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CHOLESTEROL POLICY AND THE PRIMARY PREVENTION OF CORONARY DISEASE: Reflections on Clinical and Population Strategies

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ABSTRACT

Despite billions of dollars spent on targeted and population-wide strategies aimed at reducing human consumption of saturated fat and cholesterol, aspects of the diet-heart connection remain a source of debate. At least part of the uncertainty arises from a growing appreciation that the relationship between dietary habits, serum lipids, and atherosclerosis is more complex than was previously thought. While we wait for answers from clinical and basic research, what is to be done? This review examines evidence about clinical policies and population strategies for the primary prevention of coronary disease, with specific reference to diet and dyslipidemias. It also summarizes some current policies and offers conclusions about broad directions for further policy development.

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INTRODUCTION

The concept of a link between coronary atherosclerosis and dietary intake of saturated fat and cholesterol is over thirty years old. It has been bolstered through the decades by international and cross-cultural comparisons (183), analyses of the diets and disease profiles of migrant populations (167), in-depth studies from metabolic wards (72), and a variety of randomized clinical trials. Yet, despite billions of dollars spent on targeted and population-wide strategies aimed at reducing human consumption of saturated fat and cholesterol, aspects of the diet-heart connection continue to be a source of debate (147, 151, 170). At least part of the continuing uncertainty arises not from ignorance but from growing appreciation that the relationship between serum cholesterol and plaque formation and growth is more complex than was previously thought (92, 109, 176). But while we wait for studies in cellular physiology and molecular biology to clarify how different dietary patterns affect different individuals' atherosclerotic risk, what is to be done? Decision-making under uncertainty is, of course, the cornerstone of policy formulation. Thus, our focus here is on clinical policies and population strategies with respect to diet, dyslipidemias, and coronary heart disease (CHD).

CLINICAL AND POPULATION STRATEGIES: COMPLEMENTARY PREVENTIVE PARADIGMS

Clinical strategies aim to identify and treat persons who may be at increased short-term risk of coronary events. In contrast, population strategies seek to influence general dietary habits, thereby simultaneously lowering individual and population-wide mean levels of atherogenic serum lipids. Whereas clinical strategies are usually initiated at the doctor-patient interface, population strategies typically involve one or more of three elements. "Social marketing" efforts involve the mass dissemination of dietary advice through broadcast or print media, or through school, workplace, or point-of-purchase programs. "Behavioral interventions" aim to promote the uptake and long-term maintenance of dietary recommendations. "Environmental interventions" include food advertising and labeling legislation, changes in agricultural policy, taxes on fatty foods, and subsidized production or purchase of low-fat foods.

Although clinical strategies seek to identify persons who have a reasonable probability of benefiting from treatment, the greatest proportion of incident

CHD occurs in persons who are at relatively low levels of absolute risk if assessed solely in terms of serum total cholesterol (TC). Use of other lipid markers may improve the efficiency of any clinical strategy insofar as detection of persons at high risk is concerned. But the fact remains that CHD is multifactorial in etiology. Alone, hypercholesterolemia accounts for roughly half of the excess CHD risk in a middle-aged man with a serum TC level of 6.2 mmol/liter (38, 163). Although the TC/high-density lipoprotein-cholesterol (HDL-C) ratio is a better predictor of risk of symptomatic CHD than either TC or low-density lipoprotein (LDL)-C levels alone (66, 91, 166), the relationship between various serum lipid markers and coronary risk is continuous and graded. Many persons will develop coronary disease who have minimally to moderately elevated risk if assessed solely with even the most sophisticated lipid markers. In this sense, clinical and population dietary strategies are complementary: Clinical programs identify those who may not be influenced by mass dietary advice but who need to attend to it most (many of whom will go on to drug therapy); population programs affect those with lower TC values who also are at risk of CHD, but they avoid the treatment burdens and costs of mass medicalization. In the following section, we review some of the clinical and community-wide policies that have been developed and disseminated with respect to diet, cholesterol and other lipid fractions, and CHD.

Impact on Surrogate and Clinical Endpoints

Surrogate or proxy outcomes are defined as measures that are related to, or that are a substitute for, more clinically relevant outcomes. For obvious reasons, biochemical surrogates have figured prominently in the "diet-heart" literature, especially in comparisons between the benefits of similar interventions. Serum TC has been frequently used as the primary outcome measure in trials of alternative strategies for providing dietary advice, and excellent overviews of the efficacy of cholesterol-lowering diets in terms of serum TC are available (40). However, a wide variety of dietary interventions have been shown to adversely affect HDL while lowering TC, underscoring the need for care in selecting surrogates. Even the most sophisticated biochemical surrogates, moreover, do not illuminate the absolute risks and benefits of cholesterol lowering, particularly given the multifactorial nature of CHD. For example, surrogate measures are rightly criticized for overstating potential benefits, yet the opposite has also occurred with angiographic surrogate endpoints in secondary prevention trials of lipid-altering strategies. Intriguingly, angiographic changes do not explain the large early reductions in coronary events observed in some trials (13), presumably because lipid lowering not only affects the atherosclerotic process, it also stabilizes plaques and alters platelet and endothelial function. These observations all argue for focusing on the outcomes of

greatest interest to patients and policymakers—coronary and noncoronary clinical endpoints, and their effects on quality and quantity of life.

Evidence Pertinent to Clinical Strategies

What experimental evidence should be available before adopting a clinical policy for the detection and management of dyslipidemias? Ideally, the evidence should have three elements: (*a*) It should be derived at the primary care level, for that is where the policy will be implemented; (*b*) it should prove that the program has an all-cause mortality impact with acceptable side-effects and morbidity benefits such that overall quality-adjusted life years are increased; and (*c*) to the extent that one is prepared to use economic factors in policy formulation, it should show that the program's incremental cost per life–year gained is comparable to other funded programs and interventions. Unfortunately, no trials have been performed in primary care settings to provide definitive evidence on these counts. This point is crucial because innumerable points of slippage occur that render the generalizability of the design of existing clinical trials questionable at best, independent of concerns about who was enrolled.

Most of the extant single-factor trials have started at the referral-center spout, not at the primary care funnel. They were sited in academic hospitals and clinics, took excellent laboratory facilities for granted, and also assumed that numerous nurses and dieticians would be available to enforce compliance. They used selected populations of volunteers with high lipid levels, usually middle-aged males, and took no account of persons at lower risk, e.g. premenopausal women and younger men, who would be tested and treated in aggressive programs, and for whom the risk-benefit ratio may be less favorable. Information about some key outcomes is also absent from existing trials. Some overall quality-of-life measures are absolutely necessary to capture, on the positive side, morbidity reductions from reduced CHD events and, on the negative side, the impact of other diseases, whether as inevitable background morbidity limiting the quality-of-life impact of CHD reductions or somehow induced by treatment. Other negative quality-of-life outcomes to be captured are the inconvenience and cost of continuing medical care, drug side-effects (if applicable), psychological labeling effects, and some measure of the disutility or positive health perceptions associated with adopting a different diet.

