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One of the most striking pieces of medical news in the 1980s revealed the connection between high blood cholesterol and a person’s likelihood of developing coronary artery disease. In 1985, the National Heart, Lung, and Blood Institute of the National Institutes of Health began the National Cholesterol Education Program, whose goal was to develop a national policy for reducing serum cholesterol. However, the panel that convened to formulate recommendations for screening and treatment was instructed not to consider cost in its deliberations. As Alan Garber and Judy Wagner point out in this article, failure to include costs in the development of guidelines such as these can have ‘far-reaching, unanticipated effects.” This point is especially relevant to the new Agency for Health Care Policy and Research (AHCPR), which was formed as part of the 1989 budget reconciliation law. One of AHCPR’s express mandates is to develop condition-specific treatment guidelines for nationwide use. “If the AHCPR guidelines show the same disregard for costs” that the cholesterol guidelines showed, the authors state. “they cannot be expected to guide health dollars to their most effective use.” Garber, a general internist, received his medical degree from Stanford and a doctoral degree in economics from Harvard. He is an assistant professor of medicine at the Stanford Medical School, a staff physician for the Department of Veterans Affairs, and a research associate at the National Bureau of Economic Research in Stanford, California. Garber’s research interests include technology assessment, evaluation of screening programs, and health care financing. Wagner is a senior associate at the U.S. Office of Technology Assessment, where she has been since 1982. She holds a doctorate in environmental systems engineering and public finance from Cornell University. Her last published article in Health Affairs was a commentary on well-child care.
In the past year, the federal government officially entered a new line of business: the development and dissemination of medical practice guidelines. The federal legislation that established the Agency for Health Care Policy and Research (AHCPR) also created within AHCPR a new Office of the Forum for Quality and Effectiveness in Health Care. The legislation directs the forum to sponsor panels to develop treatment- or condition-specific practice guidelines for use in patient care, educational programs, and quality assurance. Money to support the effort comes from the Medicare trust funds, and Medicare program administrators are expected to use the guidelines as appropriate.

This law marks the first time that the federal government has received a legislative mandate to develop clinical guidelines, but guideline development and dissemination are hardly new to the federal health establishment. The National Institutes of Health (NIH) have sponsored consensus development conferences since 1977, the principal products of which are often guidelines for practicing physicians. From time to time, individual NIH institutes and other health agencies such as the Centers for Disease Control and the Office of Disease Prevention and Health Promotion have sponsored the development and publication of guidelines that are clearly intended to influence clinical practice. This is the first time, however, that the federal government is explicitly directed to use the guidelines it develops as means to control medical practice.

Although the law does not specify cost containment as a goal, the public expects that the resulting guidelines will not only improve the quality of medical care but will also reduce health care costs. Proponents believe that medical practice guidelines can reduce health outlays by identifying and labeling as unacceptable medical practices that are clearly ineffective. A number of studies showing large variations in the use of medical services across geographic regions implicitly support this notion of waste in the system. Even studies that claim to find evidence of clearly ineffective practices, however, reveal that they may be less common than medical practices whose appropriateness is questionable. A study of the appropriateness of coronary artery bypass surgery in three hospitals found that 14 percent of the operations were performed for inappropriate reasons, but more than twice as many were performed for equivocal reasons.

The overall magnitude of clearly ineffective care is unknown, but it is likely that it is small compared with the frequency with which medical care of uncertain or untested efficacy is delivered. To meet the public's demand for cost containment, developers of guidelines must ultimately address the more important questions of medical practices that are not clearly ineffective but may not be cost-effective. Then the paramount issue will be how and when costs will be considered in the
process of developing guidelines.

AHCPR is currently developing the first seven sets of guidelines under its new authority, and the process, which will undoubtedly evolve over time, has been described only sketchily. Apparently, costs will be considered somehow, but a recent statement by the administrator of AHCPR is silent on this point, and the panels do not include any members representing groups, such as employers or health insurers, with a direct interest in cost containment.

One key concern of AHCPR is that the guidelines be “acceptable” to medical practitioners. Insofar as some influential practitioners resist considerations of cost in decisions governing medical practice and to the extent that acceptability is important, consideration of costs will be limited. In light of these possibilities, it is instructive to examine what can happen when an expert group sets out to develop guidelines for medical practice without a clear mandate to consider costs, without any formal process for obtaining cost data, and without any members whose expertise or interest resides in the area of health care costs.

