

Management of High Blood Cholesterol Levels in Nova Scotian Adults: Comparison With the NCEP II and European Clinical Practice Guidelines

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Abstract

Objective: To compare the prevalence of dietary and drug treatment for high blood cholesterol levels with indication for treatment according to the National Cholesterol Education Program (NCEP) II and European clinical practice guidelines.

Study Design: A population-based, cross-sectional study.

Patients and Methods: Data were from the 1995 Nova Scotia Health Survey. Patients were 2078 respondents aged 20 to 74 years who provided blood samples. Based on cardiovascular risk factors, respondents were compared with guidelines to determine eligibility for dietary and antilipemic drug therapy.

Results: According to the NCEP II and European guidelines, 21% and 13%, respectively, of the pop-

ulation were estimated to be dietary therapy candidates and 12% and 4%, respectively, were estimated to be candidates for antilipemic drug therapy. Less than half of the dietary therapy candidates, according to either guideline, reported being diagnosed, and only about half of those diagnosed reported having received dietary therapy. Overall, 6% to 15% of the NCEP II drug therapy candidates and 12% to 37% of the European drug therapy candidates were estimated to be receiving antilipemic drugs. Only about 45% of the NCEP II and 60% of the European drug therapy candidates reported being diagnosed as having high blood cholesterol levels, and only about 50% of the NCEP II- and 60% of the European-diagnosed drug therapy candidates reported having received dietary therapy. The estimated prevalence of antilipemic drug therapy among diagnosed drug therapy candidates was 12% to 29% for the NCEP II and 12% to 52% for the European guidelines.

Conclusions: Dietary therapy and antilipemic drug therapy were underused relative to the NCEP II and European guidelines as a result of underdiagnosis and low use of treatment after diagnosis. Large differences in the recommendations of the 2 guidelines, however, show lack of consensus as to who should be treated and point to the need for additional research on this issue.

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The association between high levels of blood cholesterol and coronary heart disease is well established.^{1,2} Drug therapy to lower cholesterol levels has become standard treatment for primary and secondary prevention of coronary

heart disease.³⁻⁵ Early clinical trials found that use of antilipemic drugs is effective at lowering blood cholesterol levels but did not directly demonstrate efficacy in reducing mortality and coronary heart disease events.⁶⁻⁹ Results of more recent clinical trials,¹⁰⁻¹⁴ however, show that use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors decreases the risk of cardiac events and overall mortality and lowers blood cholesterol levels. Systematic reviews and meta-analyses suggest that cholesterol lowering with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors decreases the risk of cardiac events, stroke, and total mortality for persons with and without coronary heart disease.¹⁵⁻¹⁸

Cardiovascular drugs, and antilipemic drugs in particular, are receiving close attention by public- and private-sector drug insurers because they compose a large and growing portion of the total drug budget. For example, in Nova Scotia, cardiovascular drugs accounted for 24.6% of the total senior's (≥65 years of age) drug plan expenditures in 1996,¹⁹ and the number of antilipemic drug beneficiaries is growing rapidly. Although the benefits of antilipemic drug therapy are accepted, which patients should be treated has been debated.²⁰⁻²³ This debate has been fueled by cost-effectiveness studies^{17,18,24-26} that report a wide range of cost-effectiveness ratios depending on the risk and age profiles of the population treated.

The debate over which patients should be treated with antilipemic drugs has also been fueled by the diversity of available clinical practice guidelines. Various expert groups^{3-5,27-30} have published guidelines or consensus statements on the treatment of elevated serum cholesterol concentrations using dietary modification and drug therapy. Guidelines on blood cholesterol level management attempt to account for patients' blood cholesterol levels and other cardiovascular disease risk factors, such as smoking, hypertension, diabetes mellitus, obesity, lack of physical activity, and family history of cardiovascular disease. There are considerable differences, however, among guidelines in the risk factors considered and in the levels at which treatment should be initiated. Although there is considerable debate about the practicality and effectiveness of dietary therapy,³¹⁻³⁴ practice guidelines generally recommend aggressive dietary therapy as the initial approach and drug therapy if dietary therapy fails to lower blood cholesterol to desired levels.