Of note, experience managing hypertension in asymptomatic adults suggests that detection and labeling are associated with a range of adverse psychosocial consequences, including poorer perceived health status (116, 184), greater physical symptoms and disability (116, 184), decreased time spent socializing (116), and increased illness-related absenteeism from work (27, 70, 140). Comparable effects in hypercholesterolemic adults have not been observed

(69, 85), but more research is needed. Similarly, preliminary results suggesting that health-related quality of life is unaffected by a cholesterol-lowering diet (73) need to be confirmed in light of other studies, which report loss of enjoyment of food as a primary contributor to dietary noncompliance (32, 103).

A model trial would accordingly set out two case-finding programs: one aggressive, and another more conservative. The organizers would recruit individual family physicians, or group practices, allocating the practitioners or practices randomly to one level of intervention or another. The function of trials nurses and other players would be to review the protocols with the participating primary care doctors and their office staff, not to enforce protocol compliance on the part of the patients, as such enforced compliance would exaggerate the impact of treatment. Biochemical follow-up would rely on the usual laboratories of the region. Resources for dietary therapy might be bolstered somewhat, simply to avoid unfair restraint on the potential success of the trial. But the army of trained dieticians that figure in some trials would not be in the field. There would be guidelines for family physicians to refer the patient on for endocrinologic opinions. Whether or not the referral occurred would be up to the family doctor—again, as occurs in real life—and, once a patient was referred, the specialist physician or endocrinologist would be free to follow his or her own preferred protocol. This clinical freedom would be a positive feature of such a trial, because conventional trials may underestimate effectiveness of interventions by demanding adherence to standardized drug or diet regimens even when responses are suboptimal. Patients would need to be followed for about 10 years. For simplicity, outcomes might include only three basic measures: date of death; cause of death; and regular measurements of health status (and/or quality of life) using a battery of indices. Finally, costs would be tracked using a randomly drawn subsample of patients and would include elements from the perspective of both a third-party payor and society at large (i.e. time expended by practitioners and nurses, hospitalization costs, out-of-pocket costs incurred by the patient for visits and medication, time off work, and so on).

To date, few published trials come even close to this model. Controlled trials of cholesterol screening and management in general practice have not been done, and randomized control trials (RCTs) of multifactorial screening and follow-up are rare. At least two long-term screening trials have been conducted, but these have had equivocal results. The South-East London Screening Study (162), an RCT of multifactorial screening involving 7229 men and women from two general practice groups, showed no significant changes in morbidity or mortality during a nine-year follow-up of those screened compared with those receiving conventional care. An earlier American trial of multiphasic screening also showed no demonstrable effect on CHD-related mortality after a follow-up of seven years (35). However, neither study employed a systematic

strategy for follow-up and intervention. The more recent OXCHECK Trial (81) randomly allocated 2205 men and women aged 35–64 to receive either a multifactorial CHD health check with risk factor–specific follow-up as appropriate and annual rechecks, or conventional care. Consistent with recent clinical guidelines, personal and family history of CHD, smoking status, habitual diet, blood pressure, body mass index (BMI), and TC values were assessed in all those screened. Step I dietary advice was given to all persons with a BMI >30 kg/m^2 and/or a high saturated fat or low polyunsaturated fat diet. Individualized dietary counseling and follow-up was provided for persons with a fasting TC > 6.5 mmol/liter; about 12% of intervention subjects received such counseling. After one year, mean TC was 2.3% lower in the intervention group than in the control group; this gap widened to 3.1% at year 3. A second British trial comparable in design and size, but using a more family-centered screening and treatment strategy, achieved a 4% reduction in TC over the course of one year (48), at the end of which a similar number of control and intervention patients had been given lipid-lowering drugs. These two recent studies differ from previous large multifactorial trials, such as the American Multiple Risk Factor Intervention Trial (123), the Oslo Study (74), or the Goteborg Trial (186), in that they were clinically based, included both men and women, and used no more resources than were available to general practices at the time of the trials. Thus, these results are likely to be more generalizable to clinical practice than are the results of past trials. According to Law et al (97), sustaining TC reductions of the magnitude observed in these trials for five years would reduce mortality from CHD by about 10% in persons aged 55–64 years. However, mortality projections based on risk factor changes are known to be unreliable for a single factor let alone more than one, many of the above-noted relevant outcomes are missing, and questions about the efficiency of the strategies relative to population-wide efforts remain. In the absence of ideal evidence at the programmatic primary care level, what can be said about the efficacy and safety of the cholesterol-lowering interventions they incorporate?

Almost 50 trials of cholesterol-lowering interventions aimed at reducing CHD have been reported since the mid-1960s. These trials vary considerably in terms of type of intervention (diet, drug, surgery), population (primary versus secondary prevention), degree of cholesterol lowering, duration of treatment, size, and whether or not other risk-factor interventions also were involved. Despite this heterogeneity, a relatively consistent reduction in CHD events among the clinical trials has been found.

In particular, recent trial evidence leaves little doubt about the benefit of cholesterol lowering in persons with preexisting CHD. In the Scandinavian Simvastatin Survival Study, for example, a 25% reduction in TC over 5.4 years in patients who had prior myocardial infarctions (MI) and initial TC values

between 5.5 and 8.0 mmol/liter resulted in 30% fewer deaths, 42% fewer coronary deaths, and no change in non-CHD mortality (155). Coupled with the results of the Program on the Surgical Control of the Hyperlipidemias (18), in which comparably large 12-year reductions in TC were achieved also without increases in non-CHD mortality, these findings go some way toward resolving concerns about the risk-benefit ratio of intervention in persons with established disease.

Unfortunately, because none of the primary prevention trials have been large or long enough to test conclusively for an effect on total mortality, the question of all-cause mortality and overall morbidity benefit of cholesterol lowering remains unanswered for the vast majority of persons asked to consider the Step I diet. Only very recently has a single, unifactorial, primary prevention trail had sufficient numbers of subjects and a large enough therapeutic effect to show an unequivocal effect of drug treatment on the risk of death from CHD (159a). Although a favorable trend to reduction in all-cause mortality was also demonstrated, this trial did not address dietary measures, and its mortality results should be integrated with earlier drug trials. Many quantitative syntheses of evidence from multiple sources, or meta-analyses, have already been undertaken to overcome the limited statistical power of the separate individual trials. At least ten such overviews reported in the last five years have included primary prevention trials, which are our major interest here (34, 36, 37, 62, 75, 96, 97, 107, 121, 146, 178). The principal conclusions of these overviews are summarized in Table 1; some favor primary prevention, some are more pessimistic. As Silberberg (160) points out, the divergence of opinion among overviews comes partly from commitments to different models of disease and, thus, can be attributed to nonuniform inclusion criteria and distinct approaches to the weighting of trials. With the exception of Muldoon et al (121), who focused exclusively on primary prevention trials, and Truswell (178), who reported only on dietary interventions, all of the analyses included both primary and secondary prevention trials of cholesterol-lowering drugs and diets, and some included multiple risk factor interventions (62, 75, 178).

