National improvements in low-density lipoprotein cholesterol management of individuals at high coronary risk: National Health and Nutrition Examination Survey, 1999 to 2002

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Background This study sought to evaluate national levels of elevated low-density lipoprotein cholesterol (LDL-C) before and after publication of the Adult Treatment Panel III (ATP III). The ATP III guidelines intensified LDL-C targets and defined additional high-risk conditions. These recommendations are expected to have a noticeable impact on US cholesterol levels.

Methods Coronary heart disease (CHD) risk was determined per ATP III guidelines for US residents aged 20 to 79 years in the 1999 to 2000 and 2001 to 2002 surveys. For those at high risk, the LDL-C mean percentage <100 mg/dL and percentage ≥130 mg/dL, although not taking lipid-lowering therapy, were compared between the 2 surveys. In addition, subsets with and without CHD were evaluated.

Results Of all high-risk US residents, the mean LDL-C dropped from 129 mg/dL in 1999 to 2000 to 120 mg/dL in 2001 to 2002 ($P = .003$). Those <100 mg/dL increased from 23% to 32% ($P = .003$). Those ≥130 mg/dL and not on medication dropped from 36% to 27% ($P = .001$). Goal achievement and improvements were more favorable in the subset with CHD compared with those at high risk due to high-risk equivalent conditions.

Conclusions The sharp increase in high-risk US residents at the goal and the drop in the untreated percentage of those above treatment threshold illustrate national improvements in the management of LDL-C for those at high coronary risk. High-risk subjects without CHD displayed less significant improvements, suggesting an opportunity for better recognition and management of these individuals. (Am Heart J 2008;156:284-91.)

In 2001, the National Cholesterol Education Program released the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]). This guideline emphasized risk factors and absolute risk calculation in the initial assessment of persons with dyslipidemia. Although previously, only those with known coronary disease were considered high risk, the ATP III elevated persons with diabetes mellitus (DM), noncoronary atherosclerotic vascular disease, and a Framingham risk score (FRS) of >20% to high-risk status. ATP III designated a low-density lipoprotein cholesterol (LDL-C) of <100 mg/dL as the goal for this population.[1,2]

Although some studies describe a consistent long-term decrease in total cholesterol and LDL-C levels in the US population,[3] the National Health and Nutrition Examination Survey (NHANES) III data showed that only 17% of US residents with coronary heart disease (CHD) met their ATP II–defined LDL-C goal of ≤100 mg/dL.[4] Other studies corroborate this substantial "treatment gap" between lipid levels and goals.[5-7]

To date, no studies have compared population-based data sets to evaluate change over time in lipid levels and the LDL-C treatment gap among those at high risk for future coronary events. This study compares data from the 1999 to 2000 NHANES to the 2001 to 2002 NHANES to identify changes in levels and treatment patterns of LDL-C within the ATP III–defined high-risk portion of the US population.

Methods

Participants and exclusions

The National Center for Health Statistics conducts the NHANES in recurring 2-year phases. The NHANES includes

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Submitted November 28, 2007; accepted March 4, 2008.

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0002-8703/$ - see front matter

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doi:10.1016/j.ahj.2008.03.004

Table I. Exclusions from analysis of the 1999 to 2000 and 2001 to 2002 NHANES databases

	1999-2000 NHANES * (% †)	2001-2002 NHANES * (% †)
MEC group	272.2 million	280.0 million
Aged <20 y	80.2 ± 4.8	80.4 ± 4.8
Aged >79 y	6.3 ± 0.8	7.5 ± 0.7
MEC group, aged 20-79 y	185.7 ± 7.9 (100)	192.1 ± 7.5 (100)
Currently pregnant	4.8 ± 0.6 (2.6 ± 0.3)	4.4 ± 0.3 (2.3 ± 0.2)
Recent or pending chemotherapy	1.2 ± 0.3 (0.6 ± 0.2)	–
Missing cholesterol data	9.8 ± 0.7 (5.3 ± 0.5)	10.6 ± 0.9 (5.5 ± 0.5)
Missing blood pressure data	3.5 ± 0.5 (1.9 ± 0.3)	5.3 ± 0.9 (2.8 ± 0.5)
Triglycerides ≥400 mg/dL or missing	5.4 ± 1.1 (2.9 ± 0.5)	5.7 ± 0.7 (3.0 ± 03)
Total exclusions from MEC group, aged 20-79 y	24.7 ± 1.7 (13.3 ± 0.8)	26.0 ± 1.6 (13.5 ± 0.8)
Study population	161.0 ± 7.1 (86.7 ± 0.8)	166.2 ± 7.0 (86.5 ± 0.8)