Two of the most frequently used guidelines are the National Cholesterol Education Program (NCEP) II and the European clinical practice guidelines. The

NCEP II guidelines,³ published in 1994, are widely used in the United States and Canada and are relatively simple and easy to use. They are recognized as being relatively aggressive in recommending therapy, which has generated some concern regarding their use.³⁵ The European guidelines are more conservative, are less frequently used, and use a more detailed assessment of patient risk factor characteristics in recommending dietary or drug therapy.⁵

Limited information is available comparing actual practice with published guidelines, and most information that is available is not population based.³⁶⁻⁴⁰ Population-based comparisons with guidelines can provide information on the deviation between actual and recommended clinical practice in the adequacy of detection, treatment, and control of high blood cholesterol levels. More important, population-based comparisons provide a tool for the evaluation of guidelines by examining their implications at the population level (eg, percentage of the population recommended for treatment) and permit comparisons with recent cost-effectiveness studies.^{18,41} Such information is needed to inform the current debate on clinical practice guidelines for the treatment of high levels of blood cholesterol.

The present study examines, in a population-based sample of residents of the Canadian province of Nova Scotia, (1) the prevalence and distribution of persons for whom dietary therapy and antilipemic drug therapy are indicated according to the European and NCEP II clinical practice guidelines and (2) the correspondence between actual clinical practice and that recommended by the 2 guidelines. These 2 guidelines were selected because of their popularity and because they differ in their aggressiveness. The NCEP II guideline is among the most aggressive available, whereas the European guideline recommends a much more conservative approach to therapy.

... METHODS ...

Study Design

This was a descriptive, population-based study comparing antilipemic drug use to indications for use based on the European and NCEP II clinical practice guidelines for the management of hypercholesterolemia. Using cross-sectional survey data on cardiovascular risk factors for a sample of the adult population of Nova Scotia, computer algorithms were developed to determine survey respondent's candidacy for dietary therapy and antilipemic

drug therapy according to each of the 2 guidelines. Candidacy for dietary and drug therapy according to each guideline was then compared against self-reported dietary therapy and antilipemic drug use to estimate the proportion being treated.

Data

All data for this study were obtained from the 1995 Nova Scotia Health Survey (NSHS).⁴² Respondents for the survey were selected using a stratified random sample of the Nova Scotia population 18 years and older drawn from the provincial medical register. The registry includes virtually all permanent residents of the province. Eighty-three percent of those sampled were successfully contacted, and of those contacted, 3227 (72%) participated in a face-to-face home interview, and 2658 (59%) subsequently attended a clinic where blood samples were drawn for assessment of blood lipid levels and additional clinical assessments were made. Nova Scotia public health nurses were used as interviewers. Data for this study were from the 2078 respondents aged 20 to 74 years (as stipulated by the NCEP II guidelines) who attended the clinic and provided a blood sample. Sample weights were computed to adjust for potential nonresponse bias in the survey and were used in all analyses for this study. A recent evaluation of these adjustments suggests that the weights used are effective in reducing nonresponse bias.⁴³ The NSHS, and consent procedures, were approved by the ethics review committee of the Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia. Informed consent was obtained from all study participants.

Measurement

Information on cardiovascular risk factors used in the NCEP II and European guidelines was obtained from self-report and clinical measurements obtained as part of the NSHS. Smoking status, diabetes, family history of heart disease, and previous history of heart disease were obtained from respondent self-report using pretested, structured survey questions widely used in health surveys. Although patient self-report data are subject to recall bias, they are similar to what a physician might obtain from a patient and thus were deemed appropriate for the purposes of this study. Hypertension status, body mass index, and blood lipid levels were all obtained from clinical measurements. All risk factors were defined as closely as possible to their definition in the guidelines. Where risk factor definitions were not explicit in the guidelines, some measurement assumptions had to

be made; these are outlined in a separate detailed article.⁴⁴

Persons were classified as smokers if they reported smoking an average of 1 or more cigarettes per day in the last week. Respondents were classified as diabetic if they reported being diagnosed as having diabetes mellitus by a health professional. Family history of heart disease was based on self-report of either parent having had a heart attack, stroke, or angina before age 60 years. If the respondent did not know the cause of death, it was assumed that he or she did not have a family history of heart disease. Blood pressure was assessed as the average of 4 readings: 2 during the home interview (beginning and end) and 2 during the clinic visit (beginning and end). Current or previous use of dietary therapy was measured by a self-report item on the survey: "Are you presently, or have you ever been, on a diet that was recommended by a physician or other health professional to lower your blood cholesterol level?" The survey does not contain information on the success of dietary therapy. Respondents were classified as having a previous history of heart disease if they reported having had a heart attack or stroke, coronary bypass surgery, or angioplasty or if they were currently receiving nitrate therapy.