The latest overview, by Gould et al (62), included the largest number of trials greater than two years in length and modeled outcomes in terms of the degree of cholesterol lowering achieved. It alone has shown a consistent association between cholesterol reduction and total mortality in all trials, including all unifactorial trials, and in unifactorial secondary prevention trials (62). As in earlier meta-analyses, however, the relative risk reduction for total mortality was only about 8% and was statistically nonsignificant. Ongoing concerns about adverse effects of cholesterol lowering have been sustained by a wide variety of animal experiments and human cohort studies (60, 86, 87, 120); however, in contrast to previous observational and trial reports, Gould et al (62) found no relation between non-CHD mortality and cholesterol re-

Table 1 Meta-analyses including primary prevention trials of cholesterol lowering: principal conclusions

Author (Reference)	Summary
Holme (75)	Focused on relation between TC reduction and total mortality and CHD incidence using weighted linear regression; 2.5% reduction in CHD incidence indicated for every 1% reduction in TC; estimated that TC reduction would have to be at least 8–9% over a minimum of 2 years to reduce total mortality; claimed distinction between primary and secondary prevention trials was "artificial"
Muldoon et al (121)	Focused on excess deaths from injury in treated patients; raised questions about neurochemical effects of cholesterol lowering
Davey Smith & Pekkanen (36)	Focused on the risk of cancer among those treated with drug vs. dietary therapy; suggested a moratorium on drug use pending the outcome of large primary prevention trials
Ravnskov (146)	Cited evidence counter to the diet-heart idea; emphasized the preferential citation of supportive trials in analyses
MacMahon (107)	Estimated size of "plausible beneficial effect" of several years of cholesterol lowering on total deaths to be about 5–6%, assuming no true effect on non-CHD mortality
Davey Smith et al (37)	Ranked trials according to absolute risk of CHD in control groups; defined a threshold of 3% per year below which net harm from cholesterol lowering is likely; expressed concern that results of trials involving high-risk subjects may not be generalizable to lower-risk individuals
Cucherat & Boissel (34)	Included 11 drug and 7 dietary trials, and 1 surgical trial. Performed analysis with logOR[a] method and level of significance at 0.01. Confirmed significant reductions in nonfatal MI and fatal CHD, and no effect on total mortality. Increases in deaths due to cancer and causes other than illness were nonsignificant
Law et al (96, 97)	Examined the degree and duration of cholesterol lowering and suggested close agreement between observational and trial data; argued that trial group differences in TC need to be maintained for at least 2 years for a CHD benefit to be observed; predicted a 20–30% reduction in CHD endpoints for each 10% (0.6 mmol/liter) reduction in TC over 2–5 years
Truswell (178)	Analyzed 17 dietary trials (some of which tested mechanisms other than cholesterol lowering); found fewer deaths in intervention subjects; result stronger in 5 trials achieving >10% reduction in TC for >3 years (pooled ORs: 0.89 vs. 0.94 in all trials combined); concluded, no indication of excess all-cause mortality in dietary trials
Gould et al (62)	Used a likelihood-based method of trend analysis to assess intervention-specific effects by expressing the results of 35 trials as a function of the degree of TC lowering obtained; for every 10% reduction in TC, CHD and total mortality were reduced by 13 and 10%, respectively; TC lowering per se had no effect on non-CHD mortality; expressed concern about the use of fibrates that had specific adverse effects on non-CHD and total mortality independent of TC lowering

[a] Logarithm odds ratio.

duction. This was also true in a separate analysis for unifactorial primary prevention trials. Coupled with the finding of a significant drug class–specific adverse effect for fibrates and the recent results of the West of Scotland Coronary Prevention Study (159a), which showed absolutely no adverse effects on risk of non-CHD death over a five-year follow-up period, these more recent results do not support the notion that TC lowering per se increases the risk of mortality from non-CHD causes, at least for the range of cholesterol values represented in the trials. In a comprehensive review of cohort studies and RCTs, including unpublished mortality data, Law et al (96) also found no evidence that low or lowering TC increases mortality from any cause other than hemorrhagic stroke. They concluded that even this risk was likely to be outweighed by benefits from a lowered risk of CHD. In the ten dietary trials of greater than three-years duration reviewed by Truswell (178) (seven of which were unifactorial and three were multifactorial), both major CHD events and all deaths were significantly reduced in those treated (pooled odds ratios are 0.86 and 0.94, respectively). However, this includes four trials in the setting of secondary prevention. Where do these latest analyses leave us?

It now appears that adverse effects of low or lowered cholesterol are small, if present at all, and are probably outweighed by the benefit of fewer coronary events. Unfortunately, it is unlikely that a unifactorial primary prevention trial with a potent dietary intervention will be mounted that is large and long enough to demonstrate an all-cause mortality benefit (29). In the absence of such data, a prudent strategy would be to restrict individualized dietary therapy and cholesterol-lowering drugs to persons either with established CHD or with multiple risk factors for CHD. What, then, are the current clinical guidelines?

Current Clinical Guidelines

Clinical guidelines for the prevention of CHD through serum lipid modification have been promulgated in Europe (172), Britain (12, 159), North America (21, 23, 45, 127), and elsewhere (31, 84, 110). In the past, these guidelines varied markedly among and within countries in several respects, including target populations for case finding, tests for initial screening and follow-up, threshold values leading to further testing and treatment, and the place of other risk factors in treatment decisions. However, with ongoing debate and accumulating evidence, more convergence of opinion has emerged. We focus below on the latest policy statements from five of the most influential panels (8, 24, 46, 82, 143).

The latest statements all move toward treating people with symptomatic cardiovascular disease (CVD) at milder levels of dyslipidemia and targeting them more vigorously with diet and drug therapy than asymptomatic people. Other areas of consensus among the policies are as follows: Two or more

fasting lipid profiles are needed to confirm the diagnosis; secondary causes of dyslipidemias should be excluded; dietary therapy is the first line of intervention; and at least six months of dietary therapy should be attempted before drugs are considered. In keeping with the emphasis on global CHD risk, all of the programs encourage exercise, weight reduction, and the elimination of excessive alcohol intake and smoking where applicable. All also define the ideal diet as providing no more than 30% of calories by fat, fewer than 10% of calories by saturated fat, and less than 300 mg of dietary cholesterol per day; this diet, originally defined by the American Heart Association (AHA) (67), is the Step I of the National Cholesterol Education Program (NCEP) (45). Although all the panels recommend an intensification of dietary intervention before proceeding with drugs, only America's NCEP specifies a second level of diet therapy; the Step II diet requires a further reduction in saturated fat and dietary cholesterol to 7% of calories and 200 mg/day, respectively.

Case-finding and treatment guidelines for asymptomatic adults from the five panels are summarized in Table 2. Divergence of opinion is most apparent where trial evidence is lacking, i.e. in the detection and treatment of hyperlipidemia among women, children, and the elderly. Because policy statements rarely define what is meant by dietary "advice," "counseling," and "therapy," determining the similarities and differences in the treatment guidelines is somewhat problematic. Universal first-line therapy for hypercholesterolemia—the AHA/NCEP's Step I diet—is essentially similar to the eating pattern recommended by these groups for the general public. What then constitutes dietary therapy? According to the NCEP, therapy is defined by the setting in which the message is delivered (in this case medical), and the intensity and individualization of its delivery (45). Thus, the latest NCEP guidelines differentiate between "educating" patients about the ideal diet for all, "informing" them about the Step I diet, and initiating Step I "dietary therapy" (46). For the purpose of this review, we take "education" to represent brief reinforcement of general dietary guidelines—a zone where clinical policy serves to reinforce a population-wide policy of dietary and lifestyle education. "Advice" is defined as somewhat more intensive, generally prompted by a blood lipid measure or presence of other risk factors, and as consisting in the provision of generic information about major sources of dietary saturated fatty acids and cholesterol and in guidance as to how one might use dietary means to lower blood cholesterol (see Table 7 in Reference 45). This is distinct from "therapy" or "counseling," which entails a detailed and individualized review of a patient's dietary habits with a corresponding therapeutic plan and ongoing follow-up (45).