* Survey population estimates (±SE) presented in millions of individuals.
† Percentages (±SE) are given in terms of the MEC group, aged 20 to 79 years. Percentages may not sum to 100 because of rounding.

health interviews in the home and physical examination and laboratory evaluations at a mobile examination center (MEC). Using demographic and geographical data, the NHANES assigns weights to each participant such that the sum of the weights represents the entire civilian noninstitutionalized US population at the time of the survey. The NHANES previously published a detailed account of its methods and protocols.[8]

Demographic, questionnaire, physical examination, and laboratory data on subjects from the 1999 to 2000 and 2001 to 2002 NHANES data sets were imported into a Microsoft Office Excel workbook. This database modeled a "virtual prevention clinic" using each subject's historical, examination, and laboratory information.

Subjects were limited to ages 20 to 79 years, consistent with ATP III guidelines and the FRS population.[1] Currently, pregnant women and individuals receiving cancer chemotherapy within 4 weeks of the exam were excluded. Subjects who lacked sufficient cholesterol or blood pressure data to allow for risk assessment and LDL-C stratification were excluded, as were subjects who lacked triglycerides measurements or had triglycerides ≥400 mg/dL (Table I).

Identification of high-risk subjects

The NHANES data fields representing medical history, examination, and laboratory data identifying high-risk medical conditions and ATP III–defined risk factors were parsed (see Appendix A for individual NHANES item codes and descriptions). High-risk subjects were distinguished by the presence of medical conditions including CHD, DM, or peripheral vascular disease (PVD),[1] or by having 2 or more risk factors and a 10-year FRS above 20%.[1] High-risk definitions include subjects reporting being told by a health professional that they had a myocardial infarction, coronary artery disease, or angina pectoris (CHD); reporting being told by a health professional that they had diabetes, taking insulin, or oral hypoglycemic agents; or reporting a history of a stroke or a measured ABI <0.9 in either leg.

The 5 ATP III risk factors were summed for the remaining subjects.[1] Risk factors include age (men ≥45 years; women ≥55 years), high-density lipoprotein cholesterol (HDL-C) <40 mg/dL (HDL-C ≥60 mg/dL subtracted one risk factor), hypertension (blood pressure ≥140/90 mm Hg or current antihypertensive medication use), current cigarette smoking (smoked 100 or more lifetime cigarettes and were currently smoking everyday or some days),[2] and a family history of premature CHD (a positive answer to the NHANES interview question: "Including living and deceased, were any of your biological, that is, blood relatives including grandparents, parents, brothers, sisters ever told by a health professional that they had a heart attack or angina before the age of 50?").[8]

The 10-year FRS stratified subjects with 2 or more risk factors. Those with an FRS >20% were considered high risk. The mathematical functions used were provided by members of the Framingham study (personal communication, 7/1/2002, from Lisa M. Sullivan, PhD, and Ralph B. D'Agostino, both of Boston University, Boston, MA) and exist within publicly available tools.[9,10]

Low-density lipoprotein cholesterol calculation, medication use, and target selection

Low-density lipoprotein cholesterol was calculated using the Friedwald equation (total cholesterol − HDL-C − triglycerides/5) for all subjects. Triglycerides were used in the Friedwald equation regardless of the subject's fasting status at the time of venipuncture.[11]

The ATP III guideline highlighted specific LDL-C levels for those at high risk: (1) an optimal goal of LDL-C <100 mg/dL, (2) a level for optional drug therapy between 100 and 129 mg/dL, and (3) a threshold for initiating drug therapy of ≥130 mg/dL.[1] Subjects were considered treated with lipid-lowering medications if they answered that they were following their doctor's advice to take prescribed medication to lower their high cholesterol. All other subjects were considered unmedicated.