The National Heart, Lung, and Blood Institute (NHLBI) organized the National Cholesterol Education Program (NCEP) in 1985 with the goal of developing a national policy for cholesterol reduction in the United States. As part of that program, an Adult Treatment Panel (ATP) was appointed to develop recommendations for screening adults for elevated cholesterol levels and for preventive treatment when necessary. ATP membership consisted of specialists in lipid metabolism, cardiology, endocrinology, epidemiology, dietetics, and public health. ATP was directed not to consider costs in making its recommendations. The panel issued its guidelines in 1987; NIH and other participating organizations undertook a nationwide campaign to alert physicians and the public to the guidelines, which were published in the January 1988 issue of the Archives of Internal Medicine.

In this article, we describe the ATP guidelines for detection, evaluation, and treatment of high blood cholesterol in adults. We then review the evidence on the effectiveness and risks of cholesterol reduction in specific groups of adults. Finally, we estimate the national costs of fully implementing the ATP guidelines for adult Americans who do not have symptoms of heart disease. Our calculations suggest that in health, as in other areas of public interest, questionable public policies ensue from failure to consider costs.

The ATP Guidelines

The ATP guidelines represent an ambitious attempt to lessen illness
and death associated with coronary heart disease (myocardial infarction and other disorders caused by blockages in the coronary arteries). Because coronary heart disease occurs at all adult ages and among both men and women, the screening recommendations are inclusive: all adults, age twenty and older, are to have their blood cholesterol level measured at least once every five years. If the (serum) cholesterol level is 200 mg/dl or greater, the test is repeated. If the average of at least two serum cholesterol levels is elevated, further testing is performed to estimate the low-density lipoprotein (LDL) level. For persons who have either a history of coronary heart disease or two cardiac risk factors and an LDL level of 130 mg/dl or greater, a cholesterol-lowering diet is recommended. The same recommendation is made for persons who have fewer than two risk factors and an LDL level of 160 mg/dl or greater.

Drug therapy, according to the NCEP, should be considered after six months if diet has failed to lower either the LDL or the total cholesterol to an acceptable level. For men who have one (or women who have two) or more risk factors, an unacceptable LDL level is 160 mg/dl or higher; this places them in the top 25 percent of the LDL distribution; for all other men and women, an unacceptable LDL level is 190 mg/dl or higher.

The sequence of steps leading to treatment for hypercholesterolemia consists, then, of identifying individuals who have high-risk cholesterol levels and treating with medications those who do not respond to diet. ATP advises physicians to exercise discretion in initiating drug treatment in the young, the old, and women of any age, although they do not provide an alternative algorithm for these groups, and they note that all adult men and women have an increased risk of heart disease if their LDL or total cholesterol levels are elevated. Much of the criticism of the ATP guidelines focuses on the lack of strong evidence that cholesterol reduction is effective for some of these groups.

### Effectiveness Of Screening And Treatment

The rationale for a national effort to detect and treat hypercholesterolemia has a strong scientific basis. There is no doubt that screening will frequently lead to the discovery of high blood cholesterol levels—hypercholesterolemia usually does not cause symptoms until it is far advanced, and it may first be manifested as a fatal heart attack. Hypercholesterolemia, as it is usually defined, is very common; about half of adult Americans have blood cholesterol levels that are undesirably high.

The primary reasons for screening, of course, are that people found to have the risk factor are indeed at increased risk of disease and that early intervention can prevent the disease. An extensive array of scientific
information, including laboratory experiments, animal studies, and clinical and epidemiological studies of humans, have lent support to the hypothesis that high blood cholesterol is a risk factor for coronary heart disease. The hypothesis has substantial biological credibility; cholesterol is a component of the atherosclerotic deposits that block arteries supplying blood to the heart, and experiments conducted on animals have demonstrated that a cholesterol-increasing diet can promote atherosclerosis. These findings have been confirmed in humans by a number of epidemiologic studies, which found that people with high blood cholesterol levels are at high risk of later developing heart disease.

