Implications of Changing National Cholesterol Education Program Goals for the Treatment and Control of Hypercholesterolemia

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BACKGROUND: Modifications to the National Cholesterol Education Program (NCEP) guidelines lowered optional low-density lipoprotein cholesterol (LDL-C) treatment goals.

OBJECTIVE: We evaluated the implications of widely adopting these optional goals in clinical practice.

DESIGN AND PARTICIPANTS: We performed a cross-sectional study using 1999 to 2002 data from 3,281 U.S. adults aged 20 to 79 years participating the National Health and Nutrition Examination Survey.

MEASUREMENTS: The primary outcomes were the proportions of adults whose fasting LDL-C levels exceeded NCEP recommended and optional targets from 2001 and 2004. We used survey weights to estimate the size of the U.S. population exceeding targets. We examined outcomes for 4 coronary disease risk subgroups described by the NCEP.

RESULTS: Low-density lipoprotein cholesterol values exceeded 2001 NCEP goals for 30.0% of adults, and 35.8% had levels above optional 2004 goals. An estimated 24,900,000 individuals (14.2%) exceeded 2001 thresholds for drug therapy, 46,200,000 (26.3%) exceeded optional 2001 thresholds for drug therapy, and 56,500,000 (32.2%) were above the optional 2004 thresholds for drug therapy. For lower, moderate, moderately high, and high-risk groups, 13.4%, 44.2%, 58.8%, and 71.8%, respectively, exceeded 2001 NCEP goals; 13.4%, 15.7%, 87.4%, and 96.0% of these groups exceeded optional 2004 thresholds for drug therapy.

CONCLUSIONS: In 1999 to 2002, LDL-C levels commonly exceeded 2001 NCEP goals, especially for moderately high and high-risk individuals, and cholesterol-lowering medications were underused. Optional goals promulgated by the NCEP in 2001 and 2004 moderately increased the number of adults with LDL-C above their goal, and greatly increased the number of low, moderately high, and high-risk adults who exceeded LDL-C thresholds, for cholesterol-lowering medication.

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E levated low-density lipoprotein cholesterol (LDL-C) is a major modifiable cause of coronary heart disease (CHD). The National Cholesterol Education Program (NCEP) periodically releases reports by its Adult Treatment Panel (ATP) providing recommendations for managing high blood cholesterol in adults. Since the 1993 ATP II guideline,[1] multiple clinical trials have demonstrated the benefits of LDL-C lowering in individuals at increased risk for CHD across a range of initial cholesterol levels.[2–15] Cholesterol lowering in adults with low short-term risk has not been well studied.

The 2001 ATP guideline increased the number of individuals considered to be high risk.[16,17] It also recommended using cholesterol-lowering medication in adults at moderately high risk of CHD with LDL-C levels above 130 mg/dL and to consider the option of using medication in low-risk adults with LDL-C levels between 160 and 189 mg/dL or high-risk adults with LDL-C levels between 100 and 129 mg/dL. Further optional modifications to the ATP III guideline, released by the NCEP in 2004, gave clinicians the choice of pursuing very low (<70 mg/dL) LDL-C levels for very high-risk adults and low (<100 mg/dL) LDL-C levels for moderately high-risk adults through using cholesterol-lowering medications and intensified lifestyle modifications (Table 1).[18]

We sought to determine the implications of these guideline changes for the U.S. population. Our primary goal was to determine the proportion of adults with LDL-C levels exceeding the ATP recommended and optional goals published in 2001 and 2004, and to estimate the number of adults exceeding the threshold to use cholesterol-lowering medication according to the 2001, optional 2001, and optional 2004 targets. Our secondary goal was to determine the magnitude of LDL-C reduction required to reach 2001 and 2004 NCEP goals for U.S. adults not on cholesterol-lowering therapy.