For reasons of cost and convenience, all the programs recommend using a random, nonfasting TC as the initial screening test. To increase predictive

accuracy, the NCEP has added an assessment of HDL-C. Numerous observational studies have identified the TC/HDL-C ratio as the optimal lipid predictor of clinical outcome (3, 26, 66). The ratio also appears to be a better discriminator than TC alone of those who will respond favorably to a cholesterol-lowering diet. In the Leiden Intervention Trial, for instance, TC/HDL-C was significantly more sensitive than TC alone in distinguishing between subjects who had coronary lesions that grew during two years of vegetarianism and those who had lesions that either remained unchanged or regressed (2). However, using detailed diet composition data and serum lipid values for 155 subjects, Hegsted et al (72) were able to explain only 40% of the variation in subjects' HDL-C values. Thus, the relationship between diet and HDL-C remains modest for most patients.

By far the most important change in the recent policies is the increased emphasis on CHD risk status as a guide to screening, in some cases, and, in all cases, to the type and intensity of cholesterol-lowering therapy prescribed. Although the mechanics and timing of risk assessment differ somewhat across the groups (e.g. the European Task Force advocates the use of a Framingham-based coronary risk chart versus simple risk factor counts), the principle remains the same. Implicit in this shift to risk-sensitive policies is a delay in the use of drug therapy in most young adult men and premenopausal women with high LDL-C levels who are otherwise at low short-term risk of CHD. Some authors, including the Canadian Task Force (CTF), have argued vigorously in favor of excluding these population subgroups at the screening rather than at the treatment stage on the grounds that screening makes sense only if the results affect decisions about therapy (24, 78, 127). Certainly, it seems inefficient from a societal standpoint to screen and treat low-risk persons, and to expose them to the costs and inconvenience of therapies when there is an extremely low probability of short-term benefit.

Few now argue that the move toward delaying treatment in low-risk individuals is unwise. However, since the risk of CHD rises dramatically with age, one consequence of the risk-sensitive guidelines is the increased propensity to treat elderly persons who are otherwise in good health. The conundrum here is obvious: The attributable risk of dyslipidemias in elderly persons is potentially very high, but little trial evidence has accrued to support treatment of elderly asymptomatic individuals. Trials of lipid-lowering in the elderly, currently being undertaken in the United States, should help to clarify the role of therapy in this growing subgroup.

As pointed out by both the NCEP and the British Heart Association (BHA), the use of estrogen replacement therapy (HRT) by postmenopausal women may obviate the need for cholesterol-lowering drugs. Use of oral estrogen has a favorable effect on the serum lipid profile by reversing an age-related increase in LDL-C and increasing HDL-C by 10–15% (111). In a meta-analysis com-

Table 2 Case-finding and treatment guidelines for asymptomatic persons from five expert panels

Panel (Reference)	Persons entered into program	Initial cholesterol test	Minimum lipid level in mmol/liter (mg/dl)-CHD risk thresholds for dietary advice, dietary therapy	Minimum threshold for drugs
Task Force of the ESC, EAS, and ESH (143)	Aged ≥30 yr, with the following priority given 1. With multiple CHD risk factors 2. With first-order relatives with premature CHD or other CVD 3. With asymptomatic first-order relatives at high risk of CHD	Random, nonfasting TC	•Advice: TC > 5.0 (200) •Therapy: TC > 7.0 (270) or TC > 5.0 (200) and absolute 10-yr risk > 20% if projected to age 60	TC > 7.0 (270) or lower if 10-yr risk > 20%
International Task Force for Prevention of CHD (82)	All aged ≥20 yr	Random, nonfasting TC Fasting full lipid profile for persons with diabetes or hypertension	•Single session of dietary counseling: TC 5.2–6.5 (200–250) or LDL-C 3.5–4.5 (135–175) unless patient has multiple risk factors, in which case, intensify after 3–6 mo	TC > 6.5 (250) or LDL-C > 4.5 (175) and ≥ 2 risk factors

BHA (8)	With multiple CHD risk factors, a strong family history of CHD, or clinical stigmata or a family history of hyperlipidemia	Random, nonfasting TC	•Advice: TC 5.2–6.5 (200–250) •Therapy: TC > 6.5 (250), except for those with HDL-C > 2.0 (77)	TC > 7.8 (300) or LDL-C > 6.0 (230) in persons with <2 risk factors
NCEP's Adult Treatment Panel II (46)	All aged ≥20 yr	Random, nonfasting TC and HDL-C	•Education on general population eating pattern: all tested •Advice: TC 5.2–6.2 (200–239) and HDL-C ≥ 0.9 (35) and <2 risk factors; full lipid profile for those with HDL-C < 0.9 (35) or ≥2 risk factors •Therapy: LDL-C ≥ 3.4 (130) and ≥2 risk factors or LDL-C ≥ 4.1 (160)	LDL-C ≥ 4.9 (190) for persons with <2 risk factors
CTF (24)	Men aged 30–59 yr, regardless of risk factor status Consider others with multiple CHD risk factors, or a strong family history of hypercholesterolemia or premature CHD	Random, nonfasting TC	•Advice: men aged 30–69 yr •Therapy: TC ≥ 6.2 (239) or LDL-C ≥ 4.15 (160)	TC > 6.85 (264) or LDL-C > 4.5 (173)

paring estrogen users with nonusers, use was associated with a relative CHD risk reduction of 44% (165). However, the biological actions of estrogen are complex, and the risk-benefit ratio of HRT has not been assessed by an RCT. These uncertainties mean that even with the widespread adoption of risk-sensitive guidelines, controversy about lipid screening and treatment in various adult subgroups will continue until more trials are complete (68, 77, 89, 93, 94, 164).

Recommendations regarding children and adolescents appear in two of the policy statements and, in the case of the NCEP, in a separate report (125) endorsed by the American Academy of Pediatrics Committee on Nutrition (1). The BHA advocates screening only children from families carrying the gene for familial hypercholesterolemia any time over the age of 5, the generally accepted age at which a Step I diet can be prescribed (8). The NCEP's Childrens' Panel (125) and the European Atherosclerosis Society (EAS) (82) arrived at comparable policies, both more inclusive than that of the BHA. For example, the EAS recommends screening all children over the age of 3 who have a strong family history (parent, first-degree aunt or uncle, or grandparent) of premature (aged < 60 years) CVD or a parent who has either familial hypercholesterolemia or a serum TC > 7.8 mmol/liter (300 mg/dl). A finding of TC > 5.2 mmol/liter (200 mg/dl) or LDL-C > 3.4 mmol/liter (130 mg/dl) would justify further evaluation (82). As part of their population strategies for blood cholesterol reduction, both the EAS and the NCEP recommend that all persons over the age of 2 follow a Step I diet. The guidelines for children emphasize the need to ensure that sufficient calories are provided to maintain normal growth and development, although critics have suggested that malnutrition could occasionally result (76).