The second reason for screening is the potential benefit of early intervention. The strongest and most direct evidence of benefit from cholesterol reduction comes from randomized clinical trials. In most of these studies, middle-aged men were randomly assigned to receive active treatment, usually consisting of a cholesterol-lowering diet with or without drugs, or placebo. There are two broad classes of such trials. The first, primary prevention trials, assess the effectiveness of cholesterol reduction in preventing heart disease in persons who have not experienced heart attacks or other symptoms of heart disease. Most of the participants in such trials have been men with very high cholesterol levels (averaging 280 to 285 mg/dl, placing them at about the ninetieth percentile among middle-aged American men). Collectively, these trials have found that cholesterol reduction can prevent coronary heart disease in asymptomatic men but does not increase survival.

The second class of trials assess secondary prevention. Secondary prevention trials, in contrast to primary prevention trials, test the effectiveness of a preventive intervention in a population that already has the disease; the intervention is designed to prevent further illness and death in persons who have already suffered a heart attack or otherwise exhibited manifestations of heart disease. These trials found that survivors of myocardial infarction with very high blood cholesterol levels can prevent further symptoms of heart disease if they significantly lower their cholesterol levels. In some of these studies, the treatment of hypercholesterolemia reduced overall mortality rates. Although a number of skeptics question the effectiveness of treating high blood cholesterol after extensive atherosclerosis has developed, additional support for secondary prevention comes from studies that performed x-rays of the coronary arteries. These “plaque regression” studies demonstrate that cholesterol-lowering diets and/or medications can slow or reverse the accumulation of atherosclerotic deposits in the coronary arteries. Published primary and secondary prevention trials offer little or no information, however, about the effects of treatment on women of any
age, men with borderline cholesterol elevations, younger men, and men age sixty-five and older. For the most part, women and older men were categorically excluded from enrollment in trials, and the few trials that included any elderly men or women did not have many of them.

The decision to treat members of any of the groups that were excluded from the clinical trials, particularly the elderly, is a difficult one. That is one reason why several other sets of guidelines assign a limited role to testing and treatment of elevated cholesterol levels in such groups. Epidemiologic data must serve as the main basis for evaluating the likely effects of treatment; if an elevated cholesterol level is associated with an elevated risk of heart disease, there is at least a basis for concluding that reducing the cholesterol level would prevent heart disease. But in contrast to the plethora of data about cholesterol as a risk factor in middle-aged men, few epidemiologic studies have included large numbers of older people. For many years, it seemed that cholesterol was not a risk factor for heart disease at age sixty-five and older, but the pooled results of several epidemiologic studies suggest the contrary. Furthermore, the potential benefit from cholesterol reduction might be large, because the prevalence of coronary heart disease rises with age.

However, there is also deep skepticism about treating at these ages, since older individuals are likely to have multiple chronic diseases. These diseases may exacerbate the adverse effects of cholesterol-lowering diets and medications, unfavorably altering the balance of benefits and risks of cholesterol reduction. Furthermore, low cholesterol levels, particularly at advanced ages, may be associated with increased total mortality. Because the case for treating high blood cholesterol among elderly men and women rests upon incomplete or ambiguous epidemiologic evidence, acceptance of aggressive treatment of hypercholesterolemia in the elderly is neither uniform nor enthusiastic. NHLBI is sponsoring a trial of cholesterol reduction that is designed to provide direct evidence about the effectiveness of cholesterol reduction in the elderly, but the results of the trial will not be available for several more years.

Doubts also arise about the effectiveness of cholesterol reduction in those people who have high cholesterol levels but who, because of their age, gender, or favorable risk factor profile, have only a modest excess risk of coronary heart disease. For example, at a given cholesterol level, women tend to have substantially lower rates of coronary heart disease mortality than do men of the same age. Similarly, men whose cholesterol levels are only moderately elevated have rates of coronary heart disease that only slightly exceed the rates among men who have “desirable” cholesterol levels. In either case, the predicted decline in the risk of coronary heart disease that results from cholesterol reduction is small, at
least in the near term.