METHODS

Study Population

The National Health and Nutrition Examination Survey (NHANES) conducted from 1999 to 2002 recruited a nationally representative sample of the noninstitutionalized U.S. population for a home interview, physical examination, and laboratory testing. The institutional review board of the National Center for Health Statistics approved the survey, and participants provided informed consent.[19]

We included nonpregnant morning exam participants aged 20 to 79 years old (n=4,044). We excluded participants who had fasted fewer than 8 or more than 24 hours, (n=524), had serum triglyceride levels exceeding 400 mg/dL (n=106), did not have cholesterol measured (n=67), or for whom cor-

Table 1. Summary of National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) Guidelines

	ATP III (2001)[16]	ATP III Optional Goals (2001)[16]	NCEP Optional Goals (2004)[18]
LDL-C goal (mg/dL)			
0 to 1 RF*	< 160	—	—
≥ 2 RF* and 10 y risk < 10%†	< 130	—	—
≥ 2 RF* and 10 y risk 10% to 20%†	< 130	—	< 100
≥ 2 RF* and 10 y risk > 20% or CHD, DM, or other symptomatic atherosclerosis†	< 100	—	< 70
Threshold for drug therapy, LDL-C (mg/dL)			
0 to 1 RF*	≥ 190	≥ 160	≥ 160
≥ 2 RF* and 10 y risk < 10%†	≥ 160	—	—
≥ 2 RF* and 10 y risk 10% to 20%†	≥ 130	—	≥ 100
≥ 2 RF* and 10 y risk > 20% or CHD, DM, or other symptomatic atherosclerosis†	≥ 130	≥ 100	≥ 70

*ATP III risk factors = male ≥ 45 years, female ≥ 55 years, family history premature CHD in first-degree relative (< 55 years if male, < 65 years if female), current cigarette smoking, hypertension, HDL < 40. HDL ≥ 60 counts as a negative risk factor.
†Estimated 10-year risk of fatal heart disease or nonfatal myocardial infarction using the ATP III method based on the Framingham Heart Study.[16]
LDL-C, low-density lipoprotein cholesterol; RF, risk factor; CHD, coronary heart disease; DM, diabetes mellitus.

onary risk assessment could not be performed because of missing blood pressure information ($n = 66$).

Study Variables

We classified participants' coronary risk and LDL-C goals according to the NCEP ATP III criteria (Table 1) that defined 4 risk groups. Subjects with CHD (including self-reported prior myocardial infarction or angina) were classified as high risk. Individuals with other conditions considered to carry high CHD risk—i.e., prior stroke, peripheral arterial disease (based on an ankle brachial index < 0.9 or a lower extremity amputation), or diabetes (self-reported physician-diagnosed diabetes or fasting glucose ≥ 126 mg/dL)—were also classified as high risk. For individuals with 2 or more risk factors—male ≥ 45 years old, female ≥ 55 years old, a first-degree relative with CHD before age 55 years if male or 65 years if female (only data for parents and siblings with myocardial infarction or angina before age 50 years were available), cigarette smoking, hypertension (≥ 140/90 mm Hg or taking antihypertensive medication), or serum high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL—the 10-year risk of fatal CHD or nonfatal myocardial infarction was determined using a multivariable risk assessment tool derived from Framingham Heart Study. Individuals were then classified into 1 of 3 risk groups depending on their estimated 10-year risk of fatal CHD or nonfatal myocardial infarction (< 10% [moderate], 10% to 20% [moderately high], or > 20% [high]). Those with fewer than 2 risk factors were assigned to the lowest-risk group. The number of risk factors was reduced by 1 if the HDL-C level was ≥ 60 mg/dL.[16]

LDL-Cholesterol Levels Above Guideline Goals and Thresholds for Drug Therapy

We calculated LDL-C levels from total serum cholesterol, HDL-C, and triglyceride levels using the Friedewald equation.[20] We determined the proportion of adults aged 20 to 79 years exceeding LDL-C goals from 2001 and optional goals from 2004. We also calculated the proportions exceeding 2001 guideline thresholds to use medical therapy, based on the 2001 guidelines and the 2001 and 2004 optional guidelines (Table 1).[16,18]

Sensitivity Analysis Using U.S. Preventive Services Task Force Screening Recommendations

The 2001 U.S. Preventive Services Task Force recommendations did not advocate screening men aged 20 to 34 years and women 20 to 44 years without CHD, peripheral arterial disease, stroke, diabetes mellitus, a family history of premature CHD, or multiple CHD risk factors.[21] We determined the effect of applying these guidelines on the proportion of the population exceeding NCEP guideline goals.

Data Analysis

We used SAS release 9.1 (SAS Institute Inc., Cary, NC) and SUDAAN release 9.0.1 (Research Triangle Institute, Research Triangle Park, NC) to account for the survey design and provide nationally representative proportions and accurate confidence intervals. All proportions reflect the survey weights. We used the χ^2 test to compare categorical variables and the *t*-test for continuous variables. Significance tests were 2-sided with a P value set at < .05.