Cholesterol screening policies for children have stimulated considerable debate (42, 43, 53, 95, 131, 149). Given that the adult guidelines have been revised to account for the fact that, on their own, blood lipid measures are at best modest predictors of future coronary events, the case for cholesterol screening in children is weak. It appears more sensible at present to facilitate family-wide adoption of healthful diets by discouraging detrimental eating behaviors and promoting prudent ones, beginning at an early age, through public education.

In sum, some progress has now been made toward setting clinical policies for cholesterol screening and treatment that respect evidence from both epidemiologic research and clinical trials. Not only is the increased emphasis on CHD risk as the basis for decision-making more in line with the ultimate objective of the clinical strategies as a group (i.e. to identify individuals at high risk who are likely to benefit from more intensive intervention), it has led to guidelines that are more internally consistent (64) and perhaps easier to follow than in the past. Nevertheless, some policies remain open to challenge

and debate, including the screening of young adults and children, and aggressive treatment of elderly individuals. Panels such as the CTF (24) remain wary about the extent to which the results of existing primary prevention trials have been generalized to lower-risk groups, particularly women. In our view, these deficiencies in the trial evidence strengthen the case for a targeted approach to clinical intervention and for careful community-wide promotion of dietary change.

Population Strategies: The Problem of Definition and Evaluation

Evaluating population strategies for cholesterol lowering is an exceedingly complex undertaking. As noted above, population strategies include mass dissemination of educational materials; however, media coverage will occur entirely independent of any community initiative when major agencies make policy pronouncements on dietary issues, or when studies on the relationship between diet and disease are published. The effects of behavioral interventions incorporated into a community-wide program may be difficult to separate from the effects of widespread blood screening and intervention in the clinical setting. Indeed, some community or work-site programs have incorporated blood testing for dyslipidemias, as well as individualized dietary advice that is more intense than most physicians will provide. The impact of the foregoing elements is intimately entangled with legislation about food advertizing and labeling, with changes in retail strategies, and with both market-driven and government-abetted shifts in agricultural policy. In short, one cannot easily tease apart the separate impact of specific community-based CHD programs and what might be termed the cholesterol movement with its plethora of public pronouncements from authorities of all stripes, its media coverage, and its clinical detection strategies.

General Population Policies and Trends

The modern "cholesterol movement" began gaining momentum in the 1960s. Based on broad epidemiologic evidence for the diet-heart hypothesis, American recommendations for dietary change and public policies to reduce CHD risk factors appeared as early as 1970 with the publication of the report of the Inter-Society Commission for Heart Disease Resources (83). Similar to recent advice, this report called for significant reductions in the overall consumption of fat (<35% of calories), saturated fat (<10%), and cholesterol (<300 mg/day). In 1977, the United States Department of Agriculture (USDA) assumed responsibility for a wide range of nutrition research and educational activities, including advice to the public. The first federal dietary guidelines for disease prevention, entitled "Dietary Goals for the United States," were released later

that year (181). Although its recommendations largely echoed those of earlier reports, the document was symbolically important. Official "Canadian" advice on the role of diet in CHD was released about the same time with the integration of "Nutrition Recommendations for Canadians" and "Canada's Food Guide" (124).

Evidence that consumers were listening came shortly thereafter, as sales of whole milk, eggs, and beef began to decline in both countries (142, 168, 169). As a result of public pressure, the 1970s and early 1980s also saw dramatic reductions in beef- and pork-carcass fat content (11). Not surprisingly, more visible relationships between food lobbies, the USDA, and the US Congress also began to form (130). Food-label reform initiatives began a decade later with the release of the 1988 *Surgeon General's Report on Nutrition and Health* (173). Given the North American Free Trade Agreement, it has been suggested that such initiatives may lead to international harmonization of standards, regulatory requirements, and policy in areas such as food labeling, nutrition claims, and dietary guidance (157). In the same vein, these issues are already being considered by the European Economic Community (177).

The dietary trends emerging during the 1970s and 1980s have been reinforced by health promotion coverage in the popular press, and by an upsurge of activity from voluntary health organizations such as the AHA and the Heart and Stroke Foundation of Canada, as well as by the advent of well-funded federal programs, such as the US NCEP and the Federal-Provincial Canadian Heart Health Initiative. Multiple expert panels have been convened to address the question of optimal eating patterns for the general public; as noted earlier, all have endorsed the Step I diet or its equivalent (47, 82, 135).

Evidence for the broad impact of the cholesterol movement is indeed compelling. According to national and regional surveys, the 1980s saw vast changes in cholesterol-related knowledge and behavior among US adults, particularly since the NCEP's institution in 1985 (55, 57, 132, 156). Independent cross-sectional surveys of roughly 4000 adults living in the control cities of the Stanford Five-City Project reveal a significant rise in levels of awareness of the risks and sources of dietary cholesterol (55). In similarly sized national samples, 35% of adults reported having had their cholesterol level checked in 1983 versus 65% in 1990. The proportion of respondents on physician-prescribed cholesterol-lowering diets tripled during that time, from 3 to 9%. This was temporally associated with a fall in the median range of serum cholesterol at which physicians reportedly initiated dietary therapy: 6.72–7.21 mmol/liter (260–279 mg/dl) in 1983 to 5.17–5.66 mmol/liter (200–219 mg/dl) in 1990 (156).

Since the 1960s, mean fat consumption in the United States has fallen from 40–42% of calories to less than 37%, largely because of a reduction in the consumption of saturated fat (179, 180). Coupled with a simultaneous increase

in the consumption of polyunsaturated fatty acids (from 4 to 7% of calories) and a fall in dietary cholesterol intake (from about 700 to less than 360 mg/day in men and to 260 mg/day in women), these changes have contributed to a 6% 10-year drop in the prevalence of high blood cholesterol [>6.21 mmol/liter (240 mg/dl)] among US adults—-a proportion that currently rests at about 20% (158). With these trends, and with the concomitant maelstrom of activity on the cholesterol issue, we should not be surprised that it is difficult to conclusively demonstrate the incremental effects of any community-specific intervention program let alone the component strategies within them.

Evidence for the Effectiveness of Specific Population Strategies

A large-scale controlled trial of general dietary advice was considered infeasible early on, given the results of the Diet Heart Feasibility Trial (126). Perhaps reflecting this feasibility issue, none of the unifactorial community-based programs focusing solely on cholesterol reduction have had a concurrent control group (145, 148, 161). However, three unifactorial work-site programs have had concurrent controls.

Bruno et al (16) studied the effects of eight weekly group counseling sessions with six months of periodic follow-up, and both Crouch et al (33) and Barratt et al (7) compared five sessions of individual counseling over several months with similar instruction in writing. Although all of the studies included face-to-face nutrition counseling, the courses differed in length and intensity. The most intense program produced a 6.4% reduction in TC relative to controls after three months (16). However, as seen in trials of more intensive diets (79), Bruno et al observed a parallel fall in HDL-C in treated subjects and, thus, no change in subjects' TC/HDL-C ratio. The TC reductions were 6.2 and 4.6%, respectively, after face-to-face and mail/telephone advice in a less intensive one-year study (33). There were no changes in mean TC six months after the five-week program studied by Barratt et al (7). The relative success of the earlier two studies was probably due to much higher rates of participation; both were better than 80%. Work-site programs will provide more realistic estimates of the effects of dietary education than, say, programs voluntarily attended by general citizens with a special interest in diet and CHD. Conversely, because they have a captive audience and high participation rates, work-site programs in general will tend to overestimate effectiveness relative to the average impact of community-wide education programs. Certainly, all three of these programs involved more intensive and individualized education than would be the norm in any affordable and sustainable community campaign.

