The Lipid Treatment Assessment Project (L-TAP)

A Multicenter Survey to Evaluate the Percentages of Dyslipidemic Patients Receiving Lipid-Lowering Therapy and Achieving Low-Density Lipoprotein Cholesterol Goals

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Objective: To determine the percentage of patients in the multicenter Lipid Treatment Assessment Project receiving lipid-lowering therapy who are achieving low-density lipoprotein cholesterol (LDL-C) goals as defined by National Cholesterol Education Program (NCEP) guidelines.

Methods: Adult patients with dyslipidemia, who had been receiving the same lipid-lowering therapy for at least 3 months, were assessed at investigation sites. Lipid levels were determined once in each patient at the time of enrollment. The primary end point was the success rate, defined as the proportion of patients who achieved their LDL-C target level as specified by NCEP guidelines.

Results: A total of 4888 patients from 5 regions of the United States were studied. Of these, 23% had fewer than 2 risk factors for coronary heart disease (CHD) and no evidence of CHD (low-risk group), 47% had 2 or more risk factors and no evidence of CHD (high-risk group), and 30% had established CHD. Overall, only 38% of patients achieved NCEP-specified LDL-C target levels; success rates were 68% among low-risk patients, 37% among high-risk patents, and 18% among patients with CHD. Drug therapy was significantly ($P \leq .001$) more effective than nondrug therapy in all patient risk groups. However, many patients treated with lipid-lowering drugs did not achieve LDL-C target levels.

Conclusions: Large proportions of dyslipidemic patients receiving lipid-lowering therapy are not achieving NCEP LDL-C target levels. These findings indicate that more aggressive treatment of dyslipidemia is needed to attain goals established by NCEP guidelines.

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C LINICAL AND epidemiological studies clearly establish the link between dyslipidemia and coronary heart disease (CHD).[1-13] On the basis of this compelling evidence, the National Cholesterol Education Program (NCEP) issued treatment guidelines in 1988 that identified low-density lipoprotein cholesterol (LDL-C) as a causative factor for CHD and as the target for lipid-lowering therapy.[5] These guidelines were updated in 1993[6] and 1997.[7] The NCEP guidelines emphasize that CHD risk determines the type and intensity of lipid-lowering therapy. The guidelines further define the LDL-C levels at which diet and drug therapy should be initiated for each of 3 groups: low risk (<2 risk factors, no CHD), high risk (≥2 risk factors, no CHD), and CHD.

Relatively little is known about the extent to which physicians actually follow NCEP guidelines and the extent to which their patients are able to reach LDL-C target levels. However, available data indicate that a significant gap exists between NCEP guidelines and clinical practices. The Heart and Estrogen/Progestin Replacement Study enrolled 2763 postmenopausal women with CHD, of whom 96% were candidates for lipid-lowering therapy.[14] Notably, only 47% of eligible participants took lipid-lowering drugs. Furthermore, 63% of patients did not achieve their 1988 NCEP LDL-C target level of 3.36 mmol/L (130 mg/dL), and 91% of patients had LDL-C levels that exceeded the current NCEP LDL-C target (≤2.59 mmol/L [≤100 mg/dL]). One Veterans Affairs Medical Center study showed that only 50% of 244 consecutive patients with CHD or peripheral vascular disease, who were being treated for hypercholesterolemia with diet and drug therapy, achieved LDL-C target levels of less than 3.36 mmol/L (130 mg/dL).[15] In another Veterans Affairs Medical Center study, only 30 (33%) of 90 patients achieved NCEP LDL-C target levels with hydroxymethyl glutaryl coenzyme A reductase inhibitor (statin) mono-

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PATIENTS AND METHODS

STUDY DESIGN

The L-TAP survey targeted primary care physicians who regularly treat patients with dyslipidemia. Prescription trends for lipid-lowering drugs (obtained with permission from IMS Health, Westport, Conn) were used to identify physicians who were in the top tertile of frequent prescribers by number of prescriptions for lipid-lowering medications. Invitations to participate in the L-TAP survey were sent to 25 312 primary care physicians who were frequent prescribers of lipid-lowering therapy.

Participating physicians completed a survey at the time of enrollment. The survey included questions regarding their demographic status, professional characteristics, and practice profile. Selected questions to assess awareness of NCEP guidelines and the LDL-C levels at which they start therapy were based on the 1995 Cholesterol Awareness Survey, administered to 1583 randomly selected physicians in the United States by the National Heart, Lung, and Blood Institute (NHLBI). The NHLBI survey was designed to ascertain whether physicians were aware of NCEP guidelines and used them in clinical practice.

The Institutional Review Board, Inc (San Clemente, Calif) approved the protocol and procedures for informed consent. All patients who participated in this study provided written informed consent before enrollment.

PATIENT ENROLLMENT

Dyslipidemic patients aged 20 to 75 years who were being treated with the same dietary therapy and/or lipid-lowering drug therapy for at least 3 months were eligible for inclusion. Patients who had had a major trauma, recent surgery that required anesthesia, or myocardial infarction within the 12 weeks before enrollment consideration were ineligible, as were those who had an acute infection that required current antibiotic therapy or who had had a recent or abrupt change in their usual diet within the preceding month. Women who were pregnant, breast-feeding, or 6 months or less post partum were also ineligible.