It is no accident that little is known about treating these groups. They were not included in most randomized clinical trials because the expected benefit of cholesterol reduction, on average, was smaller than for middle-aged men with very high cholesterol levels. To reliably measure a small decline in the incidence of coronary heart disease, a study would need to enroll thousands of patients or follow them for many years. Thus, the lack of information reflects the belief, at the time the clinical trials were designed, that the benefits in these groups would be relatively small. The epidemiologic data suggested that would be the case, and cost-effectiveness analyses from such data have concluded that cholesterol reduction would be much less cost-effective in these demographic groups. A recent study by Lee Goldman and colleagues found that the cost per year of life saved by low-dose lovastatin was as low as $1,600 for male survivors of myocardial infarction between the ages of fifty-five and sixty-four whose cholesterol levels were at least 250 mg/dl. For women between the ages of thirty-five and forty-four who had very high cholesterol levels (300 mg/dl or greater) but no other risk factors, the cost per year of life saved reached $1.5 million. As we argue here, the very size of the groups for which benefit is unproven means that they would account for a large fraction of the expenditures for a program for the detection and management of hypercholesterolemia.

### Expenditures Associated With The Guidelines

We estimate the expenditures associated with full compliance with these guidelines for asymptomatic adults (adults who have neither angina pectoris nor a history of myocardial infarction). The model for evaluating the expenditures is described in detail elsewhere. The number of people who would be screened is based on the projected number of Americans who do not have symptoms of heart disease in three age categories (twenty to forty-four, forty-five to sixty-four, and sixty-five and older) in 1995. We determine how many of them would require additional tests (to measure the LDL level) on the basis of the estimated distribution of cholesterol levels among asymptomatic Americans in each of these age groups. From the estimated number of persons who have elevated total and LDL cholesterol levels, complemented by information about the prevalence of other risk factors, we determine the percentage that would be eligible for dietary intervention. Finally, based on varied assumptions about the magnitude of LDL reduction from diet, we use the distribution of LDL and total cholesterol levels to determine how many would fail to achieve an acceptable LDL level after receiving the dietary intervention.
We calculate costs associated with each step of the protocol in order to estimate the overall expenditures resulting from the detection and management program. Where data on important elements of the model are unavailable, we either allow the assumed values of these elements to vary over a wide range of plausible values or make assumptions that tend to underestimate expenditures.

**Assumptions for the analysis.** The expenditures associated with the guidelines arise from initial testing, which detects high cholesterol levels (cholesterol measurements every five years for all adults and lipoprotein fractionation for people with elevated cholesterol levels), and a set of practices that are recommended for persons with high-risk cholesterol and LDL levels. These practices include further physician evaluations, dietary instruction, and medications for individuals who fail to achieve acceptable LDL levels by dieting. We assume that the prevalence of risk factors, and the associated levels of total and LDL cholesterol, are the same for all Americans in each age/sex group as in the National Health and Nutrition Examination Survey. The method for determining the presence of risk factors has been described elsewhere.24 We make the following assumptions about the costs of each component: Total cholesterol measurements cost $6.90 and lipoprotein fractionation costs $19.19, corresponding to the Medicare fee schedule prices from January 1989.25 It is possible to obtain these measurements at lower cost, but charges for testing are usually higher. Because we assume that cholesterol testing would occur as part of a patient’s visit to the physician for another purpose, our calculations do not include charges for the physician visit. Total screening expenditures include periodic retesting according to the ATP-recommended schedule. We assume that diet imposes no direct costs, an assumption that also leads to underestimates, since dietary counseling is recommended. Insofar as compliance with the guidelines leads to substitution of more expensive foods, implementation of the dietary recommendations may be costly.

The largest component of costs of the guidelines is the cost of treatment with medications for persons who fail to reach acceptable LDL levels by dieting. These costs are the product of the number of people failing diet and the costs of complying with each medication regimen. Our results assume that the dietary intervention recommended by ATP causes the average LDL level to fall by 5 percent, 10 percent, or 15 percent; 15 percent is comparable to the results of diet observed in studies of dietary control of hypercholesterolemia in institutional settings, where compliance is usually excellent. Most community-based trials of dietary treatment of hypercholesterolemia, which used interventions similar to the one recommended as part of the Adult Treatment Guidelines, have found
that diet lowers LDL levels by less than 10 percent.

