levels were achieved; costs of therapy; and cost-effectiveness defined as the cost per unit reduction in the LDL-C.**

MAIN RESULTS: **Total program costs were higher for CTP patients than for UHC patients ($659 ± $43 vs $477 ± $42 per patient, $p < .001$). However, at 24 months the patients in CTP were more likely to achieve LDL goal levels (65% vs 44%, $p < .005$), and also achieved greater reductions in LDL-C 27% ± 2% vs 14% ± 2% at 24 months, $p < .001$). Program costs per unit (mmol/L) reduction in the LDL-C, a measure of cost-effectiveness, was significantly lower for CTP ($758 ± $58 vs $1,058 ± $70, $p = .002$).**

CONCLUSIONS: **Although more expensive than usual care, the greater effectiveness of physician extenders implementing cholesterol treatment algorithms resulted in more cost-effective therapy.**

KEY WORDS: **hypercholesterolemia; physician extenders; nicotinic acid; bile acid sequestrants; lovastatin.**
J GEN INTERN MED 1996;11:277–286.

Reduction of elevated serum cholesterol levels reduces morbidity and mortality from coronary heart disease.[1,2] Recent guidelines developed by the National Cholesterol Education Program (NCEP) encourage treatment of hypercholesterolemia to achieve specific low-density lipoprotein cholesterol (LDL-C) goals, which vary depending on cardiac risk status.[3] Approximately 13 million Americans are estimated to require cholesterol-lowering drug therapy, in addition to diet, to achieve these goals.[4]

Two difficult health care delivery issues arise from these recommendations. First, hypercholesterolemia management is expensive, particularly because of the high cost of drug therapy.[5] Second, cholesterol-lowering therapy may be particularly difficult for the clinician to administer, particularly when other patient concerns compete more acutely for attention. Not surprisingly, physician performance in identifying and treating hypercholesterolemia appears to lag behind current hypercholesterolemia guidelines.[6-9]

One approach to overcome barriers to hypercholesterolemia management is to use allied health professionals as "physician extenders" to initiate and maintain patients on diet and drug therapy. Physician extenders have been previously shown to be capable of effectively implementing diet and drug algorithms to treat hypercholesterolemia,[10,11] and may perform more effectively than physicians.[11,12] In addition, physician extenders may serve to reduce treatment costs and enhance effectiveness of therapy compared with usual care for several reasons. First, physician extenders are less costly health care providers than physicians. Second, these health providers can be taught to implement treatment algorithms emphasizing the most cost-effective components of therapy, such as diet and niacin therapy. Third, physician extenders, through more intensive patient education and counseling, may improve treatment response by increasing the proportion of patients successfully maintained on diet, niacin, and bile acid sequestrant therapy.

The purpose of this randomized controlled study was to determine whether a hypercholesterolemia management program utilizing physician extenders to implement cost-effective algorithms could provide effective hypercholesterolemia management while conserving costs.

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METHODS

Design

Subjects with hypercholesterolemia were recruited from the Veterans Affairs Medical Center (VAMC) in Milwaukee, Wisconsin, and randomized into two groups for hypercholesterolemia management: (1) a group receiving usual health care (UHC) provided by the general medical clinic at the VAMC, or (2) a group entered into a cholesterol treatment program (CTP). Subjects met frequently with the study coordinator to prospectively monitor the effectiveness and costs of therapy during the 24-month study period.

Subjects

Subjects were recruited from outpatient clinics at the Milwaukee VAMC. We invited 3,112 attendees of cardiology, dermatology, ophthalmology, orthopedics, urology, hypertension, and otolaryngology clinics to have a screening of cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C) levels performed. Among 2,412 agreeing to the screening, 782 veterans had LDL-C levels above 4.14 mmol/L (160 mg/dl) and were asked to return to further determine study eligibility. At this visit, persons with triglyceride levels above 2.82 mmol/L (250 mg/dl), thyroid, liver, or kidney abnormalities, severe underlying illness, or diabetes (taking antidiabetic medications or with a fasting glucose $\geq$140 mg/dl) were excluded from further evaluation. Patients taking lipid-lowering medications who were unwilling to stop treatment for 1 month prior to study entry were also excluded. For the 375 patients meeting these criteria, two further lipid profiles were obtained. If either coronary heart disease or two or more cardiac risk factors were present, subjects were eligible if the mean of these two LDL-C measurements was at least 3.75 mmol/L (145 mg/dl); subjects without coronary heart disease and with fewer than two risk factors required a mean LDL-C of at least 4.53 mmol/L (175 mg/dl) to be included in the study. Included in the study were 247 subjects who fulfilled these lipid criteria and signed informed consent.

