Consequences of the National Cholesterol Education Program

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The expert panel report of the National Cholesterol Education Program (NCEP) provides current guidelines for detection, evaluation, and treatment of high blood cholesterol in adults.[1] Convened by the National Heart, Lung, and Blood Institute (NHLBI) in response to suggestions from a consensus conference,[2] the expert panel recommends total serum cholesterol measurements in all adults aged 20 years and older, and cholesterol-lowering treatment for persons whose low-density lipoprotein (LDL) cholesterol levels are 4.1 mmol/L (160 mg/dL) or greater and for persons with coronary heart disease or two risk factors for cardiac disease whose LDL-cholesterol levels equal or exceed 3.4 mmol/L (130 mg/dL). The consequences of applying this program to the entire adult population merit careful scrutiny.

The NCEP is endorsed by 24 national medical organizations including cardiologists, internists, family physicians, epidemiologists, dieticians, nurses, hospitals, osteopaths, life insurance directors, and pharmacists. The virtually universal acceptance of these recommendations establish them as standard medical practice. Physicians not acting in accord with the NCEP are at risk for legal action from patients who perceive suboptimal outcomes caused by failure to receive testing and treatment of hypercholesterolemia. Many physicians will concur with the recommendations. Those who disagree may nevertheless comply to reduce malpractice risks.[3] Extensive media coverage and aggressive advertising by drug manufacturers and food processors have already encouraged patient participation.

To comply with the NCEP guidelines will result in considerable costs, risks of adverse psychological consequences to patients, and an increased workload burden for physicians. Estimated initial screening and classification costs for all US adults aged 20 to 74 years will exceed $12 billion (Table 1). Treatment and monitoring of an estimated 117,572,000 hypercholesterolemic patients[4] will incur additional costs. Twenty-five percent of persons will be labeled as diseased and an additional 25% at risk for disease.[1] The effects of labeling asymptomatic patients hypercholesterolemic are uncertain. Studies of asymptomatic hypertensive patients, however, suggest that labeling is associated with increased absenteeism from work,[6] psychiatric ill health,[7] and increased hostility.[8]

Following the NCEP guidelines will increase physician workload. During the first year of screening and treatment, full implementation of the NCEP recommendations will require more than 15 additional daily office visits per 1000 adult patients (Table 2). This screening program, therefore, is warranted only if the serum cholesterol measurement is reliable and if therapy is safe and lowers both mortality and morbidity.

The interpretation of routine measurements of serum cholesterol is complicated by large variations among laboratories. Although differences are partially due to different methods used to test cholesterol, considerable variations occur even among laboratories using the same method. The National Institutes of Health Laboratory Standardization Panel specifies that all laboratories measuring cholesterol levels achieve both a coefficient of variation and an accuracy of 5% or less from the true value. These standards are met by only about one half of the laboratories.[9] Five thousand laboratories received a blood specimen whose correct cholesterol value was 6.8 mmol/L (262.6 mg/dL), but reported values ranging from 4.8 to 9.8 mmol/L (187 to 379 mg/dL).[9] Accuracy of derived LDL-cholesterol measurement is even less than that of total cholesterol.[10]

The major impetus for the NCEP guidelines was the Lipid Research Clinics Coronary Primary Prevention Trial, which compared cholestyramine with placebo.[11] The trial included 3806 men aged 35 to 59 years whose serum cholesterol after dietary intervention was at least 6.8 mmol/L (265 mg/dL), and whose LDL-cholesterol was

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TABLE 1. ESTIMATED INITIAL COSTS TO SCREEN AND CLASSIFY HYPERCHOLESTEROLEMIA IN 133,605,000 US ADULTS AGED 20 TO 74 YEARS

Group	No. (in 1000s)* (%)	Tests (in 1000s)†	Office Visits in Addition to Index Visit‡	Costs § (in $1000s)
Desirable levels <5.2 mmol/L (200 mg/dL)	57,450 (43)	Total cholesterol, 57,450 tests	57,450	2,577,781
Borderline-high levels 5.2-6.2 mmol/L (200-239 mg/dL) without CHD or 2 risk factors	21,376 (16)	Total cholesterol, 42,753 tests	42,753	1,918,327
Borderline-high levels 5.2-6.2 mmol/L (200-239 mg/dL) with CHD or 2 risk factors	18,705 (14)	Total cholesterol, 18,705 tests LDL cholesterol, 37,410 tests	37,410	2,901,894
High values >6.2 mmol/L (240 mg/dL)	36,073 (27)	Total cholesterol, 36,073 tests LDL cholesterol, 72,146 tests	72,146	5,596,364
			Total	12,994,366

CHD—coronary heart disease.
**Estimates from Sempos et al[4] and NCHS.[5]*
†Using NCEP guidlines.[1]
‡Assumptions: (1) initial screening at index visit for purpose other than cholesterol testing, and (2) additional visits required to explain findings and or initiate treatment.
§Based on informal survey of 14 family medicine clinics in 14 states distributed throughout United States.