Medication costs include costs of laboratory monitoring, physician visits, and the medications themselves. We use wholesale drug prices from the *Drug Topics Red Book*, April 1990 update, and estimate results for regimens using some of the most popular drugs for the treatment of high cholesterol. The drugs, and the estimated per patient annual costs of the drugs and required monitoring are sustained-release niacin ($434), gemfibrozil ($934), cholestyramine ($1,637 if purchased in bulk containers, $2,499 if purchased as single-dose packets), probucol ($1,005), and lovastatin ($1,078 if 20 mg/day is prescribed, $1,710 if 40 mg/day is prescribed, and $2,721 if 80 mg/day is prescribed). We assume that only one medication is used, although multiple cholesterol-lowering medications frequently are needed to attain the desired reduction. Actual wholesale prices may be lower than these figures, and patients can often purchase the medications for less money. However, average price paid by consumers is likely to be at least as large as the *Red Book* wholesale price.

Drug manufacturers recommend laboratory monitoring for drug toxicities; this monitoring can be costly. For example, monitoring costs exceed the costs of the drug itself in a niacin treatment regimen, and, for other medications, the laboratory costs are nearly as great. Charges for lovastatin are among the highest, and the costs associated with recommended monitoring are higher than for other drugs, reaching nearly $450 each year. Monitoring costs differ because cholesterol-lowering medications cause different side effects; for the most part, the drugs are not chemically related to one another, nor do they share a common mechanism of cholesterol reduction.

**Results.** Because the entire adult population will participate if the ATP recommendations are fully successful, the costs of screening itself will be in the hundreds of millions of dollars each year. Assuming full compliance, for young adults (ages twenty to forty-four), projected annual screening costs are about $424 million (in 1990 dollars); for the middle-aged (ages forty-five to sixty-four), $299 million; and for the elderly (ages sixty-five and older), $146 million.

The screening costs are roughly commensurate with the size of the populations tested. However, the greatest part of total expenditures is for treatment with medications, and the percentage of the population that will need medications is lower for young adults than for other age groups. Exhibit 1 shows the percentage of men and women, by risk-factor status and age category, who will require medications if diet lowers LDL levels by 5 percent, 10 percent, or 15 percent.

Few young adults (2 percent of men and 4 percent of women) have symptoms of coronary heart disease. Half of young men are asymptomatic
Exhibit 1
Percentage Of Screening Subjects Who Fail Diet, By Age, Risk Category, Sex, And Percentage LDL Reduction From Diet

<table>
<thead>
<tr>
<th></th>
<th>5 percent</th>
<th>10 percent</th>
<th>15 percent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>Age 20–44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>22%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Low risk</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Age 45–64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>24</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td>Low risk</td>
<td>13</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Age 65 and older</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>24</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Low risk</td>
<td>11</td>
<td>20</td>
<td>9</td>
</tr>
</tbody>
</table>

but have two or more risk factors, while 10 percent of asymptomatic young women have two or more risk factors. Thus, about half of young men and most young women are in the low-risk category, having neither the risk factors nor a history of coronary heart disease; only a small number of them will fail diet and need to be treated with medications.

In middle age, 66 percent of the men and 27 percent of the women are in the high-risk, asymptomatic category. A substantial fraction—14 to 24 percent of the high-risk men and 23 to 38 percent of the high-risk women—will require treatment with drugs. Because cholesterol levels are higher in middle age, many of the low-risk men and women are also subject to treatment with medications.

The elderly are about as likely to fail diet as middle-aged men or women in the same risk category. At advanced ages, though, the prevalence of coronary heart disease is high—19 percent of older men and 12 percent of older women have symptoms of coronary heart disease, compared with 11 percent of middle-aged men and 9 percent of middle-aged women. The risk profiles of elderly who remain free of coronary disease do not appear to differ substantially from those of middle-aged men and women.

Expenditures for drug therapy for the large number of asymptomatic adults who fail diet will be considerable. If diet lowers LDL cholesterol levels by an average of 10 percent, the total expenditures for men and women between the ages of twenty and forty-four range from $2.7 to $14 billion each year (Exhibit 2). Projected expenditures are approximately 25 percent lower if diet lowers LDL levels by 15 percent instead. Expenditures are slightly higher for people ages forty-five to sixty-four for the same regimen (Exhibit 2). The elderly would be responsible for only slightly lower expenditures—about $2 billion for the niacin regimen, and over $12 billion for the 80 mg lovastatin regimen (Exhibit 2). Of course,
Exhibit 2
Total Annual Expenditures, Millions Of 1991 Dollars, By Age Group, Medication, And Percentage LDL Reduction From Diet