Subjects were then randomized to either the UHC or CTP group by the study coordinator using a computer-generated list of random numbers. The study coordinator was blinded to the upcoming number in the list until the subject qualified for study participation and had signed informed consent.

Interventions

Within 6 weeks of randomization, subjects received appointments to attend the General Medical Clinic to receive usual health care (UHC) or a cholesterol treatment program (CTP). Participants randomized to UHC received an appointment with one of 12 general internists on the faculty at the Medical College of Wisconsin who became the UHC physician for this subject for the duration of the study. This clinic did not include medical residents or students and emphasized primary care delivery and provision of health care directly by the internist. At the initial visit, the UHC physician evaluated the patient and arranged diet or cholesterol-lowering drug therapy or both. The UHC physician would also manage other medical problems within the primary care operative in the clinic.

To provide training in hypercholesterolemia management for UHC physicians, educational sessions reviewed NCEP guidelines, and separate lectures concerning specific aspects of hypercholesterolemia management, frequently in the format of grand rounds, were also provided approximately five times per year. Lipid measurements obtained at evaluation visits for the purposes of the study (see below) were mailed to the subject's UHC physician and were also included in the patient's chart.

Subjects assigned to the CTP group were evaluated initially by the CTP physician (GS), and then introduced to CTP physician extenders, which included a nurse, clinical pharmacist, and a dietitian. At the initial visit, the patient began formal dietary instruction with the dietitian and was given a diet plan. The participant then began an intensive dietary program, which included individual diet counseling, small classes of five to eight per group encouraging group interaction, and behavioral techniques including keeping food records, positive feedback or reinforcement, and patient role modeling. This diet program generally consisted of one individual meeting with the dietitian followed by four group classes and was completed within the first 3 months of enrollment in the CTP. Other classes were offered throughout the duration of the program on a voluntary basis to provide further dietary reinforcement.

After 3 months the subject was evaluated for drug therapy. Participants failing to achieve LDL-C target levels (see Methods; Outcome Measurements) were evaluated by the nurse or clinical pharmacist or both under the supervision of the CTP physician. These subjects were prescribed medications to lower their cholesterol levels. The following algorithm served as a template for administration of drug therapy: niacin was utilized as initial therapy, followed by bile acid sequestrants (BAS), and then lovastatin if goal LDL-C levels were not achieved with previous medication. If the medication was well tolerated and effective (more than 10% reduction in LDL-C), then the medication was continued. If goal levels were not achieved, then either the dose of the medication was increased (to a maximum of 3,000 mg niacin, 30 g colestipol, and 40 mg lovastatin daily) or a second drug was added. If the drug was either not tolerated or ineffective, it was discontinued and the next drug in the algorithm was substituted. Gemfibrozil was utilized on occasion for patients whose triglyceride levels became elevated during the study and in whom niacin was either poorly tolerated or ineffective. Subjects were evaluated every 6 to 8 weeks until either goal levels were achieved or all LDL-C–lowering agents

had been initiated; subsequent visits were then scheduled at 6-month intervals.

Both niacin and colestipol were begun at low daily doses of 100 mg and 5 g, respectively, and gradually increased to 1.5 g and 20 g, respectively, over several weeks. Drug information sheets were dispensed providing education to minimize adverse side effects.[13]

During clinic hours, the CTP physician was available to evaluate unusual or acute medical problems and to assist in difficult decisions about hypercholesterolemia management not directed by the algorithm. Two thirds of all patient visits were attended exclusively by physician extenders rather than the CTP physician.

Data Collection

A study coordinator obtained lipid measurements, body weight, and demographic information and obtained informed consent for all participants before randomization. Evaluation visits were scheduled with each subject at 3 and 6 months following the initial CTP or UHC visit, and then at 6-month intervals for 24 months (total of five evaluation visits). At each evaluation visit, two fasting lipid measurements were obtained 1 week apart, and the average value was used for all analyses. Laboratory results to assess toxicity to cholesterol-lowering drugs were not obtained. At 6-month intervals, health care utilization was determined by chart audit to assess costs for the following items: physician and physician extender visits, dietary counseling, laboratory tests performed to monitor hypercholesterolemia management, pharmacy costs, and study-related hospitalizations and emergency department visits. At each evaluation visit, participants were also questioned about any medical care for hypercholesterolemia received outside the VAMC since the last visit. Evaluations were performed by the study coordinator and were not included in the analysis of study costs. Lipid measurements obtained in conjunction with the evaluation visit were also not included in the cost analysis.