This study focused on 2 clinically meaningful measures: (1) the percentage of high-risk US residents achieving goal with an LDL-C <100 mg/dL and (2) the percentage of those with LDL-C ≥130 mg/dL who were unmedicated and, thus, undertreated per the ATP III guideline.

Statistical analysis

Population totals were calculated for 5 groups in both the 1999 to 2000 and 2001 to 2002 NHANES data sets: (1) the entire survey populations, aged 20 to 79 years, less exclusions; (2) those classified as high risk through the risk stratification process, (3) those at high risk with CHD, (4) those at high risk

Table II. Percentages of the high-risk population, by clinical category and LDL-C level

Comparison group	Percentage† of high-risk group (millions*)		
	1999-2000 NHANES	2001-2002 NHANES	P‡
All high risk (% of study population)	22.2 ± 2.1 million (13.8% ± 1.0%)	23.8 ± 1.2 million (14.3% ± 0.6%)	.638
High risk with CHD	39.8% ± 2.3% (8.8 ± 0.9 million)	37.2% ± 3.1% (8.9 ± 1.0 million)	.483
High risk without CHD	60.2% ± 2.3% (13.4 ± 1.5 million)	62.8% ± 3.1% (15.0 ± 0.8 million)	.483
High risk by DM only	28.3% ± 2.3% (6.3 ± 0.8 million)	30.8% ± 2.6% (7.3 ± 0.7 million)	.469
LDL-C <100 mg/dL	22.9% ± 1.7% (5.1 ± 0.5 million)	31.5% ± 2.4% (7.5 ± 0.6 million)	.003
LDL-C 100-129 mg/dL	31.1% ± 1.7% (6.9 ± 0.9 million)	34.3% ± 1.7% (8.2 ± 0.6 million)	.193
LDL-C ≥130 mg/dL	46.0% ± 2.1% (10.2 ± 1.1 million)	34.1% ± 2.3% (8.1 ± 0.7 million)	<.001

* Estimated population presented in millions of individuals ± SE.
† Percentages below first row are given in terms of the high-risk population ± SE.
‡ *P* value compares percentages between the data sets.

without CHD, and (5) those at high risk with the diagnosis of DM as their only criterion for classification as high risk. Percentages in terms of the survey population and the high-risk group were calculated when applicable. Mean LDL-C levels were determined for all 5 groups, as were percentages of subjects achieving goal LDL-C <100 mg/dL and unmedicated subjects with LDL-C ≥130 mg/dL. Results were compared between the 1999 to 2000 and 2001 to 2002 NHANES data sets.

Estimates were weighted to produce unbiased population estimates. Standard errors of the estimates were calculated using PROC SURVEYMEANS in SAS Version 9.1 (SAS Institute, Cary, NC) to account for the complex survey design. Standard errors for the differences in percentages or means were calculated from the SEs of the individual estimates based on the independence of the 2 surveys. Differences in means or percentages between groups within each data set and differences in means or percentages between the 1999 to 2000 and 2001 to 2002 NHANES data sets were tested using the normal approximation to their sampling distributions. A 2-sided *P* value of .05 was regarded as statistically significant.

Results

Study population

The 1999 to 2000 NHANES included 4,122 subjects representing 185.7 million US adults aged 20 to 79 years. The 2001 to 2002 NHANES included 4,625 subjects representing 192.1 million US adults. After exclusions for pregnancy, chemotherapy, and incomplete data, the final study population included 3,398 subjects (161.0 million US residents) and 3,746 subjects (166.2 million US residents), respectively (Table I).

The high-risk cohorts included 13.8% (22.2 million) of the 1999 to 2000 NHANES study population and 14.3% (23.8 million) of the 2001 to 2002 NHANES study population (*P* = .638). Of these cohorts, 39.8% (8.8 million) and 37.2% (8.9 million), respectively, had CHD (*P* = .483). The remaining subjects were considered high risk because of CHD equivalent conditions. DM was the sole reason for high-risk classification in 28.3% (6.3 million) and 30.8% (7.3 million) of high-risk groups, respectively (*P* = .47) (Table II).