Each investigator enrolled consecutive dyslipidemic patients who satisfied the inclusion and exclusion criteria. For patients who met the eligibility criteria, the participating physician was instructed to interview the patient and to review the patient's medical record to obtain information specified on a case report form. This included age; sex; regional status; estrogen replacement (for women); height; weight; race or ethnicity; level of education; risk factors, including smoking, alcohol consumption, and history of CHD or atherosclerotic disease (defined by the clinical diagnosis of angina, myocardial infarction, transient ischemic attack, stroke, peripheral vascular disease, or revascularization); family history of coronary heart disease before 55 years of age in male first-degree relatives or before 65 years of age in female first-degree relatives, hypertension, and diabetes; and conditions affecting lipid levels (hypothyroidism, nephrotic syndrome, or liver disease). Whether the patient was given detailed exercise counseling and whether the patient had been counseled by a registered dietitian were also recorded. A detailed history of current lipid-lowering drugs and their doses was also collected.

Blood was collected by venipuncture into a specimen tube after the patient had been seated for approximately 10 minutes and had been fasting for at least 8 hours. The blood sample was allowed to clot at room temperature for 1 hour, and was then centrifuged for 20 minutes at 1000g. The tube was placed in the refrigerator and shipped in a special Styrofoam container with a cold pack via overnight delivery to the Lipid Laboratory at the Mary Bassett Research Institute (Cooperstown, NY) for lipid determinations. This laboratory is a participant in the Lipid Standardization Program of the Centers for Disease Control and Prevention; accuracy (±3%) and precision (±3%) are validated through Centers for Disease Control and Prevention challenge samples.

therapy.[16] Furthermore, in a study of 16 primary care practices in Upstate New York, only 9% of hypercholesterolemic patients (total cholesterol level, >6.21 mmol/L [>240 mg/dL] or 5.17-6.21 mmol/L [200-240 mg/dL] with ≥2 risk factors) attained an LDL-C level less than 3.36 mmol/L (130 mg/dL).[17] Of note, maximal doses of monotherapy or combination therapies, which included statins plus niacin or bile acid sequestrants, were used infrequently. While these studies suggest that patients with dyslipidemia are not achieving LDL-C target levels and indicate that more aggressive treatment and more effective therapies are needed, they focus on single types of patients (eg, those with CHD) from single centers and do not generally describe the scope of the problem in the United States.

The large-scale Lipid Treatment Assessment Project (L-TAP) was initiated in 1996 to ascertain whether patients in primary care settings with recognized dyslipidemia were achieving NCEP LDL-C target levels with their lipid-lowering therapies. The L-TAP survey collected data on patient and physician demographics, current lipid levels, CHD risk factors, lipid-lowering treatments, and physicians' awareness of and compliance with NCEP guidelines to determine the proportion of patients achieving NCEP LDL-C target levels, and to identify factors that predict patient success for reaching these targets.

RESULTS

PATIENT POPULATION

A total of 902 investigators agreed to participate in the L-TAP study; 896 completed surveys concerning their awareness of cholesterol lowering and risk of CHD. Overall, 5601 patients in primary care were enrolled by 619 investigators from August 1, 1996, to February 28, 1997.

A total of 4888 (87.3%) of the 5601 patients enrolled were included in the statistical evaluation. Data for the remaining 713 patients (12.7%) were deigned nonevaluable for 1 or more of the following reasons: 553 patients (9.9%) did not have current LDL-C levels available, 105 (1.9%) did not meet inclusion or exclusion criteria, and 73 patients (1.3%) did not have a fasting blood

On arrival, the serum was analyzed for total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglycerides by routine enzymatic methods on a random-access automated analyzer (MIRA; Roche Diagnostics Corporation Laboratory Systems, Indianapolis, Ind), using cholesterol reagents and calibrators from Sigma Diagnostics (St Louis, Mo).[18,19] The HDL-C level was determined after precipitation of apolipoprotein B–containing lipoproteins, with the use of dextran sulfate–magnesium chloride with a molecular weight of 50 000 (Sigma Diagnostics).[20] The LDL-C level was calculated according to the Friedewald equation.[21] If triglyceride levels were greater than 10.34 mmol/L (400 mg/dL), LDL-C level was not calculated.

STATISTICAL ANALYSIS

The primary study outcome measure was success rate, which was the proportion of patients with evaluable data taking lipid-lowering therapy who achieved their LDL-C target levels as defined by NCEP guidelines. Patients were classified into NCEP risk groups by summing the number of their risk factors. Possible risk factors included age ($\geq$45 years for men, $\geq$55 years or premature menopause without estrogen replacement therapy for women); family history of premature CHD (definite myocardial infarction or sudden death before 55 years of age in male first-degree relatives or before 65 years of age in female first-degree relatives), current cigarette smoking, hypertension (blood pressure $\geq$140/90 mm Hg or an antihypertensive medication), low HDL-C level ($<$0.91 mmol/L [$<$35 mg/dL]), and diabetes mellitus. A "negative" risk factor, which allows subtracting 1 from the number of risk factors, was an HDL-C level of 1.55 mmol/L (60 mg/dL) or more.[6] The low-risk group included patients without CHD who had fewer than 2 risk factors (LDL-C target level was $<$4.14 mmol/L [$<$160 mg/dL]). The high-risk group included patients without CHD who had 2 or more risk factors (LDL-C target level was $<$3.36 mmol/L [$<$130 mg/dL]). The CHD group included all patients with a previous heart attack, bypass surgery, or angioplasty (LDL-C target level was $\leq$2.59 mmol/L [$\leq$100 mg/dL]). The Pearson χ^2 test was used to determine whether the success rates were different between these risk groups.

Descriptive statistics for each variable by risk group were developed. As an initial step, data for each categorical variable were fitted into a $3 \times 2 \times$ level-factor framework, where 3 represents the 3 risk groups, 2 represents the outcome measure of success or failure, and *level* indicates the number of evaluation categories defined for the variable. In accordance with usual practice, the success rate for each group was analyzed separately. Univariate analyses were used to establish whether each individual variable was associated with the outcome measure of success or failure. The Pearson χ^2 test was applied to all categorical or discrete variables. These test results were supplemented by odds ratios and their 95% confidence intervals. In some cases, cells were combined where there were no or few patients, or where combining facilitated interpretation after an initial examination.

Univariate analyses were also used to assess whether each variable was associated with the outcome measure of success or failure. The Pearson χ^2 test was applied to all categorical variables and supplemented by odds ratios and their 95% confidence intervals. The success and failure rates were further compared for each physician characteristic by specialty and by risk group.

A multivariate analysis, consisting of a logistic regression, was performed with the use of all variables with a univariate $P<.30$ to determine which variables contributed to success or failure. In addition, the initial formulation included terms for risk-group interactions with these variables. Items with the highest P values were sequentially removed and a new logistic model was defined without the eliminated variable. This operation was continued until all remaining variables had P values less than .05. The adequacy of the derived equation was indicated by assessing deviance (D), Hosmer-Lemeshow goodness-of-fit test,[22] and Brier score.[23]

sample drawn. All results presented are those from patients with evaluable data.

PATIENT DEMOGRAPHICS

The average age of the 4888 patients with evaluable data (50% male, 50% female) was 60.4 years (**Table 1**). Of these patients, 90% were white, 5% were African American, 2% were Hispanic, 2% were Asian, and 1% were members of other races (Table 1).

Patients were classified into 3 groups according to the number of recorded CHD risk factors, or by the presence of established CHD. Of the 4888 patients, 1143 (23.4%) had fewer than 2 risk factors and no evidence of CHD and were, therefore, placed in the low-risk group (**Table 2**); 2285 patients (46.7%) had 2 or more risk factors and no evidence of CHD and were placed in the high-risk group; 1460 patients (29.9%) had had a heart attack, bypass surgery, or angioplasty (established CHD). Age of 45 years or more for men or greater than 55 years for women (85%) and hypertension (55%) were the most commonly reported risk factors. Diabetes mellitus was reported in 23

(2%) low-risk, 479 (21%) high-risk, and 344 (24%) CHD patients. High HDL-C was found in 284 low-risk patients (24.8%), but in few high-risk and CHD patients, 83 (4%) and 92 (6%), respectively. The majority of patients in each group (93%, low-risk group; 94%, high-risk group; and 94%, CHD group) received counseling about the importance of diet, exercise, and weight reduction. However, overall, the majority (80%) of patients did not receive counseling from a registered dietitian.

INVESTIGATOR DEMOGRAPHICS AND CHOLESTEROL AWARENESS

Of the 619 investigators who enrolled patients, 7 (1.1%) enrolled only patients with nonevaluable data and 6 (1.0%) did not complete an investigator's survey. The demographics of the remaining 606 investigators are summarized in **Table 3**. With respect to cholesterol awareness, investigators indicated that they initiated diet therapy in male patients aged 40 to 60 years without evidence of cardiovascular disease or diabetes; the investigators initiated drug therapy at a mean LDL-C level of 3.23 ± 0.54

Table 1. Demographics of Patients With Evaluable Data*

Variable	Low-Risk (n = 1143)	High-Risk (n = 2285)	CHD (n = 1460)	Total (N = 4888)
Age, mean (SD), y	54.6 (12.3)	61.2 (9.5)	63.8 (8.4)	60.4 (10.5)
Sex, No. (%)				
Male	450 (39.4)	1070 (46.8)	943 (64.6)	**2463** (50.4)
≥45 y	280 (24.5)	1005 (44.0)	912 (62.5)	**2197** (44.9)
<45 y	170 (14.9)	65 (2.8)	31 (2.1)	**266** (5.4)
Female	693 (60.6)	1215 (53.2)	517 (35.4)	**2425** (49.6)
≥55 y	376 (32.9)	1046 (45.8)	460 (31.5)	**1882** (38.5)
<55 y	317 (27.7)	169 (7.4)	57 (3.9)	**543** (11.1)
Race, No. (%)				
White	1028 (89.9)	2034 (89.0)	1347 (92.3)	**4409** (90.2)
African American	52 (4.5)	140 (6.1)	64 (4.4)	**256** (5.2)
Hispanic	32 (2.8)	55 (2.4)	24 (1.6)	**111** (2.3)
Asian	21 (1.8)	35 (1.5)	15 (1.0)	**71** (1.5)
Other†	10 (0.9)	21 (0.9)	10 (0.7)	**41** (0.8)

*Low-risk patients had 0 or 1 risk factor and no evidence of coronary heart disease (CHD); high-risk patients had 2 or more factors and no evidence of CHD, CHD patients had established CHD.
†Native Americans, Alaska Natives, and patients of other races are included.