Outcome Measurements

Effectiveness

Because the need for further cholesterol-lowering therapy when LDL-C levels closely approach NCEP-defined goal levels has not been clearly defined, data were analyzed using LDL-C target levels defined at 0.39 mmol/L (15 mg/dl) above the initial NCEP guidelines published in 1988,[14] except for subjects with preexisting coronary heart disease. Thus, goal LDL levels were set at 3.36 mmol/L (130 mg/dl) for patients with coronary heart disease, 3.75 mmol/L (145 mg/dl) for those with two or more heart disease risk factors, and 4.53 mmol/L (175 mg/dl) for those with fewer than two risk factors. In addition to assessing attainment of goal LDL-C, effectiveness of diet and drug therapy was determined by changes in LDL-C, HDL-C, and the LDL/HDL ratio compared with baseline. The LDL/HDL ratio was used as an outcome measure because it is more closely associated with coronary heart disease events than either LDL-C or HDL-C alone.[15,16]

Blood test results were obtained from patients who were fasting for at least 12 hours and total cholesterol, HDL-C, and triglyceride measurements were performed by the clinical chemistry laboratory at the Milwaukee VAMC using commercially available enzymatic methods.[17-19] Calibration of the cholesterol assay was referenced to the Abell-Kendall method and certified by standards received from the Centers for Disease Control. LDL-C was calculated using the Friedewald equation.[20]

Health Care Costs

Health care services provided by the Milwaukee VAMC and related to the treatment of hypercholesterolemia were identified from chart audit. Data were collected on the number of physician visits, physician extender visits, dietary counseling sessions, laboratory tests, medications, hospitalizations, and emergency department visits.

Average costs were derived for each service provided by the VAMC. Cost measures include administrative, overhead, staff, wholesale pharmacy, and supply costs. The average costs for each type of service were derived from the Veterans Affairs Cost Distribution Report (a detailed quarterly cost report that shows administrative, overhead, staffing, and other supply costs by service area for each VAMC). All costs were adjusted to 1992 dollars.

Costs for health care providers (e.g., physicians and physician extenders) at each visit were determined from the cost of the provider's time (calculated from the duration of the patient visit and the provider's salary, including fringe benefits) and the proportion of the visit devoted to hypercholesterolemia management, inclusive of overhead and administrative costs necessary to operate the clinic. Chart audits were used to estimate the proportion of the clinic visit devoted to hypercholesterolemia management, and the cost attributed to the clinic visit was weighted accordingly. Independent chart review by several nonstudy personnel agreed closely with estimates obtained from the initial chart audit. When sensitivity analyses were performed varying these estimates by 50%, study results and conclusions were not changed.

The costs for diet therapy were determined in a similar fashion. The actual time spent in individual and group dietary instruction was determined from chart audit. The cost of dietary instruction was valued at the dietitian's salary, inclusive of administrative and overhead costs for the service. For group instruction, the average cost per visit was divided by the number of subjects attending the group.

Pharmacy costs, estimated from wholesale drug costs, were obtained by multiplying the amount of cholesterol-lowering medication prescribed by the specific drug cost. Administrative overhead costs associated with prescription refills for cholesterol-lowering drug therapy were then added for each subject.

Laboratory costs were determined from the cost of the reagents and the technician time necessary to perform each assay, with adjustments for overhead and administrative costs and capital equipment depreciation. Because of the high volume of tests performed by the VAMC clinical laboratory and the use of highly automated equipment, the actual costs per assay were low relative to commercial laboratory charges.

Cost-effectiveness

Cost-effectiveness was evaluated by determining total program costs per unit (mmol/L) change in LDL-C and total program costs per unit change in the LDL/HDL ratio. However, to estimate recurring management costs once therapy has been initiated and optimal treatment decided, health costs incurred over the final 6 months (months 19–24) were used, rather than total program costs accrued over the entire 2 years' duration of the study. The primary cost-effectiveness measure was therefore the recurrent costs per unit reduction in LDL-C, determined by dividing the total costs of therapy for the 6-month period preceding the final lipid measurement (24 months) by the change, expressed in mmol/L, in LDL-C from the initial baseline value. The recurring cost per unit change in the LDL/HDL ratio was determined in similar fashion.

Statistical Methods

The primary comparison for all outcome measures was the difference between the CTP and UHC groups at the final 24-month evaluation visit. The unpaired t test was used to determine significant differences between groups. Differences in frequency distribution were tested with the χ^2 procedure. Because the multiple analyses conducted were not independent, no correction for multiple analyses was employed.[21] To determine whether adjustment for differences in baseline values affected study results, linear regression models utilizing LDL-C and costs per unit reduction in LDL-C as dependent variables were constructed entering the following independent variables: LDL-C and HDL-C, age, race, coronary heart disease, hypertension, and total number of cardiovascular risk factors.

Significant differences between groups were determined using a value of $p < .05$. All reported p values are two-sided. Investigators were blinded to the assigned patient group until after data analysis was completed.