We used the sampling weights (which account for the probability of selection and nonresponse) to estimate the number of noninstitutionalized nonpregnant adults aged 20 to 79 years in the U.S. population in the year 2000 in each group.

RESULTS

In total, 3,281 individuals (representing 175,600,000 U.S. adults) participated in a morning examination and had no exclusion criteria. The median age was 43.0 years and 50.7% were women (Table 2). Age, sex, race/ethnicity, income, and cholesterol-lowering medication use did not differ significantly between excluded and included subjects. The included sample was representative of 94.1% of the nonpregnant U.S. population 20 to 79 years old.

LDL-Cholesterol Levels Exceeding NCEP Guidelines

According to the 2001 ATP III guideline, 1,063 (30.0% [95% CI, 28.0% to 32.0%]) exceeded their LDL-C goal. Among high-risk individuals, 476 (71.8% [95% CI, 67.5% to 75.8%]) exceeded

Characteristic	
Age, y, median (25th to 75th percentiles)	43.0 (31.9 to 55.3)
Female sex, % (95% CI)	50.7 (49.0 to 52.3)
Race/ethnicity, % (95% CI)	
White, non-Hispanic	72.7 (68.3 to 76.8)
Black, non-Hispanic	10.6 (8.2 to 13.7)
Mexican American	6.9 (5.3 to 9.0)
Other	9.7 (6.5 to 14.4)
Hypertension, % (95% CI)	
Undiagnosed	9.2 (8.0 to 10.4)
Diagnosed	21.1 (19.2 to 23.2)
Medication for hypertension	16.5 (14.5 to 18.8)
Diabetes, % (95% CI)	
Undiagnosed	2.4 (1.8 to 3.1)
Diagnosed	6.9 (5.7 to 8.2)
Hypercholesterolemia, % (95% CI)	
Diagnosed	26.2 (23.8 to 28.7)
Medication for cholesterol	9.0 (7.6 to 10.6)
Current cigarette smoker, % (95% CI)	24.8 (22.2 to 27.6)
Parent or sibling with premature coronary heart disease, % (95% CI)	2.2 (1.8 to 2.8)
Cardiovascular disease, % (95% CI)	7.8 (6.5 to 9.3)
Diagnosed coronary heart disease	5.1 (4.2 to 6.3)
Diagnosed stroke	1.7 (1.2 to 2.5)
Peripheral arterial disease[†]	2.4 (1.9 to 3.1)
Total cholesterol, mg/dL, median (25th to 75th percentiles)	196.9 (173.4 to 223.3)
Low-density lipoprotein cholesterol, mg/dL, median (25th to 75th percentiles)	120.1 (97.9 to 143.9)
High-density lipoprotein cholesterol, mg/dL, median (25th to 75th percentiles)	47.4 (39.9 to 58.7)

Data are weighted to the corresponding portion of the U.S. population.
[†]*Ankle brachial index < 0.9 or lower extremity amputation.*
NHANES, National Health and Nutrition Examination Survey; CI, confidence interval; NCEP, National Cholesterol Education Program; RF, risk factor; CVD, cardiovascular disease.

the 2001 target LDL-C level of < 100 mg/dL. Among all participants, 534 (14.2% [95% CI, 12.7% to 15.8%]) exceeded the ATP III threshold for medication. In the 2001 ATP III guideline, medication use was considered optional for 2 groups: low-risk persons with LDL-C levels between 160 and 189 mg/dL and high-risk persons with LDL-C levels between 100 and 129 mg/dL. When we included persons in these 2 groups as being eligible for medications, 951 (26.3% [95% CI, 24.1% to 28.6%]) were above the threshold to use medication (Table 3).

The optional 2004 NCEP goals and thresholds for drug therapy include an LDL-C < 100 mg/dL for moderately high-risk adults and < 70 mg/dL for high-risk adults (Table 1). By these criteria, 1,293 (35.8% [95% CI, 33.8 to 37.9]) were above their goal and 1,181 (32.2% [95% CI, 29.9 to 34.5]) were above the threshold for drug therapy. Nearly everyone in the 2 highest risk groups exceeded their optional LDL-C goal (Table 3).

Analysis Using U.S. Preventive Services Task Force Screening Recommendations

When we examined only individuals who would be screened according to the U.S. Preventive Services Task Force (USPSTF) recommendations, the population estimates for the number of 20- to 79-year-old U.S. adults exceeding NCEP goals decreased. The proportion exceeding their ATP III LDL-C goal fell from 30.0% to 25.8% and the proportion exceeding optional thresholds for drug therapy fell from 26.3% to 23.2%. The proportion of adults exceeding optional 2004 NCEP LDL-C goals fell from 35.8% to 31.7% and the proportion exceeding the optional NCEP 2004 thresholds for drug therapy fell from 32.2% to 29.1%. Most (88.8%) persons for whom the USPSTF who would recommend no screening had LDL-C levels at ATP III goals, 97.3% had levels below the ATP III threshold for drug therapy, and 91.7% were below the optional ATP III thresholds for drug therapy.

Use of Cholesterol-Lowering Medications and LDL-C Control

Among adults aged 20 to 79 years old, 306 (9.0% [95% CI, 7.6 to 10.6]) used cholesterol-lowering medication. By ATP III risk groups, 3.5% (95% CI, 2.6% to 4.8%) of the lowest risk group, 7.7% (95% CI, 4.65% to 12.34%) of the moderate-risk group, 15.7% (95% CI, 11.18% to 21.6%) of the moderately high-risk group, and 28.6% (95% CI, 24.25% to 33.27%) of the high-risk group used cholesterol-lowering medication. Of medication users, 285 (92.6% [95% CI, 88.9% to 95.2%]) used a statin, and only 14 (5.2% [95% CI, 2.4% to 11.0%]) used more than 1 kind of cholesterol-lowering medication. Among medication users, 124 (41.8% [95% CI, 35.0% to 48.8%]) exceeded their ATP III LDL-C goals, and 195 (63.7% [95% CI, 57.2% to 69.7%]) exceeded the optional 2004 NCEP goals.

LDL-C Reduction Needed for Adults Not Already on Drug Therapy

Of the population not currently using cholesterol-lowering therapy, 538 (15.6% [95% CI, 13.6% to 17.7%]) exceeded their

Table 3. Population Estimates and Frequencies of Low-Density Lipoprotein Cholesterol (LDL-C) Levels Exceeding Guideline Goals Among Adults Aged 20 to 79 years*

	Adult Treatment Panel III Risk Categories Population Estimate in Millions (%)				
Risk group	Total	Lower	Moderate	Moderately high	High
Study participants	3,281	1,946	395	285	655
Population estimate (millions)	175.7	112.6	22.6	11.9	29.6
Guideline					
Adult Treatment Panel III (2001)[10]					
Above LDL-C goal	52.6 (30.0)	15.1 (13.4)	10.0 (44.2)	7.0 (58.8)	20.6(71.8)
Above threshold for medication	24.9 (14.2)	3.5 (3.1)	3.6 (15.7)	7.0 (58.8)	10.9 (38.1)
Above optional threshold for medication	46.2 (26.3)	15.1 (13.4)	3.6 (15.7)	7.0 (58.8)	20.6 (71.8)
NCEP optional goals (2004)[14]					
Above optional LDL-C goal	62.9 (35.8)	15.1 (13.4)	10.0 (44.2)	10.4 (87.4)	27.5 (96.0)
Above optional threshold for medication	56.5 (32.2)	15.1 (13.4)	3.6 (15.7)	10.4 (87.4)	27.5 (96.0)

Numbers represent the estimated size of the corresponding portion of the U.S. adult population from which the sample was drawn.

Table 4. Distribution of LDL-C Above ATP III (2001) and Optional (2004) National Cholesterol Education Program Goals for Persons Not Using Cholesterol-Lowering Medication, By Risk Group, Estimated Population Size in Millions (%)

Risk Group	LDL-C Goal (mg/dL)	At Goal	≤ 10% Above Goal	11% to 40% Above Goal	>40% Above Goal
Lower	<160	94.3 (86.8)	8.4 (7.7)	5.5 (5.1)	0.4 (0.4)
Moderate	<130	11.1 (53.3)	3.8 (18.2)	5.8 (28.0)	0.09 (0.4)
Moderately high	<130[*]	3.9 (39.1)	2.6 (25.7)	3.5 (34.7)	0.05 (0.5)
	<100[†]	1.2 (12.3)	0.6 (6.2)	6.9 (68.7)	1.3 (12.9)
High	<100[*]	4.6 (22.3)	2.7 (13.2)	10.1 (49.2)	3.1 (15.4)
	<70[†]	0.4 (1.8)	0.5 (2.6)	7.6 (37.1)	12.0 (58.5)

[*]*ATP III (2001) goals.*
[†]*Optional (2004) NCEP goals.*
LDL-C, low-density lipoprotein cholesterol; ATP, Adult Treatment Panel.

ATP III LDL-C target by 11% to 40%. Few people (2.3% [95% CI, 1.7% to 3.2%]) required more than a 40% reduction in their LDL-C level to achieve their ATP III goal. However, if the optional 2004 goals were widely applied, 528 (16.2% [95% CI, 14.7% to 17.7%]) would require an 11% to 40% reduction and 339 (8.6% [95% CI, 7.4% to 9.9%) would require more than a 40% LDL-C reduction to reach their optional goal. The extent of LDL-C reduction required to reach goal stratified by risk group is shown in Table 4.

DISCUSSION

We used data from 3,281 participants of the 1999 to 2002 NHANES to assess the implications of widely applying NCEP recommendations and optional thresholds. Thirty percent of the U.S. adult population had LDL-C levels exceeding ATP III goals. Furthermore, 18% of individuals not taking drug therapy exceeded their LDL-C goal by more than 10% and thus would be unlikely to reach their LDL-C target without pharmacotherapy or highly specialized diets.[21–26] Medications to lower cholesterol were underused, especially among individuals at increased short-term risk for CHD.

Our results demonstrate the impact that recent NCEP guideline changes could have on the number of individuals exceeding LDL-C goals if these recommendations were fully implemented in clinical practice. If the optional NCEP goals described in 2004 were widely adopted, 52.9 million adults (30%) not currently on medication would exceed their optional LDL-C goal, and 40 million (25%) would be more than 10% above their goal. Restricting the population screened for lipid disorders to exclude younger, low-risk individuals as described by the USPSTF guideline[27] only moderately reduced the number of U.S. adults with LDL-C levels exceeding NCEP goals.

Among adults at moderately high or high cardiovascular risk, most (68%) exceed the LDL-C goal recommended by the ATP III report. Adopting the lower optional targets would mean nearly all persons in these risk groups would have LDL-C levels exceeding their goals, despite the fact that 25% of this population already used cholesterol-lowering medication.

The downward shifts in LDL-C targets raise the proportion of adults requiring intermediate (11% to 40%) and large (>40%) reductions to achieve their target levels. The optional 2004 NCEP goals increased the proportion of the untreated 20- to 79-year-old population needing more than a 40% reduction in their LDL-C to 8.6%. For some people, maximizing therapeutic lifestyle changes and using standard dosages of statins would suffice to achieve these goals. However, many persons will be unable to reach newer optional targets using 1 of the therapeutic regimens tested in the long-term clinical trials of statins.[2–6,9–11,14] High doses of potent statins (atorvastatin 80 mg or simvastatin 80 mg daily) that reduce LDL-C by more than 40% have been tested for up to 2 years in very high-risk populations.[7,8,12,13,15] Since the publication of the 2004 NCEP update, the safety of atorvastain 80 mg daily for up to 5 years was demonstrated in 5,000 persons under 76 years of age with stable CHD.[15] Evidence of long-term safety of the potent rosuvastatin is not yet available. Widespread use of high-dose statin therapy could lead to higher rates of adverse effects such as rhabdomyolysis if individuals who were excluded from most clinical trials (i.e., the elderly, individuals with renal or hepatic impairment or who use medications that interact with statins) are exposed to high-dose statins in real-world settings.[28]

The authors of the 2004 NCEP report acknowledge that optional LDL-C goals may be out of reach for some patients given the limitations of currently available lipid-lowering agents, and their recommendations allow for individualized clinical judgment.[18] For many patients, the decision will be whether to use well-tested medications at dosages that have proven clinical benefits but cannot achieve the optional NCEP LDL-C goals, or to use drugs in combination or at higher doses. High-dose statin therapy or combination drug therapy (such as combining a statin with a bile acid sequestrant, niacin, a fibric acid derivative, and/or ezetimibe) may enable some additional individuals to achieve lower LDL-C goals but these options are likely to come at greater expense and have less long-term safety and efficacy data to support their use. Future studies should assess the long-term risks and benefits of combination cholesterol-lowering medical therapy and to determine whether combination or single drug treatment is preferred for high- and intermediate-risk individuals.