<table>
<thead>
<tr>
<th>LDL reduction from diet</th>
<th>5 percent</th>
<th>10 percent</th>
<th>15 percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 20–44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niacin</td>
<td>3,967</td>
<td>2,705</td>
<td>2,145</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>7,683</td>
<td>5,097</td>
<td>3,950</td>
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<tr>
<td>Cholestyramine, bulk</td>
<td>13,682</td>
<td>8,959</td>
<td>6,864</td>
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<td>Cholestyramine, packs</td>
<td>20,066</td>
<td>13,456</td>
<td>10,257</td>
</tr>
<tr>
<td>Lovastatin, 20 mg daily</td>
<td>9,155</td>
<td>6,045</td>
<td>4,665</td>
</tr>
<tr>
<td>Lovastatin, 40 mg daily</td>
<td>13,786</td>
<td>9,027</td>
<td>6,915</td>
</tr>
<tr>
<td>Lovastatin, 80 mg daily</td>
<td>21,585</td>
<td>14,047</td>
<td>10,703</td>
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<tr>
<td>Probucol</td>
<td>8,171</td>
<td>5,411</td>
<td>4,187</td>
</tr>
<tr>
<td>Age 45–64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niacin</td>
<td>4,669</td>
<td>3,641</td>
<td>2,553</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>9,632</td>
<td>7,435</td>
<td>5,114</td>
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<tr>
<td>Cholestyramine, bulk</td>
<td>16,652</td>
<td>12,603</td>
<td>8,736</td>
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<td>Cholestyramine, packs</td>
<td>25,268</td>
<td>19,391</td>
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<tr>
<td>Lovastatin, 20 mg daily</td>
<td>11,069</td>
<td>8,534</td>
<td>5,855</td>
</tr>
<tr>
<td>Lovastatin, 40 mg daily</td>
<td>17,383</td>
<td>13,362</td>
<td>9,113</td>
</tr>
<tr>
<td>Lovastatin, 80 mg daily</td>
<td>27,483</td>
<td>21,085</td>
<td>14,324</td>
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<tr>
<td>Probucol</td>
<td>10,344</td>
<td>7,980</td>
<td>5,481</td>
</tr>
<tr>
<td>Age 65 and older</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niacin</td>
<td>2,939</td>
<td>2,067</td>
<td>1,609</td>
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<tr>
<td>Gemfibrozil</td>
<td>6,111</td>
<td>4,247</td>
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<tr>
<td>Cholestyramine, bulk</td>
<td>10,597</td>
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<tr>
<td>Cholestyramine, packs</td>
<td>16,103</td>
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<tr>
<td>Lovastatin, 20 mg daily</td>
<td>7,029</td>
<td>4,878</td>
<td>3,752</td>
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<td>Lovastatin, 40 mg daily</td>
<td>11,064</td>
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<td>Lovastatin, 80 mg daily</td>
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<tr>
<td>Probucol</td>
<td>6,566</td>
<td>4,560</td>
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because many more of the elderly have preexisting coronary heart disease, inclusion of symptomatic individuals would raise the projected per capita expenditures for the elderly still higher.

Total expenditures are highly sensitive to the effectiveness of diet in lowering LDL levels and to the particular drug regimen selected. The least expensive regimen, niacin, is poorly tolerated. Accumulating evidence suggests that lovastatin and related drugs (known as HMG CoA reductase inhibitors) can reduce cholesterol substantially while causing few short-term side effects. Thanks in large part to patient acceptance and physician enthusiasm, lovastatin rapidly has become the most popular cholesterol-lowering drug in the United States. Even though the long-term safety and effectiveness of these drugs are unknown, and they are likely to remain expensive, they seem destined to be the most popular treatments for hypercholesterolemia. Inasmuch as expensive drugs are chosen, the higher range of estimated expenditures may be the best estimates.
Implications For Policy

In developing its guidelines for cholesterol detection and treatment, the National Cholesterol Education Program’s Adult Treatment Panel extrapolated from evidence on the effectiveness of cholesterol reduction in middle-aged men to the entire adult population. Of necessity, many aspects of the recommendations were based on limited evidence. The ATP was not asked to consider costs, so the product of their efforts represents the judgment of a distinguished group of experts about the most effective, feasible, patient-based approach to the detection and management of hypercholesterolemia.