RESULTS

Subject Characteristics at Randomization

From January 1990 to June 1992, 247 subjects were randomized into the two groups (120 CTP; 127 UHC). Baseline demographic variables, including age, gender, race, presence of hypertension and coronary heart disease, smoking status, and body mass index were equally distributed between the two groups (Table 1). During the 2-year follow-up period, 39 subjects did not complete the study. Subjects failing to complete the study were similar to those completing the study in age, race, presence of coronary heart disease, hypertension, smoking, body weight, alcohol intake, and lipid levels (not shown). Subjects who did not complete the study were included in the data analysis as of the last attended evaluation visit. Reasons for failing to complete the study included 8 deaths, 3 in the CTP (2 from cancer, 1 from myocardial infarction) and 5 in the UHC (1 from cancer, 2 from congestive heart failure, 1 from pulmonary embolus, and 1 from an unknown cause); 3 subjects withdrew because of moving to a different location (2 UHC); 7 withdrew because of severe concurrent illness (5 UHC); 11 withdrew owing to intercurrent personal problems such as illness of a family member or difficulties at work (5 UHC); and 10 for miscellaneous reasons (5 UHC).

Effectiveness of Treatment

The intensive diet program reduced LDL-C by 5% from baseline levels at 3 months and 18 CTP subjects (15%) achieved goal LDL levels with diet alone (Table 2). However, by the conclusion of the study, most patients initially successful with diet required drug therapy because their LDL-C levels eventually increased above goal levels. By 24 months, only 7% of CTP patients avoided drug therapy through adherence to diet therapy (Table 2). Among overweight subjects, there was no significant weight loss in either group.

In contrast to the CTP group, which did not use drug therapy during the 3-month diet phase, more than 34% of UHC subjects were prescribed lipid-lowering drug therapy at 3 months (Table 2). However, from 6 months until the conclusion of the study, significantly more CTP patients were on cholesterol-lowering drug therapy. At 24 months, 39% of UHC subjects were not receiving cholesterol-lowering drug therapy, and 24% of UHC patients did not receive cholesterol-lowering therapy at any time during the study.

Table 1. Baseline Characteristics of the Study Sample*

Baseline Characteristics	Usual Health Care (n = 120)	Cholesterol Treatment Program (n = 127)
Mean age	63 ± 9	63 ± 10
Race (% white)	78	87
Coronary disease (%)'	26	31
Hypertension (%)	61	66
Risk factors	2.6 ± 0.9	2.5 ± 0.9
LDL cholesterol (mmol/L)	4.66 ± 0.59	4.57 ± 0.57
HDL cholesterol (mmol/L)	1.07 ± 0.27	1.10 ± 0.31
Triglycerides (mmol/L)	2.04 ± .076	1.90 ± 0.76

**No differences between groups were statistically significant p = .05. Data are presented as means ± SD.*

Table 2. Effect of the Cholesterol Treatment Program on Lipid and Lipoprotein Levels, Utilization of Drug Therapy, and the Achievement of Goal LDL Levels

Variables	Months of Follow-Up					
	0	3	6	12	18	24
N (CTP/UHC)*	120/127	115/119	113/117	108/114	108/113	103/105
Total cholesterol (mmol/L)						
CTP	6.67 ± 0.05	6.44 ± 0.05†	6.13 ± 0.08	5.56 ± 0.08‡	5.59 ± 0.08	5.25 ± 0.08‡
UHC	6.54 ± 0.05	6.15 ± 0.08	6.08 ± 0.08	5.95 ± 0.08	5.84 ± 0.08	5.72 ± 0.10
Triglycerides (mmol/L)						
CTP	2.04 ± 0.07	2.09 ± 0.09†	1.80 ± 0.08	1.59 ± 0.07	1.62 ± 0.01	1.47 ± 0.08
UHC	1.90 ± 0.07	1.77 ± 0.07	1.79 ± 0.08	1.69 ± 0.08	1.68 ± 0.08	1.58 ± 0.08
HDL cholesterol (mmol/L)						
CTP	1.07 ± 0.02	1.04 ± 0.02	1.14 ± 0.03	1.18 ± 0.03	1.18 ± 0.04	1.16 ± 0.04
UHC	1.10 ± 0.03	1.11 ± 0.03	1.12 ± 0.03	1.14 ± 0.03	1.14 ± 0.04	1.10 ± 0.03
LDL cholesterol (mmol/L)						
CTP	4.65 ± 0.05	4.42 ± 0.05§	4.16 ± 0.05	3.65 ± 0.08†	3.67 ± 0.08*	3.41 ± 0.05‡
UHC	4.58 ± 0.05	4.24 ± 0.05	4.14 ± 0.05	4.01 ± 0.05	3.93 ± 0.08	3.88 ± 0.08
LDL/HDL ratio						
CTP	4.6 ± 0.1	4.5 ± 0.1*	3.9 ± 0.1	3.4 ± 0.1*	3.4 ± 0.1*	3.3 ± 0.1†
UHC	4.4 ± 0.1	4.1 ± 0.1	4.0 ± 0.1	3.8 ± 0.1	3.8 ± 0.1	3.9 ± 0.1
Use of drug therapy (%)‖						
CTP	0	3†	66†	82*	85†	93†
UHC	0	34	44	54	54	61
Achieved LDL goal (%)						
CTP	0	15	21	48§	54	65†
UHC	0	23	26	36	45	44