Table 2. Risk Factors Among Patient Groups*

Risk Factors	Low-Risk (n = 1143)	High-Risk (n = 2285)	CHD (n = 1460)	Total (N = 4888)
No. of risk factors				
≤1	1143 (100)	0	235 (16.1)	**1378** (28.2)
2	0	1214 (53.1)	474 (32.5)	**1688** (34.5)
3	0	802 (35.1)	478 (32.7)	**1280** (26.2)
4	0	210 (9.2)	223 (15.3)	**433** (8.9)
5	0	54 (2.4)	45 (3.1)	**99** (2.0)
6	0	5 (0.2)	5 (0.3)	**10** (0.2)
Positive risk factors				
Age (men, ≥45 y; women, ≥55 y)	676 (59.1)	2110 (92.3)	1390 (95.2)	**4176** (85.4)
Family history	167 (14.6)	927 (40.6)	671 (46.0)	**1765** (36.1)
Current smoking	64 (5.6)	441 (19.3)	188 (12.9)	**693** (14.2)
Hypertension	179 (15.7)	1608 (70.4)	914 (62.6)	**2701** (55.3)
Low HDL-C level	29 (2.5)	492 (21.5)	326 (22.3)	**847** (17.3)
Diabetes	23 (2.0)	479 (21.0)	344 (23.6)	**846** (17.3)
Negative risk factor				
High HDL-C level	284 (24.8)	83 (3.6)	92 (6.3)	**459** (9.4)

*Low-risk patients had 0 or 1 risk factor and no evidence of coronary heart disease (CHD); high-risk patients had 2 or more factors and no evidence of CHD; CHD patients had established CHD. Data are presented as the number of patients in each group who had the indicated number of risk factors or who had the indicated risk factor, with the percentage of patients indicated in parentheses. HDL-C indicates high-density lipoprotein cholesterol.

mmol/L (125 ± 21mg/dL). These responses are consistent with those given by the 1583 physicians who completed the 1995 NHLBI survey (B. Schucker, MA, unpublished data, December 1995).

According to the investigators who enrolled patients with evaluable data in the present survey, 3.47 ± 0.44 mmol/L (134 ± 17 mg/dL) is the desirable LDL-C level for adults without CHD, and 2.74 ± 0.39 mmol/L (106 ± 15 mg/dL) is the optimal level for adults with CHD. Of the 606 respondents, 384 (63.4%) thought that cholesterol lowering has a great effect on reducing the risk of future CHD and 218 (36.0%) thought it has a moderate effect. The vast majority (95%) of investigators indicated an awareness of guidelines that classify cholesterol levels, with 63% responding that they follow the guidelines "quite a bit," 31% responding that they follow them "somewhat," and 2% responding that they followed NCEP guidelines "not very much." Therefore, a similar proportion of investigators in both the L-TAP and NHLBI surveys are aware of and practice NCEP guidelines, suggesting that the patterns of L-TAP investigators may present patterns of US primary care physicians in general.

ACHIEVING TARGET LDL-C LEVELS

Of the 4888 patients with evaluable data, only 38.4% (1878) achieved their LDL-C target levels (**Figure 1**). The success rate was the highest among the low-risk group (68%), followed by patients in the high-risk group (37%). The success rate was the lowest among patients with CHD (18%) (*P*<.001 for differences between groups). Mean LDL-C levels in patients who achieved success were 3.34, 2.82, and 2.25 mmol/L (129, 109, and 87 mg/dL) for the low-risk, high-risk, and CHD groups, respectively. Mean LDL-C levels in patients who failed were 4.86, 4.22, and 3.62 mmol/L (188, 163, and 140 mg/dL) in the low-

Table 3. L-TAP Investigator Demographics Summary*

Variable	Investigators, No. (%)
Sex (N = 606)	
M	548 (90.4)
F	58 (9.6)
Specialty (N = 606)	
Family practice	254 (41.9)
General practice	31 (5.1)
Internal medicine	306 (50.5)
Other	15 (2.5)
Board certified (N = 606)	
Yes	498 (82.2)
No	108 (17.8)
Main practice (N = 606)	
Office-based	601 (99.2)
Hospital-based	5 (0.8)
Age, y (n = 605)	47.1 (9.1)†
Years practicing medicine (N = 606)	17.2 (9.2)†
No. of patients per week (N = 606)	123.8 (69.7)†

*Investigator enrolled at least one patient with evaluable data and may have enrolled patients without evaluable data. Of 619 investigators who enrolled patients, seven investigators enrolled only patients with nonevaluable data and six other investigators did not complete the survey. L-TAP indicates Lipid Treatment Assessment Project.
†Mean (SD).

Figure 1. *Percentage of patients with evaluable data achieving low-density lipoprotein cholesterol (LDL-C) target by risk group. CHD indicates coronary heart disease. Mean LDL-C levels for patients successfully achieving target and for patients not achieving target are represented by lines and the right axis. Percentage of patients achieving LDL-C targets are represented by the left axis. Target LDL-C levels were less than 4.14 mmol/L (160 mg/dL) for the low-risk group, less than 3.36 mmol/L (130 mg/dL) for the high-risk group, and 2.59 mmol/L (100 mg/dL) or less for the CHD group.*

risk, high-risk, and CHD groups, respectively, with substantial proportions of patients remaining above the threshold for initiation of therapy (eg, ≥3.36 mmol/L [≥130 mg/dL] for patients with CHD).

ACHIEVING TARGET LDL-C LEVELS BY DEMOGRAPHICS

The overall success rate of patients reaching NCEP targets in primary care was 37% among male patients and 39% among female patients. Male sex was significantly related to a successful outcome for the high-risk (P<.001) and CHD (P = .02) groups, but not for the low-risk group (P = .07).