Apart from these unifactorial studies, most of the evidence concerning our ability to promote community-wide dietary change has largely arisen in the context of community- and worksite-based intervention studies that aimed at

multifactorial CHD risk reduction. It is generally believed that, for such community-wide programs to be successful, complementary messages about the benefits of healthy eating should be available in the schools, in the workplace, at the point of food purchase, and through mass media. Each of these routes has particular strengths and weaknesses, as documented in several reviews (58, 59, 100, 187). Mass media campaigns, for example, raise awareness but rarely facilitate change in health behaviors unless they are accompanied by social support (54). Effective community-based programs have tended to capitalize on the strengths and complementarity of these modes of dissemination by including them all.

Of the multimodal community-based projects, the best-known are those implemented in North Karelia, Finland (141); California (49–51); Minnesota (118); and Pawtucket, Rhode Island (44). These first-generation "heart-health" demonstration projects, three of which were funded by the US National Heart, Lung, and Blood Institute, relied heavily on social learning theory (5). This theory holds that new behaviors result from exposure to significant role models and are sustained only by reinforcement at both the individual and the societal level. Accordingly, these five- to ten-year studies have included a broad range of educational and social strategies to achieve, among other risk factor modifications, widespread reductions in saturated fat intake and relative increases in the consumption of polyunsaturated fat and vegetables. Health education, systematic personal and group counseling, training of local personnel, and promotion of environmental changes to support new dietary habits have been among the interventions used. With the exception of the Pawtucket Project, nutrition information has been disseminated via local newspapers and radio, leaflets, posters and stickers, public meetings, and school and worksite campaigns. Broadcast media were not used in Pawtucket in order to test the effect of community activation or more grass roots approaches to education. In Minnesota, high levels of cooperation from community food retailers also meant that researchers had more direct access to the food supply itself (122).

Evaluation of these projects, as noted above, is complex. Recent attempts to minimize the contamination of reference populations have been met with only limited success (134). Similarly, problems arise when one tries to relate changes in a specific risk factor to CHD incidence without proper control for changes in other risk factors. With the possible exception of the North Karelia Project, follow-up times also have been too short for interregional differences in CHD event rates to emerge, let alone other disease outcomes likely to be responsive to multifactorial interventions, such as lung cancer or stroke. Other statistical hurdles facing community-based programs include too-few analysis units and sampling difficulties (117).

At present, hard outcome evidence in favor of the community-based CHD programs is available only for the North Karelia project. In 1983, Salonen et al reported a greater decline in coronary death rates between 1969–1979 in North Karelia compared with both its reference county and the country as a whole (154). Whether or not these trends have continued is not known. Subsequent reports have included only aggregate data of national trends in CHD incidence and mortality (153). Since none of the other community-based programs have progressed to a stage where similar outcomes can be reported, confirmation of these findings may not be available for several years.

As a proxy measure, information about risk factor changes is available for virtually all first-generation programs, including the three National Heart, Lung, and Blood Institute demonstration projects. Between 1972 and 1992, serum TC in men fell by 16% in North Karelians versus 12% in the reference population (182). During the first five years (the period of highest intervention intensity), the reduction was significantly greater in North Karelia, but since that time the trend has been similar in both regions. The early greater TC reduction in North Karelia was associated with a more marked reduction in the use of butter and a wider adoption of low-fat milk. This translated to a statistically significant net reduction in the consumption of saturated fat among North Karelians (139).

Cohort and cross-sectional surveys showed that intervention communities also experienced positive effects relative to controls in the Stanford Five-City Project: less weight gain (0.57 versus 1.25 kg); a 4% net reduction in both systolic and diastolic blood pressure; a 2% net reduction in plasma cholesterol; ; a 13% net reduction in smoking rate; and a 15 and 16% net reduction in composite total mortality and CHD risk scores, respectively (49, 175). At time of peak intervention in Pawtucket, cross-sectional surveys showed significant changes in mean BMI and CVD risk projections in favor of treatment (25). However, only a decline in smoking prevalence among women and an increased prevalence of reported regular physical activity reached statistical significance in cross-sectional surveys in the Minnesota Heart Health Program (105). Neither of these latter, well-funded, comprehensive programs was effective in reducing mean blood cholesterol levels. Authors for both studies identified secular trends in reference communities as the major stumbling block (25, 105). As pointed out by Goodman et al (61), results like these superbly illustrate the challenge of separating relative effects of community-based, regional, and national health promotion initiatives and imply that programs aimed at modifying one, or at the most two, risk factors with well-focused multilevel interventions may be more cost effective than attempts to achieve community-wide multi-risk factor change.

Should the Boundaries Be Blurred Between Clinical and Population Strategies?

The foregoing discussion illustrated that boundaries cannot always be readily drawn between clinical and population strategies with respect to their characteristics and impact. Indeed, some of the above-mentioned community-based programs included a blood screening component. The Pawtucket Heart Health Program, for example, conducted a two-month cholesterol education campaign during which a series of Screening, COunseling, and REferral (SCORE) events were held throughout the community (98). Even when volunteers are involved, such campaigns are expensive and can generate an enormous number of clinical referrals. Moreover, blood test results from a community-wide initiative may needlessly alarm some individuals, or they may be falsely reassuring, keeping people from seeking appropriate clinical guidance.

To the extent that community-wide initiatives veer away from broad education on diet and life-style, their sustainability arguably is diminished. In this respect, a recurrent criticism of the first-generation projects was that they relied on researchers and experts from outside the study communities. More recent second-generation projects, such as the Nova Scotia Heart Health Program (106) and the Heartbeat Wales Programme (134), have capitalized on existing resources and networks within the participating communities to provide the primary structure for program delivery.

If, as we believe, a population-wide or community-oriented strategy should eschew crossover into the realm of clinical testing and detailed individual counseling, what of the converse proposition? Should primary care practitioners provide passing dietary education to all patients regardless of clinical risk-factor profiles or lipid measures? Most expert bodies have suggested that the family physician or internist does have a role in reinforcing the educational messages about diet that patients receive outside the clinical context. However, the likely impact of these initiatives is unclear. Baron et al (6) randomly selected men and women aged 25–60 years from a group general practice in England and enrolled 368 volunteers in a study of general practice–based nutritional advice. The intervention group received 30 min of instruction from a clinic nurse about optimal body weight and diet, individually or in small groups. They also received an instruction booklet. Brief follow-up sessions were scheduled for one and three months postrecruitment. Most subjects found the diet tolerable and feasible, and there was evidence of compliance based on dietary records. However, effects on TC and LDL-C were absent in women and trivial in men compared with control subjects, and both sexes showed a reduction in HDL-C.

CHALLENGES AND OPPORTUNITIES

Compliance with Recommended Low-Fat Diets

Using the NCEP's cut-points for treatment, Denke & Grundy (41) have estimated that, among moderate-risk men responsible for their own food choices, Step I dietary therapy could conceivably rescue one half from potential drug candidacy. They project that a further one quarter will be biologically resistant to diet manipulation, and the remaining 25% will very likely be noncompliant. Given the huge number of adults being screened and considered for treatment under programs like the NCEP, the problems of biological resistance and noncompliance with dietary advice are clearly important for patients, physicians, and the health care system.

After 35 years (90), the area of biological resistance is still poorly understood (41). The latest set of regression equations developed by Hegsted et al (72), based on aggregate data from metabolic studies and field trials, explains up to 84% of the variation in serum TC values. Nevertheless, there continues to be substantial variability around regression lines. Among other factors, the authors identify differences in the baseline serum lipid concentrations of subjects and their physiologic responsiveness to diets as being key contributors to the variation (72). The accuracy of earlier equations in predicting the responsiveness of individual patients to the Step I diet has been variable (39, 41). It is hoped that the latest equations will produce more generalizable estimates of short-term responsiveness, but long-term predictability is uncertain.

Although metabolic studies and even short-term trials in free-living adults suggest that the Step I diet will produce the average 10% TC reduction implicit in most clinical guidelines, longer term trials of free-living subjects under usual practice conditions indicate that reductions of no more than about 5% are sustainable (81). Frustration on the part of patients and clinicians over small TC reductions may lead some patients who are at relatively low short-term risk of CHD to adopt more intensive diets or even to take lipid-lowering drugs, with questionable marginal benefit (144). As to more intensive regimens, such as the NCEP's Step II diet, there has been only one controlled trial involving free-living patients who chose their own meals. In it, mean TC levels fell significantly by about 5%, but, as noted above, so did HDL-C (79), leading to no change in lipid-related coronary risk. A more rigorous diet, such as the one used in the Oslo Study (<30% of energy by fat), has been shown to reduce TC by greater than 10%, to increase HDL, and (in combination with smoking cessation) to produce an impressive reduction in coronary events in men with TC levels >7.5 mmol/liter (74). However, even if comparable trial evidence were available for lower-risk subjects (which it is not), considerably higher

effort-yield ratios would be expected for these people, and from a patient's perspective, these more intensive diets may not be worthwhile.

Most frequently, patients report cost (19, 112, 119) and lack of taste and availability of healthful foods (28, 32, 103) as the key reasons for not adhering to reduced-fat diets. Other factors known to affect adherence include difficulties in changing eating habits, lack of motivation, and lack of family support (32, 103). In a recent British survey of the concordance between perceived and actual barriers to implementing a low-fat diet, Lloyd et al (103) found that loss of enjoyment was the most difficult barrier for subjects to overcome. Lack of family support was an unanticipated problem when it came to avoiding sweets. Contrary to subjects' expectations, only the cost of fresh fruits and vegetables was prohibitively high (103). Cost analyses by McAllister et al (112) confirm the fact that, although a direct substitution of healthier food items may be more costly, diets restructured according to recognized guidelines (such as the USDA's Food Pyramid or Canada's Food Guide) may in fact bring cost savings. However, these study results are likely to be limited in their generalizability, particularly to low-income groups for whom issues of access and cost are more meaningful. The prevalence of barriers to compliance such as healthy food's lack of taste also will be highly dependent on the characteristic diet of those surveyed, and on how easy it is for respondents to access palatable reduced-fat substitutes. The importance people place on "unhealthy" foods or eating behaviors will vary for social and cultural reasons as well. Without reinforcement, at least during the initial year of transition, not only are new eating behaviors difficult to adopt, they are generally not sustained (148, 171, 188). Although the Step I diet is easily achievable by some, others could well suffer adverse effects to their quality of life, at least in the short term (138).

In sum, the Step I diet is a reasonable guide to healthy eating and should remain both the dietary target for all adults and the initial strategy in individualized therapy. Yet, regardless of the method of delivery and for a variety of reasons (some physiologic), many people will not respond adequately to Step I. In the clinical setting, these individuals are potential candidates for more intensive diets and lipid-lowering drugs. Both options are of unproven benefit for all except those at high risk of CHD and have costs, inconveniences, and unknown risks and adverse effects that may be highly important to some people. These factors emphasize the value of informed decision making by patients.

Framing the Numbers: What Do Patients Think?

An issue of critical importance in preventive policy setting is finding appropriate ways of communicating information about risks and putative treatment effects to patients and the general public. This concern, moreover, extends to

physicians, who may also make inappropriate assessments of risks and benefits. Three interrelated areas warrant consideration: (*a*) methods to improve the accuracy of physicians' and patients' estimates of CHD risk before and after intervention; (*b*) the time preferences of patients; and (*c*) approaches to presenting risk and benefit information that will minimize the format effects induced by certain expressions.

The first area is important because, without such assistance, doctors systematically overestimate CHD risk in their patients (65), and patients underestimate risk in themselves (4, 133). Both have potentially serious consequences. Optimistic bias (185) in high-risk patients may contribute to poor adherence to interventions shown to be beneficial. Conversely, physicians' misperceptions may lead to overly aggressive treatment in those less likely to benefit. The fact that many physicians also overestimate the benefits of cholesterol lowering (65), and that a large proportion of hypercholesterolemic patients would want a greater risk reduction from drug therapy than lipid-lowering agents are likely to provide (102), provides further evidence of the need for better information on which to base treatment decisions. The latest clinical guidelines, which tend to promote the use of CHD risk assessment tools, may lead to a more realistic view of risks and benefits on all sides.

Second, all preventive programs involve investments: Patients suffer the inconvenience, costs, and side-effects of treatment now and over many years with the hope of averting some unpleasant future event. Most of us have strong time preferences, i.e. we wish to reap benefits sooner, while deferring costs or harms. Thus, patients need to know their patterns of potential risks and benefits as a function of time.

Lastly, several studies have shown that both physicians (10, 17, 52, 128) and patients (80) respond more favorably to a preventive intervention when its associated benefits are described in terms of a relative risk reduction, as opposed to a corresponding absolute risk reduction. As Hux & Naylor point out, one approach to overcoming this problem is to require that published study summaries report efficacy data in multiple formats (80). Ensuring that patients also see multiple measures of benefit will be the responsibility of physicians.

In sum, the perceptions of physicians and patients, as well as patient preferences, play an important role in ensuring that the right people agree to cholesterol-lowering therapy in the clinical setting; more attention needs to be paid to this point in research, practice, and policy setting.

Implementing Cholesterol Policy: What Do We Know?

For many reasons, the simple dissemination of clinical guidelines has seldom done much to guide practice; some reasons relate to the guidelines themselves, and others relate to the recipients and the environments in which they work

(63, 104). Moreover, those responsible for implementing public policy face a different set of challenges. An awareness of these barriers, coupled with uncertain patient compliance, allows one to appreciate why the actual yield from many preventive programs is considerably less than enthusiasts would have us believe (14).

IMPLEMENTING CLINICAL STRATEGIES Although lack of awareness of the content of guidelines is one barrier to compliance, even a knowledgeable, well-motivated family physician might have trouble deciding which guidelines to follow, particularly if they practice in North America or England. Slightly divergent pronouncements have come from four separate groups in Canada alone (21–23, 127). Nor is there any assurance that the guidelines will be comprehensive and clear. For example, the CTF on the Periodic Health Examination grades its recommendations as to inclusion in the periodic health examination as follows: A = good evidence for inclusion; B = fair evidence for inclusion; C = poor evidence for inclusion, but recommendations may be made on other grounds; D = fair evidence for exclusion; and E = good evidence for exclusion. Given a C recommendation, what is the practitioner to do?

Further confusion is created in the minds of clinicians because some guidelines are not internally consistent. This can be clearly shown by measuring the recommendations of the first Adult Treatment Panel of the NCEP against eight-year cumulative risks of any CHD event from the Framingham Heart Study (114), for a variety of age, sex, and risk-factor subgroups (115). More generally, no practitioner can adequately estimate CHD risk in the context of multiple risk factors, especially given the changing event rates across sex and age brackets. Add to this the need to estimate the reduction in risk from modifying one or more risk factors, so that the most efficient (and least disruptive) risk management strategy can be devised for a given patient, and the problem is substantial. For guideline developers, the challenge comes in striking a balance between accuracy and ease of use. Although the more simplistic cholesterol guidelines are characterized by internal inconsistencies and probably lead to an overemphasis on serum lipids, the more complex guidelines are harder for practitioners to follow in a busy office. Important progress in this regard has been made in the latest set of policy statements by recommending the use of decision support tools such as the Framingham-based risk charts or software (143). These tools also provide some sense to the patient of the potential gains with various strategies and thereby abet the process of bringing the patient's perceptions and preferences into play.

Empirical evidence confirms variable adherence to clinical policies. A national survey of American adults conducted in the two-year period following the release of the NCEP's 1988 guidelines showed that fewer than one third of persons deemed to require treatment for high blood cholesterol were receiv-

ing it (57). Although physician surveys in the United States (156) and Canada (152, 174) paint a more optimistic picture of practice than chart audits do (99, 108, 150), both confirm that the general approach to cholesterol screening and treatment taken by most general practitioners in North America is considerably more conservative than that recommended by national consensus panels.

All things considered, this conservatism and focus on highest risk patients may represent a triumph of the prudence and common sense of primary care practitioners over the zeal of those involved in cholesterol policy setting. A gap in adherence to guidelines is also understandable purely from a practical standpoint. The proportion of patients who are to receive dietary therapy, with or without drug intervention, varies from one guideline to the next according to the lipid cut-points used, but scores of adults in any given family practice might be affected. In many jurisdictions, physicians lack the training and any reasonable financial incentives to become personally involved in ongoing dietary counseling. Each patient consigned to individualized follow-up is also a source of ongoing appointments and of a certain amount of laboratory testing. Lack of time is by far the most commonly cited reason for noncompliance with guidelines (9, 56, 71). Since many general practitioners already run busy practices, it is no surprise that trials of labor-intensive educational efforts to improve physician compliance with cholesterol guidelines (one including individualized feedback on practice) have resulted in only modest improvements in detection, treatment, and follow-up behaviors (15, 71).

IMPLEMENTING POPULATION STRATEGIES Those responsible for implementing population-wide cholesterol policy face different challenges. First, there is the continuing uncertainty about just what strategies should be included in any community program and what their specific value is. Second, public policy is always developed with some view to competing private interests. Representatives from the US meat and dairy industry, for example, have lobbied vigorously against cholesterol policymakers to weaken or discredit policies and pronouncements that may reduce demand for their products (130). Nestle details how the USDA and the US Congress have been pressured over the past twenty years to revise federal recommendations for meat consumption from "eat less" to "choose lean" to "have two or three servings," a shift contrary to the goal of reducing consumption of saturated fatty acids.

Third, there are both legislative and financial barriers to improving public compliance with cholesterol policy. For example, although consumers make their most important food choices at the point of purchase, government regulations in certain jurisdictions place heavy restrictions on the use of grocery store interventions, making it difficult to support consumers in their attempt to follow guidelines (30). From a public health standpoint, traditional compliance-improving strategies [which rely heavily on group education, alone or in

combination with tailored diets, goal setting, and self-monitoring techniques (113)] are too resource intensive to apply en masse. Recent trials suggest well-designed written material is a feasible alternative to individual or group instruction (88, 101, 129) and can be improved further by tailoring messages based on a simple screening questionnaire and computer software (20). More effort is warranted to reduce legislative barriers to promotion of prudent diets, and to develop more cost-effective ways of communicating nutrition information.

CONCLUSIONS

We started this review by highlighting that policy formulation invariably consists of the art of framing recommendations and taking action in the face of incomplete evidence. Fortunately, there are some areas of cholesterol policy where the evidence has become clearer, but much doubt remains. For example, the evidence strongly supports dietary and, where necessary, drug intervention to modify serum lipids in persons who have multiple risk factors or established CHD. In all other groups, individualized treatment for high cholesterol has uncertain value in prolonging or improving life. These facts have been implicitly recognized in the latest sets of clinical guidelines from various national bodies. However, the continued endorsement of screening children and younger women is hard to understand or defend, and there is ongoing uncertainty about the best testing and treatment strategies for the elderly or for younger men. Debate will continue for many years. Longer term, it may be that new molecular markers will enable a more precise definition of lipid-related atherosclerotic risks, as well as likely responses to different treatment modalities.

As to population-wide strategies to promote dietary change, a few critics—most notably Oliver (136, 137)—have argued that the putative benefits of mass dietary change are based on inferences from observational and weak quasi-experimental evidence. Most authorities, however, accept that focusing purely on clinical detection and treatment strategies will miss an opportunity to produce beneficial changes in risk profile for the majority of those who are otherwise likely to develop CHD. It is also argued, tellingly, that gradual and widespread adoption of new eating habits is less disruptive than clinically supervised changes in diet. However, even if there is a partial consensus on the merits of community-wide dietary change, there is uncertainty about how best to accelerate existing trends. Fortunately, modest dietary changes on a population-wide basis are already occurring. In the aggregate, these changes should reduce the incidence of CHD and, perhaps, other diseases (notably some forms of cancer), without severe effects on individuals and families.

In sum, the most prudent cholesterol-related policies appear to consist in the development of separate but complementary clinical and population strate-

gies. We believe the clinical strategy should focus on adults, with extremely selective testing of older children in families at risk for genetic dyslipidemias. Adult testing for dyslipidemia itself should be opportunistic and should occur on a case-finding basis in primary care rather than through mass screening outside the clinical setting or as part of some combined clinical and community strategy. Arguably, testing might better focus on those who demonstrably have the most to gain from treatment, i.e. persons with multiple risk factors or established CHD. Even if widespread and periodic testing of adults in the clinical setting is endorsed, the treatment priorities remain selective, and dietary advice is the cornerstone of intervention. There seems to be limited yield from pressing physicians into service on behalf of a population strategy, i.e. by urging them to undertake dietary education for all patients at a time when many primary care practices are already struggling to cope with guidelines for selective and individualized treatment. Moreover, the impressive shifts in eating habits across many industrialized countries illustrate that individual clinical interactions are not the drivers of change. Instead, a concatenation of factors—legislation, regulation, publicity, and education—have all contributed to positive trends during the last two decades. Continued investment in the promotion of prudent dietary norms seems well worthwhile, along with more research into the myriad metabolic, clinical, and behavioral interrelationships among diet, health, and disease.

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