**CTP indicates cholesterol treatment program; UHC, usual health care. Standard are errors provided with mean values.*
†$p < .01$, *CTP vs UHC.*
‡$p < .005$, *CTP vs UHC.*
§$p < .05$, *CTP vs UHC.*
‖*Drug therapy is defined as prescribed use of niacin, sequestrants, lovastatin, or gemfibrozil.*

LDL-C levels were higher in the CTP group at the 3-month evaluation visit (4.42 ± 0.05 vs 4.24 ± 0.05 mmol/L, $p = .03$). However, at 6 months, LDL-C levels were similar, and from 12 months to the end of the study the CTP group was prescribed more lipid-lowering drug therapy and achieved lower LDL-C levels than the UHC group (Table 2). By 24 months, the CTP group had significantly reduced LDL-C from baseline by 27% ± 2% compared with 14% ± 2% in the UHC group ($p < .001$). Differences in LDL-C between groups were not attenuated after adjustment for differences in baseline variables including LDL-C and HDL-C, age, race, number of cardiovascular risk factors, and prevalence of coronary heart disease and hypertension. A similar pattern of improvement was noted in the LDL/HDL ratio. At the conclusion of the study, goal LDL levels were achieved more frequently by subjects assigned to the CTP group (65% vs 44%, $p = .002$). CTP subjects showed no improvement in either triglyceride or HDL-C levels compared with UHC subjects.

Utilization of Cholesterol-Lowering Drug Therapy

The distribution of drug use is shown in Table 3. Over three quarters of CTP patients were treated with niacin, usually as initial therapy. Bile acid sequestrants and lovastatin, the second- and third-line drugs of the treatment algorithm, were used with decreasing frequency in the CTP. UHC physicians used niacin, BAS, and lovastatin relatively equally and prescribed them as initial agents with similar frequency. Niacin and BAS utilization was much higher in CTP than in UHC patients, while gemfibrozil was used rarely by either group.

Despite extensive efforts among CTP personnel to improve adherence and tolerance to drug therapy, among CTP subjects, drug maintenance rates for niacin and BAS were 56% and 42%, respectively, and not significantly different from those obtained in the UHC group. On the other hand, the lovastatin drug maintenance rates were greater than 90% for both groups, and at study conclusion more patients were taking lovastatin than any other agent. At the final evaluation visit, niacin and BAS use, but not lovastatin use (47% vs 35%, $p = .10$, χ^2), was significantly higher among CTP patients than among UHC patients.

Among CTP patients, maintenance of niacin therapy spared the use of further and more expensive cholesterol-lowering drug therapy, as only 49% of those taking niacin at the final evaluation visit were also taking BAS, lovastatin, or gemfibrozil, compared with 88% of those not taking niacin who were prescribed these drugs ($p < .001$). In

Table 3. Characteristics of Cholesterol-Lowering Drug Use

	Niacin	Sequestrants	Lovastatin	Gemfibrozil
Initiated during study (% of subjects)				
CTP	77*	54*	43	11
UHC	28	29	34	13
Prescribed as initial agent (% of subjects treated with drug therapy)				
CTP	74*	13†	8†	5
UHC	34	29	25	13
Used at final evaluation visit (% of subjects)‡				
CTP	46*	25†	47	8
UHC	22	11	35	6
Drug maintenance rate‡§				
CTP	56	42	96	62
UHC	72	34	93	35

*$p < .001$.
†$p < .01$.
‡*Includes only subjects appearing at final evaluation visit.*
§*Among patients begun on drug, the proportion maintained on therapy at final evaluation visit.*

contrast, the proportion of UHC patients using the more expensive cholesterol-lowering agents was similar regardless of whether or not the patient was successfully maintained on niacin at the study conclusion (50% vs 57%, $p = .6$; data not shown).

Substantial practice variation was noted among 12 UHC physicians (mean 6.2 ± 3.0 patients per physician), as the proportion of patients treated with drug therapy varied from 46% to 81%, the proportion treated with niacin ranged from 8% to 56%, and achieving goal LDL-C levels varied from 15% to 56%.