White and Hispanic patients had similar overall success rates: 39% and 40%, respectively (**Figure 2**). The success rate among African American patients was 29%. The remaining races had too few patients for comparison. Race was significantly associated with the success rate for the patients in the low-risk and CHD groups (P = .006 and P = .03, respectively), but not in the high-risk group (P = .30).

The success rate was influenced by the patient's level of education in the CHD group (P = .02) but not in the low-risk or high-risk groups. Overall, patients with a college degree or higher had a 44% success rate, patients with some college or technical school education had a 40% success rate, high school graduates had a 37% success rate, and patients who completed some high school or less had a 32% success rate. The success rate for achieving target LDL-C levels was independent of the patient's height, weight, place of residence, and whether the patient had medical insurance.

RISK FACTORS AND TARGET LDL-C LEVELS

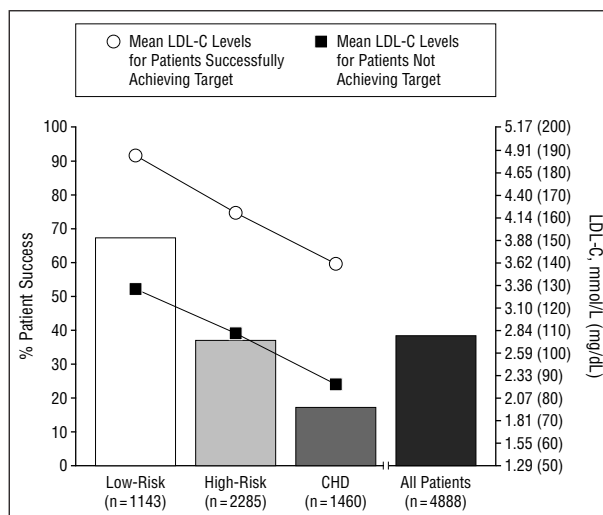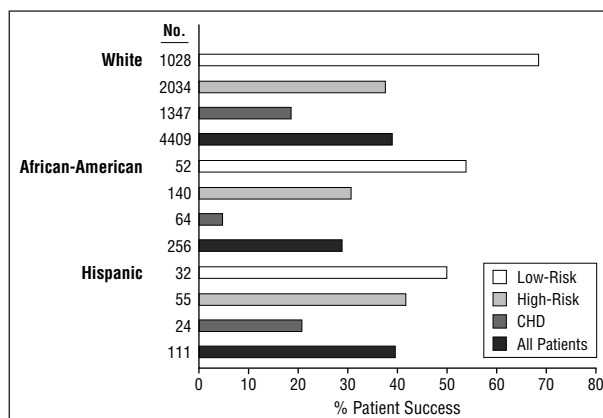The number of risk factors did not significantly affect the success rates among patients in the low-risk and CHD

Figure 2. *Effect of race on the proportion of patients achieving target low-density lipoprotein cholesterol (LDL-C) levels. CHD indicates coronary heart disease; see Figure 1 for target LDL-C levels. Low-risk group, P = .006; high-risk group, P = .30; and CHD group, P = .03, univariate analysis comparing success rates among white, African American, and Hispanic patients in each risk group.*

groups. However, the number of risk factors was directly and significantly (P<.001) related to a successful outcome among high-risk patients. Among high-risk patients with 2 risk factors, the success rate was 33%, which was lower than that among patients with 3 risk factors (40%), 4 risk factors (45%), 5 risk factors (50%), and 6 risk factors (60%).

A univariate analysis evaluated the relationship between CHD risk factors and patients' success at achieving LDL-C target levels. Age group (≤39, 40-49, 50-59, 60-69, ≥70 years) was not significantly related to a successful outcome for any of the 3 risk groups. Patients in the high-risk group with either diabetes (41%) or hypertension (39%) were significantly (P = .04 and P = .005, respectively) more likely to achieve target LDL-C levels than patients with diseases (36% and 33%, respectively).

Patients receiving insulin or an oral antidiabetic agent were more likely to be at target LDL-C levels, whereas the success rate for diabetic patients being treated with diet alone was comparable with that of the nondiabetic patients. There were no differences between diabetic and nondiabetic patients or between hypertensive and non-hypertensive patients in the low-risk and CHD groups. Patients with a family history of CHD had a success rate that was not significantly different from that of patients without a family history of CHD. In all 3 risk groups, patients who currently or formerly smoked had success rates comparable with those of patients who had never smoked.

LIPID-LOWERING THERAPY AND TARGET LDL-C LEVELS

A total of 4137 patients (84.6%) received treatment with lipid-lowering drugs. The remaining 751 patients (15.4%) received nondrug lipid-lowering therapy. The
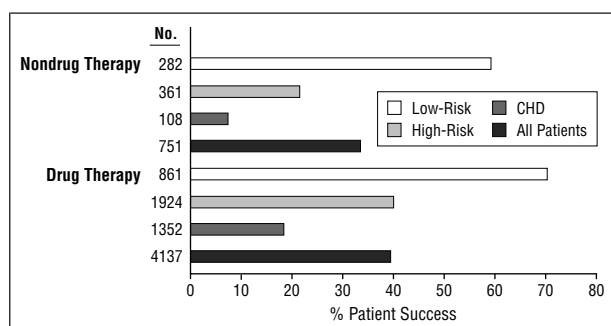

Figure 3. *Effect of treatment on the proportion of patients achieving target low-density lipoprotein cholesterol (LDL-C) levels: nondrug vs drug therapy. CHD indicates coronary heart disease; see Figure 1 for target LDL-C levels. Low-risk group, P = .001; high-risk group, P<.001; and CHD group, P = .004, univariate analysis comparing success rates among patients receiving lipid-lowering drug therapy and those who did not receive drug therapy.*

proportion of patients in the drug and nondrug groups who achieved target LDL-C levels was 39% and 34%, respectively (**Figure 3**). Drug therapy was significantly ($P<.004$) more effective than nondrug therapy overall and in each risk group. However, compliance with diet still contributed to LDL-C lowering and remained a significant predictor of success in the multivariate analysis.

The relationship between the type of lipid-lowering drug therapy and a successful patient outcome was also investigated (**Figure 4**). Of the patients who received statins as their only drug therapy, 40% achieved LDL-C target levels; the success rates were 32% for fluvastatin, 36% for lovastatin, 39% for pravastatin, and 46% for simvastatin ($P<.001$). Overall, compared with patients receiving statin therapy, far fewer were receiving other classes of lipid-lowering drugs as monotherapy. The success rates for patients receiving monotherapy were 32% for those taking gemfibrozil, 43% for patients taking bile acid sequestrants, 39% for patients taking niacin, and 28% for patients taking psyllium fiber. Only 500 patients (10.2% of total) received combination drug therapies, including 434 patients treated with a combination that included at least 1 statin plus another lipid-lowering drug, as well as 66 patients treated with a combination of lipid-lowering drugs that did not include a statin; the success rate for the 500 patients was 40%.

Among patients receiving lipid-lowering monotherapy, the type of drug significantly affected outcome in the low-risk ($P<.001$) and high-risk ($P = .02$) groups. These patients were significantly more likely to achieve a successful outcome if they were treated with any statin than if treated with drug therapy that did not include a statin. In the CHD group, the type of drug therapy did not affect outcome; the success rate for statin treatment was 18%.
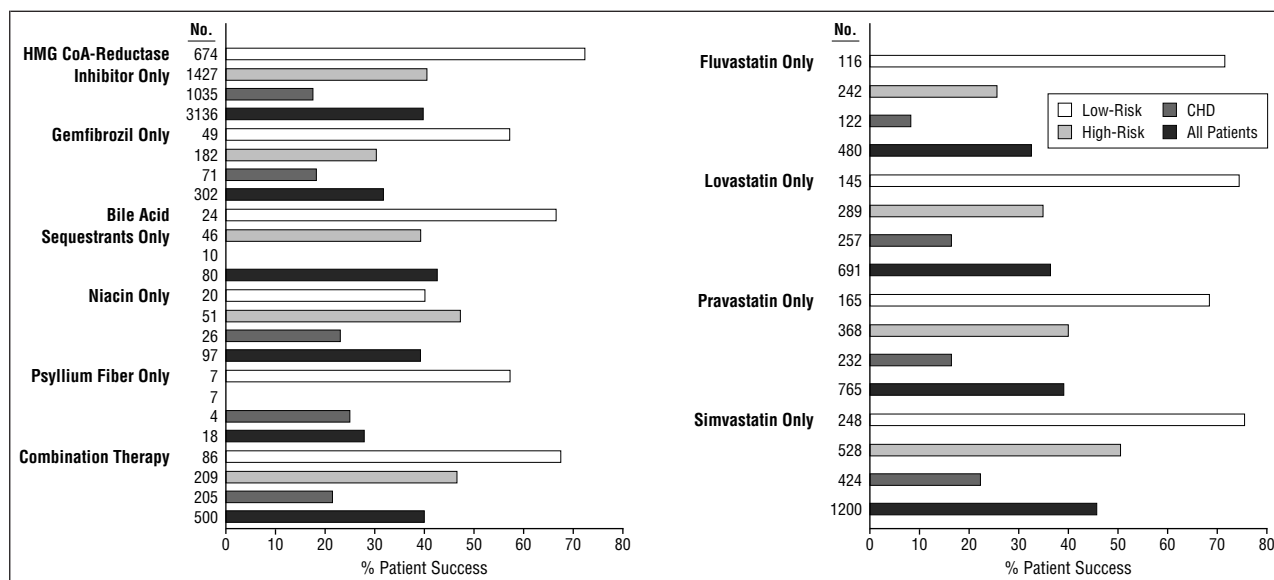

Figure 4. *Effect of treatment on the proportion of patients achieving target low-density lipoprotein cholesterol (LDL-C) levels. CHD indicates coronary heart disease; see Figure 1 for target LDL-C levels. Left, Hydroxymethyl glutaryl coenzyme A (HMG-CoA) reductase inhibitors, gemfibrozil, bile acid sequestrants, niacin, psyllium fiber, and combination therapies. Low-risk group, P<.001; high-risk group, P = .02; and CHD group, P = .62, univariate analysis comparing success rates among patients receiving any HMG-CoA reductase inhibitor drug therapy and those receiving other types of lipid-lowering drug therapy. Right, Fluvastatin, lovastatin, pravastatin, and simvastatin.*

PHYSICIAN DEMOGRAPHICS AND PATIENT SUCCESS RATE

The success rate of patients achieving NCEP LDL-C target levels was not affected by physician demographics. Therefore, the success rate was comparable for male and female physicians; for those in family practice, general practice, or internal medicine; and for those who were board certified.

MULTIVARIATE ANALYSIS

Logistic regression indicated that several demographic and clinical variables were significantly related to patient outcome (**Table 4**). The following variables were significantly related to achieving LDL-C target levels: risk group ($P<.001$); sex and menopausal status ($P<.001$); race ($P = .002$); instruction to reduce serum cholesterol level ($P = .002$); and diabetes ($P = .009$). In addition, there was a significant interaction between risk group and dietary compliance ($P = .001$) and between risk group and statin vs nonstatin vs nondrug therapy ($P = .03$). Dietary compliance influenced success in the low-risk CHD groups, but not in the high-risk groups. The choice of therapy influenced success differently in the low-risk group compared with the high-risk and CHD groups. The average Brier score for all 3 risk groups was 0.20, which indicates a satisfactory fit of the logistic equation. Furthermore, the Hosmer-Lemeshow χ^2 was not statistically significant ($P = .91$), which indicates that the final model is a good fit of the data.

COMMENT

The NCEP guidelines, first issued in 1988[5] and subsequently revised in 1993,[6] define LDL-C target levels for patients with dyslipidemia to reduce the risk of continued or future CHD. The updated 1997 NCEP guidelines reaffirm these target levels based on the results of the landmark studies.[7] For patients in the low-risk group (no evidence of CHD and <2 risk factors), the LDL-C target level is less than 4.14 mmol/L (160 mg/dL). In the present survey, 68% of low-risk group patients achieved LDL-C target levels, with a mean LDL-C level of 3.34 mmol/L (129 mg/dL). Although the majority of patients in this group reached LDL-C target levels, one third (32%; mean LDL-C level, 4.86 mmol/L [188 mg/dL]) failed. For high-risk group patients (no evidence of CHD and ≥2 risk factors), the LDL-C target level is less than 3.36 mmol/L (130 mg/dL). Even fewer patients in the high-risk group (37%; mean LDL-C level, 2.82 mmol/L [109 mg/dL]) reached the LDL-C target than in the low-risk group. The mean LDL-C value for the 63% of high-risk patients who failed to reach target was 4.19 mmol/L (162 mg/dL). Finally, the results of this survey indicate that patients with established CHD—patients whose risk of future CHD events is highest and whose NCEP-recommended LDL-C target level is 2.59 mmol/L (100 mg/dL) or less—have the lowest success rate. Only 18% of the patients with CHD achieved their LDL-C target levels (mean LDL-C level, 2.25 mmol/L [87 mg/dL]), while 83% (mean LDL-C level, 3.62 mmol/L [140 mg/dL]) failed. These results clearly

Table 4. Multivariate Analysis Variables Significantly Affecting Patient Success Rate at $P<.05$

Variable	*P* Main Effect	Interaction With Risk Group*
Risk group	<.001	. . .
Sex or menopausal status	<.001	NS
Race	.002	NS
Treatment with any statin vs nonstatin vs nondrug therapy	<.001	.03
Compliance with dietary therapy	<.001	.001
Instructed to reduce cholesterol level	.002	NS
Diabetes	.009	NS

*Ellipses indicate not applicable; NS, no significant interaction with risk group.

demonstrate that a large proportion of dyslipidemic patients across all risk groups are not achieving NCEP-recommended levels of LDL-C, with the proportion of patients who fail being highest in the group of patients at greatest risk of future CHD events.

To some extent, the reason for the lower rates of success in reaching LDL-C goals in the high-risk and CHD groups is their lower LDL-C goals, namely, less than 3.36 mmol/L (130 mg/dL) and less than 2.59 mmol/L (100 mg/dL), respectively. Therefore, the LDL-C levels were examined relative to the groups' respective goals. In fact, LDL-C levels were well above the recommended target levels in patients who did not achieve NCEP goals. The mean LDL-C level of patients who failed in the low-risk group was 4.86 mmol/L (188 mg/dL), which was 0.72 mmol/L (28 mg/dL) higher than the target level. More importantly, mean levels for patients who failed in the high-risk and CHD groups were 0.83 mmol/L (32 mg/dL) and 1.03 mmol/L (40 mg/dL) higher than the respective target levels. These results indicate that substantial numbers of patients who failed were far from their LDL-C target levels. In fact, the majority of patients failing to reach LDL-C goals had levels that exceeded the threshold for initiation of drug therapy.

The results of the L-TAP survey demonstrate that the lipid management available at the time of this survey (1996) was not used optimally. This may be due to a number of reasons, including use of low dosages of drugs, limited drug effectiveness, inappropriate choice of drug, other drug limitations (eg, tolerability), and noncompliance of patients with recommended treatment. In this survey, there was little difference between the success rates for patients judged by the investigator to be compliant and rates for patients considered noncompliant with various lipid-lowering nondrug and drug treatments (data not shown). Although compliance was not quantified by pill count or prescription tracking, it is unlikely that poor patient compliance accounted for the high proportion of dyslipidemic patients whose LDL-C levels were above NCEP target levels. Rather, the results of the present survey suggest that patients are not receiving adequate lipid-lowering treatment or the lipid-lowering treatments themselves are not adequate. This is supported by the observation in L-TAP that high doses

of lipid-lowering drugs were seldom used. Therefore, a more aggressive approach to cholesterol and, specifically, LDL-C reduction is required.

This survey targeted physicians who write large numbers of prescriptions for lipid-lowering drugs, suggesting a potential for bias in the pattern of care. This selection bias is likely to influence the results of the present survey, but in the direction of providing evidence of higher success rates than are actually present in the community. Therefore, an even greater percentage of dyslipidemic patients than that indicated by the present survey may not be achieving NCEP-specified LDL-C target levels.

Approximately 95% of the investigators indicated that they were aware of NCEP guidelines and follow them in practice. Furthermore, these investigators believe that LDL-C levels influence risk of CHD. Nevertheless, only small proportions of patients are actually reaching LDL-C levels that the investigators consider desirable. Therefore, the results of the investigator survey suggest that factors other than knowledge of and attitude toward NCEP guidelines account for the low success rates.

The presence of multiple risk factors has a major influence on the proportion of high-risk patients who achieve LDL-C target levels. Patients with a greater number of risk factors might be expected to receive more aggressive therapy to bring LDL-C levels to NCEP targets. This finding is supported by the observation that high-risk patients with 2 risk factors had a success rate that was significantly lower than rates for patients who had 3, 4, or 5 risk factors (data not shown). Presence of hypertension or diabetes significantly improved the success rate among patients in the high-risk group. The proportion of high-risk group patients with diabetes and hypertension who were at target LDL-C levels was still unsatisfactory, being only 41% and 39%, respectively.

Nonpharmacologic therapy, including diet and exercise, has frequently been maligned as inefficient in its ability to lower total cholesterol and LDL-C levels. The L-TAP study assessed the provision of advice by physicians to lower cholesterol with diet, and the extent to which the patient complied with the diet. Interestingly, both factors were independent predictors of success in reaching LDL-C goals. Compliance with diet appeared to be especially important in the CHD group. These results may be interpreted in several ways, including the possibility that individuals who comply with the diet are also compliant with drug therapy, thereby improving their success rate. Nonetheless, a cholesterol-lowering diet remains a cornerstone of lipid-lowering therapy. These results suggest the role of dietary therapy, especially in conjunction with drug therapy, as a means to reach LDL-C goals.

No attempt was made to estimate the socioeconomic status of the patients in this survey. The high proportion of patients who do not reach LDL-C target levels presumably spans all socioeconomic classes. Estimation of socioeconomic status based on the level of education indicated that highly educated persons were more likely to reach their LDL-C goal than the less educated (data not shown). The success rate was low for all races, with African American patients being less likely to reach their LDL-C goal than white or Hispanic patients. This find-ing is supported by the results of the Heart and Estrogen/Progestin Replacement Study, in which nearly half of African American women failed to use lipid-lowering medicine, a figure that was significantly higher than that for women who were white or of other races.[14] This may reflect an underappreciation of the importance of LDL-C as a risk factor for CHD among African Americans, in whom the primary focus has been the treatment of hypertension. Despite these differences, more aggressive cholesterol-lowering therapy is needed for patients in all socioeconomic classes and ethnic groups.

THE EFFICACY OF statin therapy in both primary and secondary prevention of CHD mortality and other CHD events has been established by the West of Scotland Coronary Prevention Study,[8,9] the Cholesterol and Recurrent Events Trial,[10] the Scandinavian Simvastatin Survival Study,[11] and, more recently, the Air Force/Texas Coronary Atherosclerosis Prevention Study[12] and the Long-Term Intervention with Pravastatin in Ischaemic Disease[13] study. In the present survey, 3136 patients received statin monotherapy, which included various doses of fluvastatin, lovastatin, pravastatin, and simvastatin. The success rates ranged from 32% for fluvastatin to 46% for simvastatin. In the CHD group, which corresponds to those patients who participated in the Scandinavian Simvastatin Survival Study, Cholesterol and Recurrent Events Trial, and Long-Term Intervention with Pravastatin in Ischaemic Disease study, statin monotherapy produced a success rate of 18%. In the high-risk group, which corresponds to those who participated in the West of Scotland Coronary Prevention Study, statin monotherapy was associated with a success rate of 40%. These results demonstrate that a large number of patients treated with these statins—in whom these drugs have been shown in prospective, placebo-controlled clinical trials to affect CHD morbidity and mortality significantly—are not achieving NCEP-specified LDL-C target levels. Only in the low-risk group, which in part is reflected by the Air Force/Texas Coronary Atherosclerosis Prevention Study, was a majority of patients treated to their LDL-C goal (<4.14 mmol/L [<160 mg/dL]) by current statin therapy.

In a placebo-controlled study performed at 2 academic, urban, tertiary care hospitals, patients with CHD received stepped-care therapy with pravastatin, niacin, cholestyramine, and gemfibrozil over 2.5 years.[24] Of the 44 patients receiving treatment, 35 were above the NCEP LDL-C target levels at baseline, with a mean LDL-C level of 3.85 mmol/L (149 mg/dL). Of these patients, 51% achieved target LDL-C levels after statin monotherapy, an additional 43% required addition of niacin, and 3% required the addition of both nicotinic acid and cholestyramine. Only 1 patient failed to achieve the target LDL-C level after combination lipid-lowering drug therapy. The results of this study illustrate the potential benefits of a lipid-lowering drug approach that includes dose maximization and combination drug therapy.

The NCEP guidelines were originally formulated to reduce the risk of CHD as both primary and secondary

prevention. Landmark clinical trials have reaffirmed the validity of these guidelines. The L-TAP survey clearly demonstrates that only 38% of patients being treated in community practice are achieving their NCEP LDL-C target levels. More aggressive treatment will be required if the NCEP objectives are to be fully realized. This includes more use of drug therapy after failure of diet, more use of statins relative to other lipid-lowering drugs, and greater use of higher doses of drugs.

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