The 2001 and 2004 ATP reports have major economic ramifications. The expense of statins has been implicated in their underuse by Medicare beneficiaries with CHD.[29] Without cost reductions, purchasing standard-dose statin therapy[18] for the 25 million people in the U.S. who exceed the ATP III threshold for drug therapy could be prohibitively expensive. At current retail prices, a year's supply of generic lovastatin 40 mg daily can cost at least $450 to $700. For the nearly 40 million people not currently using cholesterol-lowering medication who exceed their optional NCEP 2004 goals by more than 10%, drug treatment could cost $18 billion annually. Using name-brand statins would raise this estimate 3- to 4-fold.[30] Using high-dose statin and combination drug therapy would increase costs further. Greater availability of generic statins, group purchasing, or other cost reducing measures

may enable more individuals to benefit from cholesterol-lowering therapy. Furthermore, much of the cost of cholesterol treatment for high-risk individuals may be offset by reductions in the direct and indirect cost of CHD; for some high-risk subgroups, drug therapy to lower cholesterol may even be cost-saving.[31,32]

The ATP III recommendation to consider medication use for adults with fewer than 2 concomitant risk factors and an LDL-C level between 160 and 189 mg/dL (6.6% of adults) warrants comment. These individuals have lower short-term CHD risk than the participants in primary prevention trials who were middle-aged and had other risk factors such as hypertension, current smoking, or low HDL-C.[3,6,7] The cost-effectiveness of using cholesterol-lowering drug treatment depends on treatment costs, the population's CHD and stroke risk, and the age of the population (for persons with similar CHD risk, cholesterol lowering is more cost effective for younger adults).[21] For persons in this optional ATP III treatment group with LDL-C levels between 160 and 189 mg/dL, the 10-year CHD risk is low (approximately 2%). If statin therapy is assumed to reduce the CHD event rate by 30%, 1,670 person-years of treatment would be required to prevent 1 CHD event. At $450 per person per year, the medication costs to prevent this event would be at least $750,000 and subsequent office visits and monitoring would raise costs further. While a formal cost-effectiveness analysis is beyond the scope of our investigation, we believe that treating people in this low-risk group with cholesterol-lowering medication is unlikely to be cost effective at current statin prices.

Our study has several limitations. The number of individuals studied was modest. While our findings are generally in accord with analyses performed with the larger NHANES sample from 1988 to 1994,[33] we could not accurately estimate the size of some population subgroups. Results from this survey are weighted to account for the chance of selection, nonparticipation, and excluding nonfasting persons; however, our findings might be less generalizable if excluded persons or nonparticipants had fasting LDL-C levels substantially different from study participants. Our population estimates of the number of adults with LDL-C levels exceeding goals may be underestimates for several reasons. We did not account for the proportion of the population represented by the 5.9% of the sample meeting exclusion criteria. In addition, we did not estimate the number of adults 80 years and older who may be eligible for cholesterol-lowering therapy.[9] We likely underestimated the proportion of adults with LDL-C levels above guideline goals because we may have classified some of the subgroup using cholesterol-lowering medication as lower risk when their pretreatment lipoprotein values would have placed them in a higher risk group. We did not have a precise measure of atherosclerotic cerebrovascular disease. We may have misclassified some patients with carotid atherosclerosis as lower risk, and may have misclassified some subjects with nonatheroembolic strokes as high risk. Lastly, we may have misclassified the risk group for some individuals because the medical and family history data were self-reported.

In summary, many U.S. adults, especially those at increased cardiovascular risk, have uncontrolled LDL-cholesterol by 2001 ATP III guidelines. Optional LDL-C targets from 2004 greatly increased the number of individuals for whom drug therapy may be needed to reach therapeutic targets. A substantial number of people are unlikely to achieve optional NCEP LDL-C goals with standard-dose statins. Current costs of these drugs may place them out of reach for many patients likely to benefit from them. Research is needed to define long-term risks, benefits, and cost-effectiveness of combination cholesterol-lowering drug therapy compared with high-dose statin therapy alone.

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