Costs of Cholesterol-Lowering Care

Costs of therapy for the CTP and UHC groups are shown in Table 4. Although total costs for the UHC group were relatively constant over the 2-year study period, costs for the CTP group increased from $129 ± $7 for the first 6-month period to $181 ± $13 by the final 6-month period. Most of this increase in cost was due to progressively larger expenditures for drug therapy. Although costs of drugs accounted for only 29% of total costs for the CTP during the initial 6-month period when diet and niacin were initiated, by the final 6-month evaluation pharmacy expenses for drug therapy were responsible for 79% of total costs. During the final study period (19–24 months), costs for the CTP group were significantly higher than costs for the UHC group for each of the following categories: health provider services, pharmacy, and laboratory monitoring. Most of the higher costs observed for the CTP group during this period were due to increased use of drug therapy.

Most pharmacy costs during the last 6 months of the study were due to lovastatin, which accounted for 55% of total pharmacy costs in the CTP group and for 69% in the UHC group. Sequestrants were the second most costly drug, accounting for 19% and 11% of total pharmacy costs for the CTP and UHC groups, respectively. Of the total pharmacy costs, only 12% and 7% were attributable to niacin use in the CTP and UHC groups, respectively.

Cost-effectiveness

The CTP was significantly more cost-effective than UHC when evaluated by either measure of cost-effectiveness, the cost per unit reduction in LDL-C ($758 ± $58 vs $1,085 ± $70 per mmol/L reduction in LDL-C, $p < .005$) or the cost per unit change in the LDL/HDL ratio ($420 ± $11 vs $452 ± $10 per unit change in the LDL/HDL ratio, $p < .05$). These significant differences persisted following adjustment for baseline variables including LDL-C, HDL-C, age, race, number of cardiovascular risk factors, and prevalence of hypertension and coronary heart disease. The CTP was also more cost-effective when costs incurred only during the final 6-month evaluation period (months 19–24) were analyzed ($304 ± $44 vs $578 ± $75 per unit reduction in LDL-C, $p = .001$).

To assess effectiveness, costs, and cost-effectiveness among subjects selected to receive cholesterol-lowering drug therapy, separate analyses were performed. Among subjects receiving drug therapy, CTP participants had greater LDL-C reductions at 24 months (27% ± 2% vs 19% ± 2%, $p = .003$). Despite the greater reductions in LDL-C achieved, drug costs and overall program costs were similar (drug costs for 19–24 months; CTP $160 ± $12 vs UHC $144 ± $16, $p = .4$; total drug costs; CTP $444 ± $33 vs UHC $511 ± $50, $p = .27$; total program costs; CTP $733 ± $44 vs UHC $734 ± $57, $p = .9$). Among these subjects, the CTP remained more cost-effective than UHC (total program costs per unit LDL-C reduction; CTP $764 ± $59 vs UHC $1,040 ± $77, $p = .02$).

Table 4. Effect of the Cholesterol Treatment Program on Mean Costs per Patient for Each 6-Month Treatment Period (in 1992 dollars)*

	Study Periods (Months)				
	0–6	7–12	13–18	19–24	Entire Study
Total costs ($)					
CTP	129 ± 7	170 ± 24†	179 ± 18‡	181 ± 13§	659 ± 43‡
UHC	139 ± 11	107 ± 11	119 ± 12	112 ± 12	477 ± 42
Itemized costs ($)					
Health provider services					
CTP	46.9 ± 1.6	40.1 ± 1.8§	33.9 ± 1.8§	29.4 ± 1.9§	150.3 ± 4.6§
UHC	47.4 ± 1.9	21.7 ± 1.6	20.4 ± 1.8	15.5 ± 1.4	105.0 ± 4.7
Diet					
CTP	36.1 ± 1.1§	0.8 ± 0.3§	0.7 ± 0.4‡	0.3 ± 0.2	37.9 ± 1.3§
UHC	14.8 ± 1.1	4.4 ± 0.6	2.7 ± 0.5	1.2 ± 0.4	23.1 ± 1.9
Pharmacy					
CTP	37 ± 5‡	96 ± 10	120 ± 11†	143 ± 12§	396 ± 31
UHC	67 ± 10	78 ± 10	91 ± 11	92 ± 12	327 ± 38
Laboratory					
CTP	6.3 ± 0.5	9.2 ± 0.5§	8.3 ± 0.5§	8.4 ± 0.6§	32.1 ± 1.4§
UHC	6.5 ± 0.5	3.6 ± 0.4	3.5 ± 0.4	2.9 ± 0.3	16.5 ± 1.1
Adverse events					
CTP	2.7 ± 1.9	23.5 ± 20.1	15.9 ± 14.6	0.0 ± 0.0	42.0 ± 25.4§
UHC	3.8 ± 2.2	0.0 ± 0.0	1.3 ± 1.3	0.0 ± 0.0	5.0 ± 2.5

**Values are average costs ± SE.*
†$p < .05$, *CTP vs UHC.*
‡$p < .01$, *CTP vs UHC.*
§$p < .005$, *CTP vs UHC.*

Toxicity Related to Cholesterol-Lowering Drug Therapy

Significant adverse events requiring either emergency or urgent care visits occurred in six CTP subjects and in four UHC subjects. Emergency department visits among CTP patients were for glycosuria while taking niacin (one patient), rash while taking niacin (three patients), and gout while taking niacin (two patients). Among UHC patients, emergency department visits were for a rash secondary to gemfibrozil, a rash secondary to niacin, dizziness while taking lovastatin, and abdominal pain thought to be secondary to lovastatin.

Hospital admissions were required in two CTP patients. One patient taking niacin and nonsteroidal anti-inflammatory drugs had gastrointestinal bleeding requiring a 6-day hospitalization. The other patient developed anaphylaxis shortly after taking niacin, requiring a 2-day hospital admission. The average cost per patient of these events is shown in Table 4.

Cardiac Events

Cardiac events, defined as emergency department visits for angina, cardiac catheterizations, coronary bypass surgery, or angioplasty, or any combination of these, occurred in 12 CTP patients (10%) and 16 UHC patients (13%). This difference between groups was not significant.

DISCUSSION

This study evaluated effectiveness and costs of a multidisciplinary team of allied health professionals operating under the direction of a physician to manage hypercholesterolemia. The physician extender–based cholesterol treatment program was more effective than usual health care in reducing LDL-C, improving the LDL/HDL ratio, and achieving LDL-C goals. In addition, this program reduced the cost per unit reduction in LDL-C, and was therefore more cost-effective. However, despite efforts to reduce costs through implementation of effective yet relatively inexpensive therapies, such as diet and niacin, the total cost for the physician extender–based program was 40% greater than standard care.

Findings from this study are consistent with those of other studies evaluating the effectiveness of physician extenders in treating hypercholesterolemia. In an uncontrolled study treating military personnel with hypercholesterolemia, physician extenders reduced total cholesterol by 25% through implementation of a diet and drug algorithm.[10] In a retrospective chart audit conducted in a VAMC, physician extenders achieved LDL-C goals in 44% of patients, compared with only 11% of matched controls treated in a general medical clinic. Costs were not evaluated in this study, and clinicians administering "usual health care" were not provided with education concerning the use of cholesterol-lowering therapy to achieve defined

goals.[12] Debusk and coworkers randomized patients following myocardial infarction to either usual care provided in a large HMO or to a physician extender–operated cardiac rehabilitation program that included aggressive dyslipidemia management. The physician extenders achieved a 19% greater reduction in LDL-C compared with usual care.[11] Our findings are consistent with these results and confirm that physician extenders, through implementation of effective diet and drug treatment algorithms, can provide better hypercholesterolemia management than general internists practicing in the general medical clinic.

One of the most important differences between physician extender–based and physician–based hypercholesterolemia management systems appears to be that physician extenders treat more patients and utilize greater amounts of cholesterol-lowering therapy. In our study, 93% of CTP patients but only 61% of UHC patients were treated with cholesterol-lowering therapy, similar to results reported previously.[11,12] Undertreatment of hypercholesterolemia by physicians has been well recognized.[22-24] In our study, this failure of UHC physicians to treat many hypercholesterolemic patients occurred despite the provision of seminars to review NCEP guidelines treatment and the mailing of all lipid results obtained during evaluation visits to each UHC physician to serve as treatment reminders. We conclude that physician education and simple reminder systems are likely to be insufficient to optimize cholesterol-lowering therapy administered by physicians. On the other hand, these measures may have been partially successful because the treatment rate for hypercholesterolemic UHC patients was improved relative to routine care reported in other settings.[6,12]

To reduce reliance on more expensive and less cost-effective therapeutic strategies, physician extenders implemented algorithms emphasizing the use of diet and niacin, rather than BAS and lovastatin. Despite extensive dietary instruction including behavior modification techniques to promote healthful eating habits, diet therapy reduced LDL-C only 5%, sparing less than 10% of patients from further drug therapy. This response is consistent with that in other studies evaluating the role of diet therapy in hypercholesterolemia,[25,26] and it suggests that even an intensive dietary program may have only a minor role in lipid disorder management compared with drug therapy. Although we did not formally compare the intensive diet program with the routine diet referral, similar LDL-C reductions may have occurred using this simpler and less costly approach.

Niacin, an agent with beneficial effects similar to those of lovastatin on the LDL/HDL ratio,[27,28] was the initial drug used in 77% of CTP patients. Among CTP patients successfully maintained on niacin, significantly fewer required treatment with other more expensive agents, and their drug treatment costs were reduced (data not shown). Because more than half of the CTP patients were able to tolerate niacin for the duration of the study, niacin remained an important therapeutic agent contributing to the greater effectiveness and enhanced cost-effectiveness of the CTP.

However, despite extensive efforts to alleviate niacin-induced side effects by the CTP, the CTP drug maintenance rate was no better than that achieved by UHC and similar to that reported in the HMO setting.[29] Therefore, reliance on physician extenders to provide counseling and education about niacin did not improve patient tolerance. Identification of alternative strategies to improve patient adherence to niacin therapy will be necessary to further extend the usefulness of this effective and inexpensive agent. Until such strategies are identified, use of niacin routinely as an initial agent to treat more severe LDL-C elevations may not be necessarily more cost-effective than use of a statin.[30]

Because implementation of the physician extender–based program, although cost-effective compared with usual care, was not cost-saving, we estimated the impact that this degree of cholesterol lowering might have on reduction of specific cardiovascular events. The Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT) randomized 3,806 nondiabetic, nonhypertensive middle-aged subjects to receive either diet and cholestyramine or diet and placebo for an average of 7.4 years. Diet and cholestyramine reduced LDL-C by 12% compared with diet and placebo,[31] a decrease very similar to the results in our study. In the LRCCPPT, coronary heart disease mortality and nonfatal myocardial infarction were reduced by 19%, the incidence of angina or a positive exercise stress test decreased by 20% and 25%, respectively, and the need for coronary artery bypass grafting was lowered by 21%. Assuming similar event rates in our study, treatment of 1,000 individuals for 7 years would save 4 men from coronary heart disease death, 15 men from nonfatal myocardial infarction, 49 men from a positive exercise stress test, 27 men from developing anginal symptoms, and 10 men from coronary artery bypass surgery. To treat 1,000 patients for 7.4 years, we estimate that the incremental cost burden of the cholesterol treatment program compared with usual health care would be $927,200. Patients enrolled in our study, similar to many patient populations treated elsewhere in the ambulatory clinic setting, were older and had more cardiovascular risk factors than LRCCPPT subjects, and would be predicted to have a higher coronary heart disease incidence rate than that of LRCCPPT subjects. Therefore, the number of patients likely to benefit from cholesterol treatment assignment compared with usual care would be higher than suggested by LRCCPPT data. These anticipated reductions in cardiovascular disease complications, and related improvements in quality of life, should help to offset the increased cost burden imposed by physician extender–based programs utilizing aggressive cholesterol-lowering measures.

Several limitations of this study deserve mention. First, the study was conducted at a VAMC and primarily included men over age 50. Therefore, our results may not

be fully generalizable to younger men or to women. However, neither age nor gender significantly affects response to cholesterol-lowering drugs,[32] and therefore treatment programs employing allied health professionals to administer cost-effective therapy would appear to have utility in other populations. Second, the economic analysis for this study was performed from a VAMC perspective. Therefore, the cost estimates used do not reflect hospital charges, which may be considerably higher, especially if obtained from non-Department of Veterans Affairs institutions. Although the absolute costs would be different if the cost analysis were done in other settings, it is likely that the relative dollar amounts allocated between the UHC and the CTP groups would be similar, and that the costs for a physician extender–based program would be greater than those for usual care regardless of the treatment setting. Therefore, our conclusions that the CTP is more costly and more effective than usual health care should persist independent of treatment setting. On the other hand, conclusions regarding relative cost-effectiveness (i.e., cost relative to LDL-C reductions) between programs will depend on absolute costs for health provider services, drugs, and laboratory tests, which may vary widely in different practice settings. Our cost-effectiveness data should be generalizable to similar patient populations treated in Department of Veterans Affairs hospitals, but will require confirmation in other settings.

Our findings suggest that, in addition to being more effective, and potentially more cost-effective, physician extender–based programs are also likely to be more costly. Therefore, risk factor reduction to decrease morbidity and mortality from coronary heart disease will most likely entail an increased short-term cost burden to reduce long-term and potentially expensive coronary heart disease events. Recognition that increased fiscal resources are required for prevention, even when model cost-effective programs are implemented, may contribute to better planning and allocation of resources in the future.

The authors thank the study coordinator, Ms. Leslie Voigt, for her untiring efforts and meticulous attention to detail, which ensured the successful completion of this project.

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