Blood lipid levels were assessed based on a blood sample drawn during the clinic visit. Blood samples were analyzed at the Alick J. Little Lipid Laboratory at the University of Toronto, Toronto, Ontario, a US Centers for Disease Control and Prevention reference laboratory that conforms to strict, monitored quality control standards. When information on low-density lipoprotein was required, respondents were dropped from the analysis if they had not fasted for at least 8 hours. This resulted in the exclusion of 165 respondents from the NCEP II analyses. We did not exclude nonfasting respondents from either guideline when only information on total cholesterol or high-density lipoprotein was required because fasting has little effect on these measurements.

Data on dietary and drug therapy were obtained from patient self-report. Receipt of dietary therapy was obtained from an interview question that asked patients if they had ever been on a diet recommended by a health professional to reduce their cholesterol level. Data on antilipemic drug use at the time of the survey were obtained, during the home interview, from assisted self-report data on drug use. The nurse interviewer asked respondents to gather all their medications and then reviewed them with the respondent. Information on instructions for use (name, strength, dose, and frequency), indication

for use, and actual use (dose and frequency) were recorded for each medication. Procedures used for the coding of drugs and indications for use are described elsewhere.⁴⁴ Seven patients receiving cholestyramine resin for other indications were reclassified as non-antilipemic drug users. Data on previous use of drugs to lower blood cholesterol level were obtained from patient self-report.

Development of Guideline Algorithms

Table 1 contrasts the basic recommendations of the NCEP II and European guidelines in terms of the cholesterol levels at which treatment is recommended and the risk factors that are taken into

consideration in recommending treatment. This table does not present all the recommendations of the 2 guidelines but highlights key differences. The original sources should be examined for the full guidelines.^{3,5}

A computerized algorithm was developed for the NCEP II and European guidelines based on the published guidelines.^{3,5} Because the NCEP II guideline recommends testing total cholesterol and high-density lipoprotein only for persons aged 20 to 74 years, we only compared respondents in this age range to the guidelines. The European guideline provided no information on age cutoff values for cholesterol testing, so the same age restriction as

Table 1. Comparison of Treatment Criteria for the NCEP II and European Clinical Practice Guidelines

Guideline/Year of Publication	Dietary Therapy (Step II Diet)	Drug Therapy
NCEP/1994 Primary prevention	Total cholesterol <5.2 mmol/L, HDL<0.9 mmol/L, LDL >4.1 mmol/L	Adequate trial and failure of diet therapy and LDL >4.9 mmol/L with no RFs
	Total cholesterol <5.2 mmol/L, HDL<0.9 mmol/L, LDL 3.4-4.1 mmol/L, >2RFs	
	Total cholesterol 5.2-6.2 mmol/L, HDL<0.9 mmol/L, LDL 3.4-4.1 mmol/L	
	Total cholesterol 5.2-6.2 mmol/L, LDL 3.4-4.1 mmol/L, 2 RFs	LDL >4.1 mmol/L with >2 RFs
	Total cholesterol 5.2-6.2 mmol/L, HDL<0.9 mmol/L, LDL >4.1 mmol/L	
Secondary prevention	LDL >2.6 mmol/L	LDL >3.4 mmol/L, or LDL 2.6-3.3 mmol/L with clinical judgment
European/1994* Primary prevention	Total cholesterol 5-7 mmol/L and risk of CHD event >20%	Total cholesterol 5-7 mmol/L and risk of CHD event is very high
	Total cholesterol 7-8 mmol/L	Total cholesterol 7-8 mmol/L and risk of CHD event >20%
		Total cholesterol >8 mmol/L
Secondary prevention	Same as for primary prevention, except risk of CHD event for people with overt cardiovascular disease is increased by at least 10	

NCEP = National Cholesterol Education Program II; HDL = high-density lipoprotein; LDL = low-density lipoprotein; RF = risk factors; CHD = coronary heart disease.

*Coronary risk chart used in the guidelines is based on risk function derived from the Framingham study.

used in the NCEP II guidelines was used to enhance the comparability.

In some cases, variables necessary to apply a guideline were missing in the survey data (respondent refused to answer or did not know). For several variables, assumptions that would mirror those that would be made by a clinician were applied in the presence of missing data. For example, patients who did not know if they had a family history of heart disease were assumed not to have a family history, and respondents who did not know if they had been diagnosed as having diabetes were assumed not to have diabetes. In some cases, however, such assumptions could not be made and patients were excluded from components of the analysis. The most common reason for exclusion was missing data on low-density lipoprotein cholesterol. We report the sample sizes that were used for each component of the analysis where appropriate.

Applying the guidelines using cross-sectional data was problematic because both guidelines include decision points that depend on outcomes from previously conducted tests or therapies. For example, the NCEP II guidelines call for the testing of all persons aged 20 to 74 years for total cholesterol, and then the subsequent assessment of fasting low-density lipoprotein if the total cholesterol level is >5.2 mmol/L. We handled this problem by applying the total cholesterol/high-density lipoprotein rules for all persons in the age range and then examining low-density lipoprotein for those whose total cholesterol level was >5.2 mmol/L.

A more problematic issue resulting from the use of cross-sectional data was the handling of dietary therapy. Both guidelines first define candidates for dietary therapy and subsequently recommend pharmacologic therapy if unsuccessful. Data on the timing, type, duration, or effectiveness of dietary therapy was not available. Accordingly, we used the guidelines to define dietary candidates and then liberally defined "potential drug candidates" as persons who would be drug therapy candidates if dietary therapy was unsuccessful. In addition, we applied a more restricted definition in which we excluded "drug candidates" who did not report having been on a diet to lower their cholesterol level. We expect that the latter definition conforms closely to the guidelines but erroneously misclassifies some persons.

Another problematic issue resulting from the use of cross-sectional data was the handling of respondents who were currently taking an antilipemic drug. If their blood cholesterol levels were successfully con-

trolled, they would not qualify as dietary or drug therapy candidates. Ideally, longitudinal data would be used to determine candidacy based on respondents' pretreatment lipid levels and risk factor status. Our approach to the problem defined a lower (conservative) and an upper (liberal) bound estimate of the prevalence of drug therapy candidates. For the lower bound estimate, we applied the lipid levels at the time of the survey to the guidelines, thus excluding persons taking antilipemic drugs whose lipid levels were successfully managed. For the upper bound estimate, we assumed that all persons taking antilipemic drugs at the time of the survey were valid drug candidates. Because it is expected that physicians primarily prescribe antilipemic drugs to patients at high risk, we believe that the true prevalence is closest to the upper bound estimates. For defining dietary therapy candidates, we assumed that all antilipemic drug users were valid dietary therapy candidates because both guidelines indicate that all pharmacologic therapy should follow dietary therapy.

Analyses

The analysis included several steps. First, we estimated the percentage of the adult Nova Scotia population that could be classified as dietary therapy candidates and as potential drug therapy candidates under each guideline. Second, we estimated the percentage of dietary therapy candidates who reported having been told by a health professional that they have a high cholesterol level and the percentage who reported having been on a diet that was recommended by a health professional to control their cholesterol level. Third, for each guideline we computed lower and upper bound estimates of the number of drug therapy candidates and the percentage of these candidates taking antilipemic drugs. To assess the rate of diagnosis, the percentage of drug candidates who reported being told by a health professional that they had a high cholesterol level (the percentage "aware") was computed. Treatment of diagnosed drug therapy candidates was assessed by computing the percentage of aware drug therapy candidates who reported having undergone dietary therapy and the percentage of those receiving antilipemic drug therapy. Because discontinuation of drug therapy may account for many people who should have been but were not treated according to the practice guidelines, the percentage reporting ever having taken drugs to reduce their cholesterol level was also computed.

All prevalence estimates were weighted and 95% confidence intervals were computed. The weights

account for differences in the probability of selection caused by the sample design and nonresponse and help ensure that the prevalence estimates are unbiased and reflect the true rates for the population.⁴⁵ Because standard statistical programs assume simple random sampling, they do not correctly estimate standard errors and 95% confidence intervals for most survey data. We thus used the statistical program STATA (StataCorp, College Station, TX), which uses the linearization method, to compute 95% confidence intervals that take into account the complex sample design in the NSHS.^{42,46} Where appropriate, binomial confidence intervals were computed.

... RESULTS ...

Recommended Treatment According to the NCEP II and European Guidelines

Table 2 shows estimates of the population prevalence of dietary and potential drug therapy candidates according to the NCEP II and European guidelines. In this and all other tables, reported numbers are unweighted and prevalence estimates are weighted to represent the population. The percent-

Table 2. Prevalence of Dietary and Potential Drug Therapy Candidates According to the NCEP II and European Clinical Practice Guidelines

	NCEP II	European
Dietary therapy candidates*		
No. (%) [†]	2031 (21)	2078 (13)
95% CI	19%-23%	12%-15%
Drug therapy candidates [‡]		
No. (%) [†]	2017 (12)	2077 (4)
95% CI	10%-13%	3%-4%

NCEP = National Cholesterol Education Program; CI = confidence interval.

*Antilipemic drug users are included as dietary therapy candidates but not as drug therapy candidates.

[†]Numbers are unweighted and percentages are weighted.

Deviations in the numbers from the total number included in the study (N=2078) reflect exclusions caused by missing data on variables needed to apply the guidelines.

[‡]Definition of drug therapy candidates is based on risk factors only and does not include previous use of dietary therapy.

age of the population classified as potential drug therapy candidates by the NCEP II guidelines is more than 3 times the percentage classified as such according to the European guidelines. For dietary therapy, there is less than a 2-fold difference between the 2 guidelines. In absolute terms, the percentage of the population classified by the guidelines as candidates for drug and dietary therapy is large, particularly for the NCEP II guidelines, where 12% of the population aged 20 to 74 years are potential drug therapy candidates and 21% qualify as dietary therapy candidates.

The Diagnosis and Management of Dietary Therapy Candidates

Table 3 presents information on the management of dietary therapy candidates for each clinical practice guideline. A minority of those classified as dietary therapy candidates by either guideline reported having undergone dietary therapy (21% according to NCEP II and 27% according to the European guidelines). This is a product of both underdiagnosis and nonuse of dietary therapy for those diagnosed. Only 42% of the NCEP II and 49% of the European dietary therapy candidates reported having been told by a health professional that they have a high blood cholesterol level. Of those who reported being diagnosed as having a high blood cholesterol level, only 50% of the NCEP II and 55% of the European dietary therapy candidates reported having been on a diet to lower their cholesterol level.

The Diagnosis and Management of Drug Therapy Candidates

The prevalence of antilipemic drug use in the sample was low. Of 2078 respondents included in this study, only 69 (3.3%) reported currently using antilipemic drugs. Table 4 displays lower and upper bound estimates of the prevalence of antilipemic drug use among respondents classified as drug therapy candidates according to each of the clinical practice guidelines. The prevalence of antilipemic drug use among drug therapy candidates, defined according to either guideline, is low. For the NCEP II guidelines, the lower bound estimate is 6% and the upper bound estimate is 15%. The prevalence estimates for antilipemic drug therapy are higher based on the European guidelines, in which the lower bound estimate is 12% and the upper bound estimate is 37%. Regardless of which guideline is used, the results indicate that

a clear minority of potential drug therapy candidates in the population are receiving antilipemic drugs.

An important factor contributing to the low antilipemic drug use rates is that many candidates have not been diagnosed. Only one half to one third of all drug therapy candidates reported having been told by a health professional that they had a high cholesterol level (point estimates of 45%-47% according to NCEP II and 56%-69% for the European guidelines). The prevalence of antilipemic drug use, however, in the population of potential drug therapy candidates who reported that they had been diagnosed as having a high cholesterol level is also low. According to the NCEP II guidelines, only an estimated 12% to 29% are taking an antilipemic drug, and according to the European guidelines, an estimated 12% to 52% are taking an antilipemic drug.

Both guidelines recommend that drug therapy be used only if dietary therapy fails to bring cholesterol levels within the acceptable range. Further restricting the pool of eligible drug therapy candidates to those who are diagnosed and who report having received dietary therapy results in somewhat higher estimates of the prevalence of antilipemic drug use. The estimated prevalence of antilipemic drug use according to the NCEP II guidelines is 18% to 38%, and the estimated prevalence according to the European guidelines is 21% to 60%. As a result of small numbers, however, the confidence intervals are broad for the European guidelines.

For diagnosed drug therapy candidates who have previously been on a diet, the last row in Table 4 shows the percentage who report ever having been prescribed a drug to lower their cholesterol level. These estimates are somewhat higher than the percentage who are currently taking antilipemic drugs.

... DISCUSSION ...

Practice guidelines for the management of blood cholesterol levels may play an important role in targeting antilipemic drug therapy in a

cost-effective manner. However, few previous studies have examined adherence to such guidelines. Moreover, many of these studies are not population based, are based on small sample sizes, or were conducted in the context of an intervention to alter physician behavior.^{36,37,39} In the largest and most comprehensive study to date, Shepherd³⁸ investigated the influence of cholesterol-lowering guidelines in 6 European countries using physician surveys. Data were obtained from a large sample of physicians participating in a market intelligence instrument. Although not necessarily representative of national physician or patient populations, this study found that the thresholds for intervention were considerably higher (>1 mmol/L) than suggested in either the European or NCEP II guidelines. Similar results were obtained in a survey of Canadian physicians.⁴⁰ The present study provides one of the most comprehensive studies to date on adherence of a population to 2 frequently used clinical practice guidelines. We found that the NCEP II and European guidelines yield large differences in the percentage of the adult population who are candidates for treatment with either dietary or drug therapy. The NCEP II guidelines classify 13% of persons aged 20 to 74 years as potential drug therapy candidates. This is more than 4 times the percentage of the same population classified as drug therapy candidates by the European guidelines. Using data for the Canadian population,

Table 3. Diagnosis and Treatment of Dietary Therapy Candidates: NCEP II and European Guidelines*

	NCEP II	European
Dietary therapy candidates (No.) [†]	498	354
Candidates who are/have been undergoing dietary therapy	21% (17%-24%)	27% (22%-32%)
Candidates who have been diagnosed	42% (37%-46%)	49% (43%-55%)
Diagnosed candidates who are/have been undergoing dietary therapy	50% (42%-57%)	55% (47%-63%)

NCEP = National Cholesterol Education Program.

*95% confidence intervals are shown in parentheses.

[†]Antilipemic drug users are included as dietary therapy candidates. Numbers are unweighted and percentages are weighted.

MacLean et al⁴¹ also documented that there are major differences in the impact of various guidelines with respect to the percentage of Canadian adults recommended for testing and treatment. Durrington et al⁴⁷ studied 570 patients referred to a lipid clinic who did not have preexisting evidence of atherosclerosis. Candidacy for therapy according to the NCEP II and United Kingdom guidelines was examined in 386 patients. Sixty-two percent of men and 72% of women met the NCEP II guidelines, whereas only 9% of men and <1% of women met the United Kingdom criteria. Although the patients were not compared with the European guidelines, only 32% of men and 11% of women had a >20% risk of coronary events (the risk cutoff value used in the European guidelines).⁴⁷

The broad difference between guidelines in the percentage of the population eligible for treatment

highlights the need to consider population-based implications and cost effectiveness as a part of guideline development.⁴¹ Large differences in the percentage of the population recommended for drug therapy imply large differences in potential drug costs. The high cost of treating according to the NCEP II guidelines prompted the Kaiser Permanente health maintenance organization in the United States to adopt its own set of guidelines, which are considerably less aggressive than the NCEP II guidelines.³⁵ In Britain, considerable debate has resulted from recent recommendations by the National Health Service Medical Advisory Committee on the use of lipid-lowering drugs, much of it focusing on cost implications.²⁰ The National Health Service report implies treating 8.2% of the population aged 35 to 69 years.

Table 4. Prevalence Estimates of Antilipemic Drug Use for Potential Drug Therapy Candidates: NCEP II and European Guidelines*

	NCEP II		European	
	Lower [†]	Upper [‡]	Lower [†]	Upper [‡]
Drug therapy candidates (No.) [§]	275	317	95	145
Drug therapy candidates taking antilipemic drugs	6% (3%-8%)	15% (11%-19%)	12% (4%-21%)	37% (28%-45%)
Drug therapy candidates who have been diagnosed	45% (39%-52%)	47% (41%-52%)	56% (46%-67%)	69% (61%-77%)
Diagnosed drug therapy candidates who are taking antilipemic drugs	12% (6%-18%)	29% (22%-36%)	12% (4%-21%)	52% (41%-62%)
Diagnosed drug therapy candidates who are undergoing dietary therapy [¶]	52% (43%-61%)	56% (49%-65%)	59% (46%-73%)	65% (55%-75%)
Diagnosed drug therapy candidates with dietary therapy taking antilipemic drugs	18% (8%-27%)	38% (29%-49%)	21% (7%-34%)	60% (47%-73%)
Diagnosed drug therapy candidates with dietary therapy who reported ever using antilipemic drugs	25% (14%-36%)	44% (33%-55%)	26% (12%-41%)	63% (50%-75%)

NCEP = National Cholesterol Education Program.

*95% confidence intervals are shown in parentheses.

[†]For lower bound estimates, respondents taking antilipemic drugs with controlled blood cholesterol levels are not treated as drug therapy candidates.

[‡]For upper bound estimates, all respondents taking antilipemic drugs are assumed to be drug therapy candidates.

[§]Numbers are unweighted and percentages are weighted.

^{||}Reported being told by a health professional that they have a high cholesterol level.

[¶]Reported presently or ever having been on a diet recommended by a physician or other health professional to lower their cholesterol level.

The consideration of cost effectiveness in guideline development is critical. Given the broad range of cost-effectiveness ratios published in the literature, however, and differences in the populations incorporated into cost-effectiveness studies, applying evidence from cost-effectiveness studies to the evaluation and development of guidelines is difficult. What is clear is that the cost effectiveness of treatment recommended by practice guidelines is highly sensitive to the level of risk in the population recommended for treatment. The cost effectiveness of lipid-lowering drugs is extremely sensitive to differences in the risk factors, age, and sex of patients treated.^{18,24} Lipid therapy is more cost effective for secondary prevention than for primary prevention, and is more cost effective the more likely the chance of experiencing a coronary event. For primary prevention, cost-effectiveness studies related to drug therapy have been conducted that estimate the cost per life-year gained, ranging from \$13,000 to \$1 million depending on the drug used, the blood cholesterol level, and risk factors for cardiac disease.^{10,17,18,24,25,48} The treatment of the additional population classified as potential drug therapy candidates by more aggressive guidelines, such as the NCEP II, will be less cost effective because of their lower level of coronary heart disease risk.

Comparison of the population classified as drug therapy candidates by various guidelines with the populations incorporated into cost-effectiveness studies in terms of annual coronary heart disease risk would assist in guideline evaluation and development. For example, in a cost-effectiveness study associated with the West of Scotland study,¹³ it was noted that the average coronary heart disease risk was 1.5% vs a coronary heart disease event rate of 2% to 4% in the population targeted by the European guidelines.¹⁰ A systematic way to make such comparisons would be to apply the populations recommended for treatment under various guidelines, and the populations incorporated into various cost-effectiveness studies, to models of risk assessment (eg, the Sheffield tables^{49,50}) to determine the average annual risk of a coronary heart disease event.

In examining treatment relative to the 2 guidelines, this study found that most candidates for therapeutic intervention to lower blood cholesterol levels are not receiving dietary therapy. According to both guidelines, only about 25% of all candidates for dietary therapy report having been on a diet recommended by a health professional to lower their cholesterol level. Undertreatment was found to be

about equally reflective of lack of diagnosis, and lack of treatment once diagnosed. The degree to which these results reflect error in patient self-report is not known. It is likely that patient recall leads to at least some underestimation of diagnosis and treatment. Lack of use of dietary therapy may also reflect practitioners' lack of confidence in its effectiveness. There continues to be controversy and mixed findings about the efficacy and effectiveness of low-fat, high-carbohydrate diets.³¹⁻³⁴

Similarly, we found that most potential candidates for drug therapy were not receiving antilipemic drug therapy. Only about 15% of NCEP II candidates and 40% of European candidates were receiving antilipemic drug therapy. As with dietary therapy, this in large part reflects lack of diagnosis. Only about half of the drug therapy candidates according to either guideline reported being diagnosed. The true percentage diagnosed, however, might be higher in the absence of patient recall error. Among diagnosed candidates, less than half of the NCEP II candidates and <60% of the European candidates were receiving antilipemic drug therapy, even when the pool of drug therapy candidates was further restricted to those who reported ever having received dietary therapy.

Our study was not able to determine the degree to which low use of antilipemic drugs among diagnosed drug therapy candidates is caused by patient nonadherence to therapy or physician prescribing practices. Because our data capture current use, it is possible that many of the diagnosed patients not currently receiving antilipemic drug therapy may have previously been receiving antilipemic drug therapy. Results of Canadian and international studies suggest that discontinuation rates are approximately 20% to 30% for statin drugs and >50% for other antilipemic drugs, such as niacin and cholestyramine.^{17,18,30,51-53} We still found, however, only moderately higher self-reported rates of ever having been prescribed medications to manage high blood cholesterol levels.

This study has advantages and disadvantages relative to other studies that have examined adherence to guidelines. Some of our data were based on patient self-report and may be subject to recall error. Previous myocardial infarction and stroke, previous dietary therapy, and diagnosis of high cholesterol level and diabetes mellitus were all based on patient self-report. When respondents reported having undergone dietary therapy, we did not know the aggressiveness of the recommended dietary therapy

or how effective the therapy was. Measurement of angina was based on nitrate use and therefore may be underestimated. It is possible that this study underestimated the prevalence of previous history of coronary heart disease and therefore underestimated the number of potential candidates for therapy. Most other studies obtained data from physician questionnaires.³⁷⁻⁴⁰ Both types of designs may be subject to recall error and reporting bias, although the types and extent of bias are likely to be different. A comparison of survey data with medical records or administrative data would be useful.

This study has the advantage of being population based, whereas previous studies have limited generalizability because of small samples sizes, nonrandom samples, and data collection in the context of interventions to improve adherence to guidelines. Nonresponse might be a source of bias in this study as well because only 59% of those contacted participated in the clinic visit. Sample weights for the NSHS, however, were poststratified to census data, and a recent analysis suggests that use of these weights is effective in minimizing nonresponse bias. Moreover, by studying adherence from a patient perspective, this study incorporates patients who have not been screened or diagnosed, thus providing a more comprehensive picture of adherence to guidelines.

This study was cross-sectional and therefore did not permit us to follow up patients over time. For patients receiving drug therapy, we did not know their cholesterol levels before initiation of therapy. Our assessment of patients is based on a single, high-quality assessment of blood cholesterol levels. It is possible that the use of multiple profiles would result in a smaller percentage of persons being classified as candidates for therapy. Also, we did not determine the timing of dietary therapy or assess whether it was effective, and we were not able to fully assess the history of previous antilipemic drug therapy. A longitudinal survey, or linkage of survey data to patient medical charts, would permit some of these issues to be addressed.

... CONCLUSIONS ...

This study documented large differences in the percentage of the population recommended for treatment by the NCEP II and European clinical practice guidelines. This study also shows that the percentage of the population receiving dietary or drug treatment is well below that recommended by either guideline and that to a large degree this is a

reflection of underdiagnosis. However, because of the uncertainty our results cast on the guidelines themselves, it would be premature to conclude from the results of this study that antilipemic drugs are underused. The divergent recommendations of the 2 guidelines we examined highlight the need to carefully evaluate and revise practice guidelines based on their population impact and evidence from economic evaluations and recent clinical trials.

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