Test	Mean Cost $	Range $
Total cholesterol	16.62	6.50–34.00
LDL	41.01	22.00–73.90
Limited office visit, established patient	28.25	20.00–45.00

at least 4.9 mmol/L (190 mg/dL). The dietary intervention was continued throughout the trial in both groups. The group receiving cholestyramine had an 11.8% reduction in total serum cholesterol levels and a decrease in mortality from coronary heart disease of 2% to 1.6% (statistically not significant) over a 7-year period. All-cause mortality was nearly identical (3.7% and 3.6% in the control and cholestyramine-treated groups, respectively). The major benefit for the cholestyramine-treated group was an attributable risk reduction of 1.5% for definite nonfatal myocardial infarctions. This group, however, experienced a trend for increased gastrointestinal cancers. The Helsinki Heart Study[12] in which 4081 asymptomatic hypercholesteremic men aged 40 to 55 years were randomly assigned to receive either a placebo or gemfibrozil obtained similar results. The gemfibrozil-treated group had an attributable risk reduction for definite nonfatal myocardial infarction of 1.31% over the 5 years of the study and statistically insignificant differences from the placebo group in cardiac and all-cause deaths. In this study, too, there were trends for more adverse consequences in the group receiving active treatment when compared with those given placebo.

The cholesterol intervention trials were limited to men within a narrow age band, but results were extrapolated to all persons aged 20 years and over. The extrapolation may be unwarranted, however, because women have less morbidity from coronary heart disease than do men and tend to be older when they develop symptoms; health effects of cholesterol-lowering treatment in women are unknown. In the elderly, total cholesterol levels appear not to predict coronary heart disease, cardiovascular mortality, or overall mortality.[13] Furthermore, in all age groups there is an association between low cholesterol levels and increased mortality.[13,14]

Dissent from the NCEP is beginning to appear but has received little attention from the media and has not yet affected the increasing demand for cholesterol testing and treatment from the general population. After a thoughtful and comprehensive review of the evidence, Garber and colleagues[10] recommend individualized testing and treatment with optional screening in women and the elderly. The Royal College of Physicians rejected cholesterol screening for the United Kingdom, concluding that "screening programs in which doctors approach apparently healthy individuals to make them patients for a lifetime, ethically must insure that treatment facilities are available, that treatment is of proven efficacy and that it

TABLE 2. ESTIMATED OFFICE VISITS PER 1000 PATIENTS TO SCREEN FOR, CLASSIFY, AND MANAGE HYPERCHOLESTEROLEMIA DURING THE FIRST PROGRAM YEAR

Group	Number of Patients*	Visit Function†	Number of Visits‡
Desirable levels <5.2 mmol/L (200 mg/dL)	430	Give test results, dietary advice, return 5 y	430
Borderline-high levels 5.2–6.2 mmol/L (200–239 mg/dL) without CHD or 2 risk factors	160	Give initial test results and repeat cholesterol test	320
		Second test result, dietary advice, and return 1 y	
Borderline-high levels with CHD or 2 risk factors and those with high values >6.2 mmol/L (240) mg/dL)	410	Give initial test results and schedule 2 LDL cholesterol tests	410
		Give results of LDL tests, clinical evaluation, and begin step 1 diet	410
		Recheck LDL cholesterol at 4–6 wk and 3 mo	820
		10% respond. Two additional quarterly monitoring visits	123
		Nonresponders given step 2 diet	369
		Recheck LDL cholesterol at 3–4 wk and 3 mo	738
		10% respond. Measure LDL cholesterol and 1 additional quarterly monitoring visit	37
		Begin drug therapy on nonresponders and recheck LDL cholesterol at 4–6 wk and 3 mo	644
		Total visits/1000 patients	4301

CHD–coronary heart disease.
**Estimates from Sempos et al[4] and NCHS data.[5]*
†Assuming initial screening at index visit for purpose other than cholesterol testing and following NCEP guidelines.[1]
‡Additional visits for adverse consequences of dietary and or drug treatment not estimated.

does more good than harm. These requirements have not yet been satisfied by cholesterol screening."[15] The Committee on Nutrition 1988–1989 recommends against universal cholesterol testing in children because improvements in cholesterol levels from diet are likely to be obscured by errors of measurement.[16] In a recent editorial in the *Journal of the American Medical Association*[17] Palumbo states that "at this point to avoid bankrupting our health care system and medical credibility, clinical judgement based on age, sex, family history and other risk factors must be emphasized as a necessary component of the NCEP for individuals older than 60 years and, in fact, for those of all ages."

A change in the course recommended by the NCEP is needed but will be difficult to achieve. Cholesterol screening in physicians' offices is becoming established, and it is available even at supermarkets. The minimal decrease in morbidity in middle-aged men treated with cholesterol-lowering drugs does not warrant the costs and potential adverse consequences to patients, their physicians, and the general public. We call on the NHLBI to convene an expert panel to reconsider the issues at stake in universal cholesterol screening. National medical organizations should reconsider their unqualified endorsement of this national program.

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