We believe that no aspect of the ATP recommendations has been proved to be ineffective. Yet most of the expenditures generated by the guidelines will be for indications of uncertain effectiveness. Women of all ages, young men, and elderly men have not been well represented in randomized clinical trials of cholesterol reduction. The value of treatment in these groups has been questioned, and cost-effectiveness studies that extrapolate from data from clinical trials and epidemiologic studies have concluded that, for the most part, treating hypercholesterolemia in these groups would not be cost-effective. Thus, if all Americans rigorously follow the ATP guidelines, many billions of dollars each year will be spent on treatment for hypercholesterolemia. The effectiveness of much of this treatment is uncertain and, even if proven, will not be cost-effective.

The extraordinarily high health care costs of the NCEP guidelines raise questions about how and by whom guidelines for medical practice should be developed, while they provide lessons for guideline development more generally. NCEP is a creation of the National Heart, Lung, and Blood Institute, whose mission is to conduct biomedical research and to transfer the results of new information to the medical community. Its function is not to make decisions about the allocation of health care dollars. Yet, in fulfilling its mission of disseminating medical research, NCEP has implicitly recommended greatly increased health expenditures, with uncertain benefits for specific groups of adults. Other federal programs (notably Medicare and Medicaid), private insurers, and the public itself will be asked to pay for the interventions recommended under the NCEP guidelines.

If the AHCPR guidelines show the same disregard for costs, they cannot be expected to guide health care dollars to their most effective uses. Clinical expertise may be all that is needed to produce guidelines that proscribe clearly ineffective or harmful practices. There can be no doubt that such practices exist and should be avoided.

But the more difficult challenge for guidelines development is clinical
practices whose effectiveness is small or unknown, particularly those practices whose costs are large in relation to the anticipated health benefits. Our calculations illustrate the consequences of implementing guidelines that are designed without attention to costs. As a program of an NIH institute, NCEP never had a mandate to consider how its authoritative recommendations regarding medical practice might change the allocation of health care dollars. AHCPR clearly does have such a mandate. If it interprets its mandate narrowly, seeking only to expose and put a stop to useless practices, its contribution to US. health care will fall far short of its potential.

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NOTES


2. AHCPR defines practice guidelines as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.” Agency for Health Care Policy and Research, Program Note, August 1990.

3. Subsection (d) (103 Stat. 2190) of the law directs the secretary of health and human services to provide for the use of the guidelines produced under the law to improve the quality, effectiveness, and appropriateness of care for Medicare beneficiaries.


7. J.J. Clinton, “From the Agency for Health Care Policy and Research,” Journal of the American Medical Association 265 (1991): 1508. Most panel members are subspecialty physicians with expertise in the clinical areas pertinent to the technologies and diseases under evaluation. For example, the fourteen-member panel on guidelines for benign prostatic hyperplasia includes nine urologists, one family practice specialist, two internal medicine specialists, one radiologist, and one nurse. Although experts in economics, cost-effectiveness analysis, and related areas are participating in the methodology development, they are not represented on most of the panels.


11. The risk factors are: male sex, family history of premature coronary heart disease, current cigarette smoking, hypertension, low level of high-density lipoprotein (HDL) cholesterol, diabetes mellitus, history of definite cerebrovascular disease or occlusive peripheral vascular disease, and severe obesity.


16. The American College of Physicians, for example, does not recommend routine cholesterol testing above age seventy. The U.S. Preventive Services Task Force only recommends consideration of drug therapy of hypercholesterolemia for middle-aged men; see U.S. Preventive Services Task Force, Guide to Clinical Preventive Services (Baltimore, Md.: Williams and Wilkins, 1989). A 1989 King’s Fund consensus conference reported that “[t]he panel is not convinced that offering blood cholesterol testing to all individuals is justified” and called for selective testing on the basis of risk factors; see Consensus Statement, “Blood Cholesterol Measurement in the Prevention of Coronary Heart Disease,” Lancet 2 (1989): 115–116. A joint commission of the Ontario Ministry of Health and the Ontario Medical Association also called for a limited role for testing and treatment of hypercholesterolemia; see A. Basinski et al., Detection and Management of Asymptomatic Hypercholesterolemia (Toronto: Ontario Ministry of Health, 1989).

17. T.A. Manolio et al., “Cholesterol and Heart Disease in Older Persons and Women:


