Cholesterol Risk Management: A Systematic Examination of the Gap from Evidence to Practice

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Hypercholesterolemia is a major risk factor for coronary heart disease, and data indicate that aggressive cholesterol reduction decreases mortality and morbidity associated with this disease. Many patients with hypercholesterolemia, however, are not screened, prescribed appropriate lipid-lowering therapy, or treated to target cholesterol levels. Practice patterns are particularly inadequate for those patients at highest risk for having a cardiac event. We performed a literature search to identify studies of practice patterns in the management of patients with hypercholesterolemia with regard to screening, implementing lipid-lowering therapy, and treating to lipid goals. The findings highlight the potential for substantial opportunities to improve patient outcomes. Future studies should evaluate reasons for suboptimal cholesterol management as well as provide steps to improve management.
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Coronary heart disease (CHD) is the most common cardiovascular disease, which is the leading cause of mortality in western countries.[1] Hypercholesterolemia is a strong, independent, and modifiable risk factor for CHD.[2, 3] Although numerous randomized, controlled trials conclusively established the efficacy of aggressive cholesterol reduction in decreasing mortality and morbidity associated with CHD,[4–8] there is increasing recognition that the real-world management of hypercholesterolemia (i.e., application of this evidence) is suboptimal.[9–33]

Cholesterol risk management is a continuum that includes screening and diagnosing patients with hypercholesterolemia, initiating appropriate lipid-lowering interventions, and implementing follow-up to ensure that patients are adherent to therapy, are achieving target lipid goals, and are not experiencing adverse effects. Evidence points to treatment gaps in each step of these processes, especially with regard to those patients at greatest risk for cardiac events.[9] We reviewed the literature that evaluated practice patterns in the management of hypercholesterolemia to define the scope of the problem and suggest improvements.

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Methods

Articles published in English from January 1966–July 2000 were identified through MEDLINE and EMBASE by using the following combinations of keywords and medical subject headings: coronary artery disease, hypercholesterolemia, low-density lipoprotein, cholesterol management, and practice patterns. The reference lists of published articles were reviewed for additional pertinent papers. All relevant articles assessing practice patterns (either physician or other health care professional) were reviewed. Articles that did not provide quantitative data on cholesterol management

Table 1. Assessment of Screening Practices in Patients with CHD

Method	Percentage of Patients Screened
Retrospective chart audit of 154 inpatients with CHD and surveys of 184 physicians on knowledge, attitudes, and practice patterns[11]	High cholesterol noted as a risk factor for CHD in 53% of charts; 18% of charts had complete lipid profile documented.
Retrospective chart audit of 100 consecutive inpatients with CHD under the care of three cardiac surgeons[12]	Total cholesterol recorded for 83% of patients.
Retrospective chart audit of 3304 inpatients with CHD admitted to four acute care hospitals in 1993[13]	Lipids documented in 28% of charts either during patient hospital stay or anytime in 1988–1993.
Retrospective chart audit of 2583 inpatients with CHD from 12 specialty hospitals and 12 district general hospitals and a cross-sectional survey[14]	64% men (n=1284) and 59% women (n=1299) had documented total cholesterol measured.
Retrospective chart audit of 934 patients with CHD in lipid and nonlipid clinics[15]	51% women (n=271) and 68% men (n=663)had documented LDL.
Retrospective chart audit and survey of 603 patients with CHD in primary care practices[16]	Total cholesterol documented in 96% of charts; lipid panels documented in 67%.
Retrospective chart audit of 225 patients admitted to the coronary care unit in 1996[17]	Lipid panels performed in 50% of patients in whom they were indicated based on NCEP criteria.
Retrospective outpatient chart audit of 48,586 patients with CHD[18]	Total cholesterol documented in 66% of charts; LDL documented in 44% of charts.
Retrospective chart audit of 390 patients with CHD before institution of heart care project and 140 inpatients with CHD and 641 ambulatory patients with CHD[19]	LDL documented in 61% of charts before project institution; LDL documented in 55% of inpatient charts and 93% of outpatient charts.

CHD = coronary heart disease; LDL = low-density lipoprotein; NCEP = National Cholesterol Education Program.

practice patterns in the areas of screening, implementation of lipid-lowering therapy, or treatment to target lipid levels were excluded. Studies involving pediatric populations or with data available only in abstract form also were excluded.

Due to the number of articles and the wide ranges of results in variable sample sizes, the utilization rates of therapies and the proportion of patients achieving target lipid levels are reported as weighted averages.

Results

Screening

The first indication of the presence of CHD is sudden cardiac death in 50% of men and 63% of women. This statistic illustrates the importance of early detection and treatment of hypercholesterolemia.[34–36] An estimated 36–50% of the general population have hypercholesterolemia warranting treatment with, at a minimum, dietary modifications.[1, 37] Therefore, screening the population is a crucial first step in the early detection and subsequent management of hypercholesterolemia to prevent the onset and progression of CHD.

Reports from the National Cholesterol Education Panel (NCEP) recommend that all adults aged 20 years or older have their total cholesterol and high-density lipoprotein (HDL) assessed at least once every 5 years.[34, 35] Depending on initial screening results and an individual's risk factors, a full lipoprotein analysis may be required. Despite wide dissemination of the NCEP guidelines, population-based data indicate that only approximately 8% of the population is screened annually, much lower than the 20% expected if the guidelines were followed.[10]

Since the publication of the NCEP II guidelines, controversy has arisen regarding the rationale and cost-effectiveness of mass cholesterol screening of adults in the general population.[38, 39] Proponents suggest that mass screening of all adults over 20 years of age is necessary due to evidence that atherosclerosis commences early in childhood.[38] Screening provides patients with a complete cardiac assessment, identifies individuals who would benefit from lipid-lowering interventions, and promotes public awareness of the role of cholesterol in cardiac risk.[38] On the other hand, others recommend selectively screening those individuals most likely to benefit from lipid-lowering interventions if they are found to be hypercholesterolemic.[39] This practice would be consistent with Canadian, European, and British

clinical practice recommendations.[40–42] Furthermore, recommendations published since NCEP II suggest limiting screening to men and women over the ages of 35–40 years and 45–50 years, respectively; any individual with more than two risk factors; and persons with a family history of familial hypercholesterolemia.[40, 43] All recommendations state that any patient with documented CHD should undergo an aggressive screening strategy (i.e., yearly testing), given the great benefit of early detection and management of hypercholesterolemia in patients with established CHD.[34, 35, 40–43]

Data from numerous retrospective audits of medical records from both inpatients and outpatients with CHD indicate that only 64% (range 28–96%) of these high-risk individuals had cholesterol measurements documented (Table 1).[11–19] Based on these data, approximately 36% (and as many as 72%) of patients with CHD are not screened for hypercholesterolemia. Two studies did report exceptionally high proportions of patients being screened: 93%[19] and 96%,[16] respectively; however, one used protocols and care maps to guide lipid management,[19] and the other included only those physicians who agreed to participate.[16] Although all of these studies relied on retrospective chart documentation of cholesterol levels as indicators for screening, they nevertheless highlight the possibility of significant missed opportunities for intervention and improvement in patient outcomes.

Although it is evident that the implementation of screening strategies for hypercholesterolemia is suboptimal, the proportion of patients screened seems to have increased over time.[11] Furthermore, screening practices appear to increase as patients move from primary to secondary prevention.[13, 14] Still, improvements are needed to increase screening, at least for patients at the greatest risk for CHD events. This measure is a crucial first step in the identification and subsequent management of those with hypercholesterolemia.

Implementation of Therapy

Given the suboptimal rate of screening for cholesterol risk, it is perhaps not surprising that many investigators suspect that patients are undertreated for hypercholesterolemia.[11–18, 20–27] A 1993 study involving a database of 154,735 adults estimated that 72% of those eligible for lipid-lowering therapy with diet or drugs failed to receive either form of treatment.[23] Although this study was completed before the publication of the NCEP II guidelines and the pivotal statin trials, the rate is consistent with a 1998 survey of 7423 adults, which found that 71% of treatment-eligible patients in the general population received no therapy.[25] Studies that evaluated the implementation of treatment interventions are described in Table 2.

Nonpharmacologic Therapy: General Population

Published guidelines suggest that nonpharmacologic therapy, including diet, exercise, and smoking cessation, be initiated in all patients requiring treatment for hypercholesterolemia, with the addition of lipid-lowering drugs in select groups of patients.[35, 40–42] Despite these recommendations, data indicate wide variation in the implementation of such therapy.

Data from several studies show that 34% (range 11–79%) of patients receive counseling for nonpharmacologic interventions.[10–14, 16, 20–23, 25] The largest of these studies found that of 85 million physician visits by patients with documented hypercholesterolemia, only 34% of patients received nonpharmacologic counseling for hypercholesterolemia, defined as any counseling (including dietary) related to cholesterol.[10] This may be an underestimate as nonphysician and community services were excluded from the analysis or counseling may not have been documented.[10] The most optimistic estimate of patients started on dietary therapy was 79%.[23] The study yielding this estimate was the only prospective assessment of cholesterol management practices (telephone interviews of 154,735 adults in the United States) that we found. It is likely an overestimate because the study addressed only a minority (10.3%) of highly selected patients (i.e., those who were aware of having hypercholesterolemia).[23]

Nonpharmacologic Therapy: Patients with CHD

Studies that specifically evaluated the use of nonpharmacologic therapy in patients with documented CHD reveal that only 32% (range 11–55%) of patients receive counseling on the therapy.[11–14, 16, 20, 22, 25] One would expect this estimate to be much higher, given the well-established benefits of cholesterol reduction in these high-risk patients. Based on a survey of 7423 patients, the fraction of U.S. adults with CHD eligible for and receiving dietary therapy is only 29%. This percentage is identical to that estimated in the general population.[25] A related

Table 2. Evaluation of Therapy Implementation

Method	Percentage of Patients Started on Therapy
Retrospective chart audit of 154 inpatients with CHD and surveys of 184 physicians on knowledge, attitudes, and practice patterns[11]	53% of patients had elevated cholesterol; 11% treated with dietary therapy.
Retrospective chart audit of 100 consecutive inpatients with CHD under the care of three cardiac surgeons[12]	Overall, 36% of patients referred to dietician; 29% of patients with total cholesterol > 259 mg/dl (6.7 mmol/L) were referred to dietician; 14% were treated with drug therapy.
Retrospective chart audit of 3304 inpatients with CHD admitted to four acute care hospitals in 1993[13]	22% were prescribed dietary therapy; 5% had lifestyle adjustments recommended; 8% were prescribed drugs.
Retrospective chart audit of 2583 inpatients with CHD from 12 specialty hospitals and 12 district general hospitals and a cross-sectional survey[14]	50% of patients with total cholesterol > 251 mg/dl (6.5 mmol/L) received therapeutic intervention.
Retrospective chart audit of 934 patients with CHD in lipid and nonlipid clinics[15]	51% of women and 55% of men were on drug therapy.
Retrospective chart audit and survey of 603 patients with CHD in primary care practices[16]	55% received dietary counseling; 32–37% received drug therapy.
Retrospective chart audit of 225 patients admitted to the coronary care unit in 1996[17]	14%, 62%, and 52% of eligible patients with CHD received drug therapy on admission, during hospitalization, and on hospital discharge, respectively.
Retrospective outpatient chart audit of 48,586 patients with CHD[18]	39% were prescribed lipid-lowering drug therapy.
Retrospective chart audit of 120 inpatients with cardiovascular disease[20]	30% of patients had known elevated cholesterol: 11% treated with dietary therapy; 6% with drugs; 6% with both.
Retrospective chart audit of 217 patients with hypercholesterolemia (i.e., > 259 mg/dl [6.7 mmol/L])[21]	29% treated with diet therapy; 7% treated with drug therapy; 64% received no treatment at all.
Interviews of 95 patients on admission to hospital for angiography, and 1 mo. and 12–24 mos. after admission[22]	17% treated before angiography[a]; 26% treated after angiography[a]; 33% treated 12–24 mo after angiography[a]
Telephone interviews of 154,735 adults in 37 U.S. states[23]	10% reported being treated for hypercholesterolemia: 79% had low-fat diet recommended; 19% had drug therapy recommended; 72% of eligible patients received no treatment at all.
Cross-sectional measurement of lipids in 2763 women with CHD[24]	35% with LDL > 160 mg/dl (4.1 mmol/L) received drug therapy; 39% with LDL > 130 mg/dl (3.4 mmol/L) received drug therapy
Survey and physical examination of 7423 respondents to phase 2 of the NHANES III questionnaire[25]	28% of patients were eligible for treatment. Overall, 29% received dietary therapy; 6% received drug therapy; 65% received no therapy. In patients with CHD, 29% received dietary therapy; 13% received drug therapy; 58% received no therapy.
Retrospective chart audit of 1710 patients hospitalized for recurrent acute myocardial infarction during 1986–1995 to determine receipt of lipid-lowering drugs before and after myocardial infarction[26]	0.8% received drug therapy in 1986 and 11.5% received drug therapy in 1995.
Retrospective chart audit of 348 outpatients followed in a primary care health maintenance organization[27]	14% of eligible patients received drug therapy.

CHD = coronary artery disease; LDL = low-density lipoprotein; NHANES III = third National Health and Nutrition Examination Survey.
[a]Treatment was with diet and/or drug therapy.

study, a retrospective chart audit of 3304 inpatients with cardiovascular disease, found that only 5% of the patients had documentation of recommendations for lifestyle adjustments and only 22% had recommendations for dietary therapy.[13]

Interpretation of data on nonpharmacologic therapy is difficult, as these interventions are continuous variables (e.g., patients may only partially modify their diet) rather than simple dichotomous outcomes, and various degrees of success in implementation are possible. Furthermore, counseling and nonpharmacologic therapies may be used more frequently than reported, given that these recommendations may be poorly documented in patients' medical

records.

It is important to note that investigators have found dietary therapy alone may be ineffective at reducing cholesterol levels.[44, 45] In fact, some suggest that the step I and II diets recommended by the NCEP II guidelines may not be aggressive enough at reducing cholesterol levels,[46] perhaps making documentation of dietary recommendations irrelevant. Still, lifestyle adjustments are cost-effective when patients are compliant and are healthy initiatives that should be encouraged and reinforced in all patients.

Lipid-lowering Agents: General Population

A large proportion of the population requires lipid-lowering agents to achieve optimal cholesterol levels. General population surveys evaluating the use of these drugs indicate that only 23% of patients receive drug therapy for hypercholesterolemia.[10, 23, 25] Furthermore, these surveys suggest that 65–77% of the general population receive no therapy (drug or nondrug) at all for hypercholesterolemia.[10, 23, 25]

A national survey of randomly selected, office-based physician visits reported the highest rate of prescriptions for lipid-lowering agents at 23%.[10] This report may overestimate the actual administration because individuals were captured on a per-visit basis rather than a per-patient basis and because patients prescribed drug therapy are more likely to require follow-up with their physician.[10] Another study reported the use of lipid-lowering agents to be 19% among a select group of patients who were aware of their elevated cholesterol (only 10.3% of the total population surveyed).[23] Consistent with data on population screening, the studies suggest that only a minority of patients eligible for lipid-lowering pharmacologic therapy actually receive it.

A limitation of these data is that they do not account for the degree or duration of cholesterol elevation or the appropriateness of lipid-lowering drug therapy. It is conceivable that some patients surveyed had cholesterol levels for which drug therapy was not indicated and that many may have received nonpharmacologic therapy, such as dietary counseling.

Lipid-lowering Agents: Patients with CHD

The absolute benefits of lipid-lowering agents are greatest among those patients with established CHD.[4–6] Drug therapy is recommended immediately, in conjunction with diet and nonpharmacologic therapy, in high-risk patients with lipid levels above target.[35, 30, 41] Published data from 12 studies involving 68,446 patients with established CHD indicate that only 35% (range 6–62%) received therapy with a lipid-lowering agent.[12–18, 20, 22, 24–26]

Again, this literature must be interpreted cautiously, given that the majority of studies did not present the cholesterol levels of the patients; therefore, not all patients may have required drug therapy. A study of 2763 high-risk patients did identify lipid levels and reported that only 39% of patients with low-density lipoprotein (LDL) levels greater than 130 mg/dl (3.4 mmol/L; a level at which drug therapy should be initiated according to guidelines[35, 40, 42]) were prescribed drug therapy.[24]

Whereas most of reported studies retrospectively documented the administration of hypolipidemic agents at single time points, it is possible that prescriptions for these drugs may increase over time as physicians become more familiar with clinical trial data and practice guidelines. Two studies evaluated the prescription of lipid-lowering therapy over time.[22, 26] The first reported that of 95 patients hospitalized for cardiac catheterization, 25.9% with known hypercholesterolemia were treated with drugs before the procedure.[22] This figure increased to 32.8% between 1 and 2 years after the procedure. The second study examined trends in cholesterol management over more than 9 years among 1710 patients hospitalized with recurrent acute myocardial infarction.[26] Significantly more patients received lipid-lowering drugs in 1995 compared with 1986 (0.8% vs 11.7%, $p<0.001$).[26] Still, in 1995, 36% of patients had elevated cholesterol levels and thus many patients remained untreated.[26] These studies provide encouragement that practice patterns may improve, but it is important to remember that approximately one-third of high-risk patients are untreated with lipid-lowering agents.

Treatment to Cholesterol Targets

Even when hypercholesterolemia is identified and treatment is instituted, many patients are not treated to target cholesterol levels (Table 3). The British, NCEP II, and Canadian guidelines all recommend target LDL cholesterol concentrations in accordance with an individual's cardiac risk stratification; the greater the risk for cardiovascular events, the lower the LDL target.[35, 40, 41] For example, British guidelines recommend LDL targets of 160 and 130 mg/dl (4.1 and 3.4

Table 3. Evaluations of Treating to Target Cholesterol Levels

Methods	Percentage of Patients Achieving Target
Retrospective chart audit of 934 patients with CHD in lipid and nonlipid clinics[15, a]	24% of women and 34% of men achieved target.
Retrospective chart audit and survey of 603 patients with CHD in primary care practices (target LDL = 100 mg/dl [2.6 mmol/L])[16]	14% of patients achieved target.
Retrospective outpatient chart audit of 48,586 patients with CHD (target LDL = 100 mg/dl [2.6 mmol/L])[18]	25% of patients achieved target.
Cross-sectional measurement of lipids in 2763 women with CHD (target LDL = 100 mg/dl [2.6 mmol/L])[24]	10% of patients achieved target.
Surveys of 7423 patients and physician exam in respondents to phase 2 of the NHANES III questionnaire[25, a]	18% of patients with CHD; 45% with two risk factors; 87% with < two risk factors.
Most recent database of the NHANES III analyzed to estimate proportion of adults requiring drug therapy (33,994 people interviewed)[28, a]	Overall, 71% achieved target; with CHD: 17%; CHD and > two risk factors: 30%; no CHD and < two risk factors: 79%.
Retrospective cohort of 244 lipid clinic patients with CHD and taking lipid-lowering agents (target LDL < 130 mg/dl [3.4 mmol/L])[29]	56%, 44%, and 35% of patients with mild, moderate, and high cholesterol achieved target, respectively.
Retrospective chart audit of 90 patients treated with statin monotherapy[30, a]	Overall, 33% achieved target; with CHD: 24%; no CHD and < two risk factors: 100%; no CHD and > two risk factors: 52%.
Randomized controlled trial of 125 patients with CHD (target LDL < 100 mg/dl [2.6 mmol/L])[31]	39% of patients achieved target.
Retrospective chart audit of 622 patients admitted to hospital with myocardial infarction and established hyperlipidemia (target LDL < 100 mg/dl [2.6 mmol/L])[32]	15% of patients achieved target.
Retrospective cohort of 4888 outpatients with or without CHD and on the same treatment program for 3 mos.[33, a]	Overall, 38% achieved target; with CHD: 18%; no CHD and > two risk factors: 37%; no CHD and < two risk factors: 38%.

CHD = coronary heart disease; LDL = low-density lipoprotein; NHANES III = third National Health and Nutrition Examination Survey.
[a]LDL target defined as < 100 mg/dl (2.6 mmol/L) with CHD, < 130 mg/dl (3.4 mmol/L) with > two risk factors, and < 160 mg/dl (4.1 mmol/L) with less than two risk factors.

mmol/L) or less in patients without and with CHD, respectively.[41] Guidelines from NCEP II identify LDL targets of 160, 130, and 100 mg/dl (4.1, 3.4, and 2.6 mmol/L) or lower for patients with less than two risk factors, more than two risk factors, and established CHD or diabetes, respectively.[35] Although the recently published Canadian guidelines are similar, targets of less than 97 mg/dl (2.5 mmol/L) for patients with CHD or diabetes are recommended.[40]

An estimated 83% (range 38–100%) of patients with fewer than two cardiac risk factors, compared with 39% (range 30–52%) of patients with more than two risk factors, reach their cholesterol targets.[25, 28, 30, 33] Among patients at high risk for cardiovascular events, only 21% (range 9–39%) achieve their cholesterol targets.[16, 18, 30, 33] A large study of 48,586 patients with CHD (39% of whom were taking lipid-lowering agents) reported that only 25% achieved a target LDL of less than 100 mg/dl (2.6 mmol/L).[18] This study may have overestimated the population reaching target because it included physicians who were frequent prescribers of 3-hydroxy-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. These studies should be interpreted cautiously because they did not specify whether patients were receiving lipid-lowering therapy at time of assessment, which is important given the treatment gaps in screening and implementation of therapy. Paradoxically, the proportion of patients achieving target appears inversely associated with patients' risk for cardiovascular events.

Only a few studies specifically evaluated the proportion of patients who achieved target while receiving lipid-lowering therapy. Surprisingly, the proportion remained unchanged at 21% (range 18–35%).[29, 30, 33] The largest and most recently published study enrolled 4888 patients with CHD.[33] It reported that only 18% of patients achieved their LDL targets, despite receiving lipid-lowering agents for the previous 3 months.[33]

Application of Results

Figure 1 illustrates cholesterol management practices for a hypothetical cohort of patients at high risk for CHD events. Based on weighted averages calculated from available data, only 64% of patients will be screened for dyslipidemias. From a sample of 100 high-risk patients and based on the published literature,[24] only 39% requiring lipid-lowering therapy would receive it. Applying this figure to the hypothetical cohort, only 39 patients (39%) would be started on lipid-lowering therapy, and only 8 (21%) of these patients would receive the necessary follow-up and titration to achieve their cholesterol goal.

Reasons for Suboptimal Management of Cholesterol

Although ample evidence suggests that patients are not adequately managed for hypercholesterolemia, few studies explore the reasons. Insights into the mechanisms of undertreatment of elevated cholesterol would help in the development of interventions to improve patient care. One study found that patients were more likely to receive therapy if they had an LDL measurement documented; history of acute myocardial infarction, coronary artery bypass grafting, or hypertension; or were followed by cardiologists.[18] Other studies have shown that younger patients[13, 26] and men are more likely to receive lipid-lowering agents,[13] as are those patients with a history of revascularization.[13, 24] Factors significantly associated with the achievement of targets include a lower baseline LDL cholesterol, administration of combination drug therapy, and patient adherence to treatment.[29, 31] The lower proportion of high-risk patients reaching their target LDL levels simply may indicate that cholesterol management is more difficult in these patients, given that the target is much lower. Alternatively, such patients may be poorly adherent with their drugs or simply undertreated. Many patients are either lost to follow-up in the community setting or do not have their lipid-lowering therapy assessed routinely. Overall, factors contributing to the suboptimal achievement of targets can be broadly classified into three categories: patient related, physician related, and health care system related (Table 4).

Patient-related Factors

Patient-related factors include drug adherence, side effects or intolerance to prescribed therapies, and drug costs. Approximately 50–79% of patients discontinue their lipid-lowering drugs within 12 months of initiation.[29, 47–49] Generally, adherence is poorer in patients treated with therapies other than HMG-CoA reductase inhibitors, such as bile acid sequestrants or niacin, likely due to adverse effects.[48, 49] A few studies evaluated the influence of adherence or drug side effects on the achievement of lipid

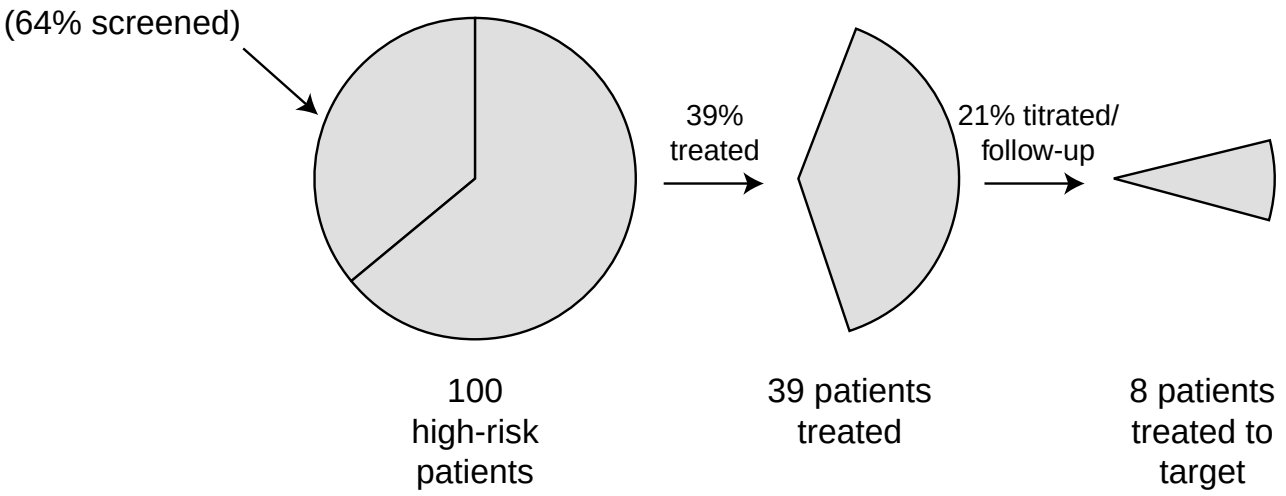

Figure 1. Cholesterol management practices in patients with coronary heart disease based on a hypothetical cohort of 100 patients.

Table 4. Factors Contributing to Suboptimal Cholesterol Management

Patient-related	Physician-related	Health Care System-related
Drug adherence	Reliance on laboratory flags to alert to presence or absence of hypercholesterolemia	Lack of system for monitoring and follow-up
Adverse drug effects	Failure to measure cholesterol levels	Illness, rather than prevention, driven
Inadequate patient knowledge of their hypercholesterolemia	Lack of guideline awareness	Inadequate dosage titration
Cost of lipid-lowering agents	Overestimation of actual treatment of high-risk patients	

goals.[30] One such study found that 31% of patients were nonadherent; 72% of those patients failed to achieve their target cholesterol levels.[30] Other than drug side effects, the reasons for poor adherence with cholesterol-lowering agents are largely unknown. It may be secondary to a lack of patient knowledge about the importance of cholesterol reduction or the requirement for lifelong therapy. In addition, the cost associated with lipid-lowering drugs may negatively affect adherence rates, although the clinical significance of this factor is unknown.[49, 50]

Numerous studies show that patients are often unaware of having hypercholesterolemia.[21, 51–53] One study assessed 15,800 patients in the general population (aged 45–64 yrs) with regard to awareness of the presence of hypercholesterolemia (total cholesterol > 240 mg/dl [6.2 mmol/L]) during 1987–1989.[51] It found that 42% of patients were aware of their condition.[51] A related study reported that 53% of patients with elevated total cholesterol, defined as greater than 220, 240, and 259 mg/dl (5.7, 6.2, and 6.7 mmol/L) for patients aged 22–29, 30–39, and 40 years and over, respectively, had no prior knowledge of these elevations.[20] A third study reported that public awareness of elevated cholesterol levels increased over time, although more than 80% of those surveyed were still unaware of their own condition.[53] Patients also may simply fall through the cracks and be lost to monitoring and follow-up. Clearly, initiatives are needed to improve public awareness of the need for cholesterol monitoring.

Physician-related Factors

Numerous physician-related factors may affect the management of patients with hypercholesterolemia. Reliance on laboratory reports to confirm the presence or absence of hypercholesterolemia may cause some patients with abnormal lipid levels to be missed. For instance, a study reported that physicians were more likely to recognize hypercholesterolemia if it were marked as abnormal on the laboratory report.[21] Many laboratory reports indicate a range of normal cholesterol values without taking into account the level of risk for individual patients.

Lack of knowledge about guidelines and the clinical trials reporting the efficacy of lipid-lowering drugs may contribute to suboptimal cholesterol management. A 1998 study reported that only 54% of physicians would prescribe lipid-lowering agents to a patient with documented CHD and an LDL greater than 130 mg/dl (3.36 mmol/L), despite evidence and guideline recommendations to initiate therapy in these patients.[16] A study published in 1988 reported that only 48% of physicians stated that lowering blood cholesterol reduces coronary disease risk "often" or "always,"[11] but the study was conducted before publication of the major lipid-lowering trials.

Physicians may overestimate the adequacy of treatment in their patients with hypercholesterolemia. They reported performing lipid panels in 86% of their patients, yet on chart audit, lipid panels were available for only 67% of patients.[16] Another study reported a prevalence of hypercholesterolemia of 24% in family practice patients, yet the condition was documented in only 13% of cases.[21] Although the reasons for physician nonadherence with guidelines are largely unknown, one report cited physician time constraints, lack of skills for behavioral modifications, patient inattentiveness, and the urgency of the patients' concomitant medical problems as potential factors.[11, 53]

Health Care System Factors

Traditionally, health care systems were driven by illness, not prevention. A survey of family physicians identified the following two assertions as barriers to the provision of preventive services: "patient is well and does not present" and

"priority was given to the presenting complaint."[54] Although few trials have evaluated the impact of health care system factors on patients' achievement of target cholesterol measurement, some evidence suggests that lack of appropriate monitoring and follow-up may contribute to poor response rates. One study found that 88% of patients treated with lipid-lowering therapy and who had not reached their target had been on the same dose of statin for at least 1 year.[30] Another study found that 65% of patients not achieving their target goals were taking the starting (low) dosage of their lipid-lowering drug.[18] These data suggest that more aggressive dosage titrations, the use of combination therapy, and aggressive follow-up may be needed to help patients achieve target measurements.

Limitations of Data

Most studies in this review were conducted in North America, making it difficult to generalize to other settings. There is a potential for publication bias in which only reports of poor cholesterol management practices are published. Given that data from the population-based studies, which provide estimates for millions of people, are remarkably consistent with most smaller studies, it is likely that the data presented here are representative of general practice patterns. Most of the studies were retrospectively conducted and are limited in their ability to capture undocumented interventions (i.e., screening and treatment initiation). At least two of the studies required physicians to consent to being involved; this may have introduced a volunteer bias because those who agreed to participate may have had a greater interest in hypercholesterolemia than other physicians.[14, 16] These studies, however, involved small numbers of the total patients in this review and did not greatly affect the calculated weighted average. Most published papers evaluated events at a single point in time rather than accounting for temporal changes over time. Practice patterns likely have improved since publication of the major clinical trials and guidelines, but few published studies have evaluated temporal changes to practice patterns. Many studies evaluating the proportion of patients reaching target did not define the LDL goal. In addition, cholesterol targets were set by consensus guidelines, even though there is little randomized, controlled trial evidence for screening recommendations or specific numeric goals. Still, randomized trial evidence does suggest that patient outcomes are improved at lower cholesterol levels, a finding that is consistent with considerable epidemiologic evidence.[5]

Future Directions

Emphasis must be placed on screening, documenting results, initiating therapy, and following patients to improve the proportion of patients achieving target lipid goals. Recognition of the gap between evidence and practice in cholesterol risk management is increasing; this awareness is an important first step. Innovative approaches to the management of patients with or at risk for CHD are required to improve the application of appropriate lipid-lowering interventions to eligible patients.

Multidisciplinary team involvement at the level of the community may improve the proportion of patients screened, started on appropriate therapy, and followed to target lipid goals. For example, dieticians can provide appropriate dietary counseling and community pharmacists can identify patients who would benefit from pharmacologic therapy and work with patients and family physicians to optimize the proportion of patients achieving target lipid goals.[55] Use of advanced measurement technology, such as point-of-care technology involving fingerstick blood samples, may assist in the identification, monitoring, and follow-up of patients.[55] Furthermore, reminder systems for both patients and physicians may help ensure that repeat lipid panels and appropriate monitoring and follow-up are conducted. Further studies should investigate the reasons why patients are not reaching targets and evaluate ways to optimize therapy. In light of the enormous public health importance of CHD and the availability of safe and efficacious therapies, our next step must be to improve the process of cholesterol risk management.

References

1. Heart and Stroke Foundation of Canada. The changing face of heart disease and stroke in Canada 2000. Available from http://www.hc-sc.gc.ca/main/lcdc/web/bcrdd/hdsc2000/pdf/card2ke.pdf.
2. Anderson KM, Castelli W, Levy D. Cholesterol and mortality. JAMA 1987;257:2176–80.
3. Stamler J, Wentworth D, Neaton JD. Is the relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? JAMA 1986;256:2823–8.
4. Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian simvastatin survival study.

Lancet 1994;344:1383–9.
5. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996;334:1001–9.
6. The Long Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998;339:1349–57.
7. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. N Engl J Med 1995;333:1301–7.
8. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. JAMA 1998;279:1615–22.
9. Pearson TA, Peters TD. The treatment gap in coronary artery disease and heart failure: community standards and the post-discharge patient. Am J Cardiol 1997;80(8B):45H–52.
10. Stafford RS, Blumenthal D, Pasternak RC. Variations in cholesterol management practices of U.S. physicians. J Am Coll Cardiol 1997;29:139–46.
11. Boekeloo BO, Becker DM, LeBailly A, Pearson TA. Cholesterol management in patients hospitalized for coronary heart disease. Am J Prev Med 1988;4:128–32.
12. Northridge DB, Shandall A, Rees A, Buchalter MB. Inadequate management of hyperlipidaemia after coronary bypass surgery shown by medical audit. Br Heart J 1994;72:466–7.
13. The Clinical Quality Improvement Network (CQIN) Investigators. Low incidence of assessment and modification of risk factors in acute care patients at high-risk for cardiovascular events, particularly among females and the elderly. Am J Cardiol 1995;76:570–3.
14. ASPIRE Steering Group. A British cardiac society survey of the potential for the secondary prevention of coronary disease: ASPIRE (action on secondary prevention through intervention to reduce events). Heart 1996;75:334–42.
15. Bramlet DA, King H, Young L, Witt JR, Stoukides CA, Kaul AF. Management of hypercholesterolemia: practice patterns for primary care providers and cardiologists. Am J Cardiol 1997;80:39H–44.
16. McBride P, Schrott HG, Plane MB, Underbakke G, Brown RL. Primary care practice adherence to national cholesterol education program guidelines for patients with coronary heart disease. Arch Intern Med 1998;158:1238–44.
17. Frolkis JP, Zyzanski SJ, Schwartz JM, Suhan PS. Physician noncompliance with the 1993 National Cholesterol Education Program (NCEP-ATPII) guidelines. Circulation 1998;98:851–5.
18. Sueta C, Chowdhury M, Boccuzzi SJ, et al. Analysis of the degree of undertreatment of hyperlipidemia and congestive heart failure secondary to coronary artery disease. Am J Cardiol 1999;83:1303–7.
19. LaBresh KA, Owen P, Alteri C, et al. Secondary prevention in a cardiology group practice and hospital setting after a heart-care initiative. Am J Cardiol 2000;85:23A–9.
20. Watt P, Gecker DM, Salaita K, Pearson TA. Hypercholesterolemia in patients undergoing coronary bypass surgery: are they aware, under treatment, and under control. Heart Lung 1988;17:205–8.
21. Madlon-Kay DJ. Family physician recognition and treatment of severe hypercholesterolemia. J Fam Pract 1987;24:54–6.
22. Cohen MV, Byrne M, Levine B, Gutowski T, Adelson R. Low rate of treatment of hypercholesterolemia by cardiologists in patients with suspected and proven coronary artery disease. Circulation 1991;83:1294–1304.
23. Giles WH, Anda RF, Jones DH, Serdula MK, Merritt RK, DeStefano F. Recent trends in the identification and treatment of high blood cholesterol by physicians: progress and missed opportunities. JAMA 1993;269:1133–8.
24. Schrott HG, Bittner V, Vittinghoff E, Herrington DM, Hulley S. Adherence to national cholesterol education program treatment goals in postmenopausal women with heart disease: the heart and estrogen/progestin replacement study (HERS). JAMA 1997;277:1281–6.
25. Hoerger TJ, Bala MV, Bray JW, Wilcosky TC, LaRosa J. Treatment patterns and distribution of low-density lipoprotein cholesterol levels in treatment-eligible United States adults. Am J Cardiol 1998;82:61–5.
26. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, β-blockers, and lipid-lowering medications before recurrent acute myocardial infarction: missed opportunities for prevention? Arch Intern Med 1999;159:561–7.
27. Lai LL, Poblet M, Bello C. Are patients with hyperlipidemia being treated? S Med J 2000;93:283–6.
28. Jacobson TA, Griffiths GG, Varas C, Gause D, Sung JC, Ballantyne CM. Impact of evidence-based "clinical judgment" on the number of American adults requiring lipid-lowering therapy based on updated NHANES III data. Arch Intern Med 2000;160:1361–9.
29. Schectman G, Hiatt J. Drug therapy for hypercholesterolemia in patients with cardiovascular disease: factors limiting achievement of lipid goals. Am J Med 1996;100:197–204.
30. Marcelino JJ, Feingold KR. Inadequate treatment with HMG-CoA reductase inhibitors by health care providers. Am J Med 1996;100:605–10.
31. Allison TG, Squires RW, Johnson BD, Gau GT. Achieving national cholesterol education program goals for low-density lipoprotein cholesterol in cardiac patients: importance of diet, exercise, weight control, and drug therapy. Mayo Clin Proc 1999;74:466–73.
32. Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. J Gen Intern Med 1999;14:711–17.
33. Pearson TA, Laurora I, Chu H, Kafonek S. The lipid treatment assessment project (L-TAP). Arch Intern Med 2000;160: 459–67.
34. NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Report of the National Cholesterol Education Program expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Arch Intern Med 1988;148:36–69.
35. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Summary of the second report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. JAMA 1993;269:3015–23.
36. American Heart Association. 2000 Heart and stroke statistical update. Dallas, Texas: American Heart Association, 1999.
37. Sempos C, Fulwood R, Haines C, et al. The prevalence of high blood cholesterol levels among adults in the United States. JAMA 1989;262:45–52.
38. Cleeman JI. Adults aged 20 and older should have their cholesterol measured. Am J Med 1997;102(2A):31–6.
39. Garber AM. Cholesterol screening should be targeted. Am J Med 1997;102(2A):26–30.
40. Frohlich J, Fodor G, McPherson R, Genest J, Langner N. Recommendations for the management and treatment of hypercholesterolemia: report of the working group on hypercholesterolemia and other hypercholesterolemia. Can Med Assoc J 2000;162:1441–7.
41. Betteridge DJ, Dodson PM, Durrington PN, et al. Management of hyperlipidaemia: guidelines of the British Hyperlipidaemia Association. Postgrad Med 1993;69:359–69.
42. Pyorala K, De Backer G, Graham I, et al. Prevention of coronary heart disease in clinical practice: recommendations of the task force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension. Atherosclerosis 1994;110:1212–61.
43. Garber AM, Browner WS. American college of physicians guidelines for using serum cholesterol, high-density lipoprotein cholesterol, and triglyceride levels as screening tests for preventing coronary heart disease in adults. Ann Intern Med 1996;124:515–17.
44. Marcus AO. Rationale for effective treatment of hypercholesterolemia. Am J Cardiol 1996:78(suppl 6A):4–12.
45. Ramsay LE, Yeo WW, Jackson PR. Dietary reduction of serum

cholesterol concentration: time to think again. Br Med J 1991;303:953–7.
46. Aquilani R, Tramarin R, Pedretti RFE, et al. Despite good compliance, very low fat diet alone does not achieve recommended cholesterol goals in outpatients with coronary heart disease. Eur Heart J 1999;20:1020–9.
47. Saskatchewan Health Services Utilization and Research Commission. Adherence to lipid-lowering medication in Saskatchewan. In: Cholesterol testing and treatment in adults. Final report. JSIRC 1995:41–5.
48. Schectman G, Hiatt K, Hartz A. Telephone contacts do not improve adherence to niacin or bile acid sequestrant therapy. Ann Pharmacother 1994;28:29–35.
49. Andrade SE, Walker AM, Gottlieb LK, et al. Discontinuation of antihyperlipidemic drugs: do rates reported in clinical trials reflect rates in primary care settings? N Engl J Med 1995; 332:1125–31.
50. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. Arch Intern Med 1990;150:841–5.
51. Nieto FJ, Alonso J, Chambless LE, et al. Population awareness and control of hypertension and hypercholesterolemia: the atherosclerosis risk in communities study. Arch Intern Med 1995;155:677–84.
52. Bairey CN, Felando MN, Klein J. Cholesterol awareness and treatment in patients with coronary artery disease participating in cardiac rehabilitation. J Cardiopulm Rehabil 1996;16: 117–22.
53. Luepker RV. Current status of cholesterol treatment in the community: the Minnesota heart survey. Am J Med 1997;102(2A):37–42.
54. Hutchison BG, Abelson J, Woodward CA, Norman G. Preventive care and barriers to effective prevention: how do family physicians see it? Can Fam Phys 1996;42: 1693–1700.
55. Tsuyuki RT, Johnson JA, Teo KK, et al. Study of cardiovascular risk intervention by pharmacists (SCRIP): a randomized trial design of the effect of a community pharmacists intervention program on serum cholesterol risk. Ann Pharmacother 1999;33:910–9.