Low-density lipoprotein cholesterol levels

Low-density lipoprotein cholesterol levels among high-risk individuals dropped between the 1999 to 2000 and 2001 to 2002 NHANES data sets. The mean LDL-C ± SE for all high-risk individuals decreased from 129 ± 2 mg/dL in 1999 to 2000 to 120 ± 2 mg/dL in 2001 to 2002 (*P* = .003). When separated by high-risk diagnosis, those with CHD dropped from 123 ± 3 to 112 ± 4 mg/dL (*P* = .01), and high-risk individuals without CHD went from 133 ± 3 down to 126 ± 2 mg/dL (*P* = .03). Individuals at high risk solely due to a diagnosis of DM trended down from 125 ± 3 to 119 ± 2 mg/dL (*P* = .06).

Within the same NHANES, mean LDL-C levels were significantly lower among individuals with CHD compared with those without CHD: 123 ± 3 versus 133 ± 3 mg/dL (*P* = .01) in 1999 to 2000 and 112 ± 4 versus 126 ± 2 mg/dL (*P* < .001) in 2001 to 2002.

Low-density lipoprotein cholesterol goal achievement

Achievement of LDL-C <100 mg/dL among all high-risk individuals improved from 23% in 1999 to 2000 to 32% in 2001 to 2002 (*P* = .003) (Tables II and III). Increased goal achievement was greatest in individuals with CHD from 27% to 41% (*P* = .02) (Table III, horizontal comparison). Smaller trends occurred in all high-risk individuals without CHD from 20% to 26% (*P* = .07) and in individuals at high risk solely due to DM (from 26% to 32%, *P* = .15).

Within the 1999 to 2000 NHANES high-risk group, LDL-C goal achievement in those with and without CHD was not statistically different (27% vs 20%, *P* = .16). However, in the 2001 to 2002 survey, LDL-C goal achievement in those with CHD was significantly higher than those at high risk without CHD (41% vs 26%, *P* = .002) (Table III, vertical comparison).

Medication use in individuals with LDL-C ≥130

The percentage of high-risk individuals with LDL-C ≥130 mg/dL decreased from 46% (10.2 million) in the 1999 to 2000 NHANES to 34% (8.1 million) in the 2001 to 2002 NHANES (*P* < .001) (Table II). Within these subsets,

Table III. Percentage of high-risk individuals achieving LDL-C goal of <100 mg/dL and exceeding the treatment threshold without receiving medication

	Percentage* at LDL-C goal of <100 mg/dL (million†)			Percentage* of both unmedicated and LDL-C ≥130 mg/dL (million†)		
Comparison group	**1999-2000 NHANES**	**2001-2002 NHANES**	***P* value‡**	**1999-2000 NHANES**	**2001-2002 NHANES**	***P*‡**
All at high risk	22.9% ± 1.7% (5.1 ± 0.5 million)	31.5% ± 2.4% (7.5 ± 0.6 million)	.003	36.3% ± 2.2% (8.1 ± 1.0)	26.5% ± 1.9% (6.3 ± 0.6)	.001
High risk with CHD§	27.0% ± 4.3% (2.4 ± 0.4 million)	40.9% ± 4.2% (3.6 ± 0.5 million)	.022	25.1% ± 3.5% (2.2 ± 0.4)	15.7% ± 2.7% (1.4 ± 0.3)	.033
High risk without CHD§	20.2% ± 2.3% (2.7 ± 0.4 million)	26.0% ± 2.3% (3.9 ± 0.4 million)	.073	43.6% ± 2.5% (5.8 ± 0.8)	33.0% ± 2.1% (4.9 ± 0.4)	.001
High risk by DM only	25.5% ± 3.3% (1.6 ± 0.3 million)	32.3% ± 3.3% (2.4 ± 0.3 million)	.152	38.2% ± 3.8% (2.4 ± 0.4)	29.0% ± 3.4% (2.1 ± 0.3)	.069
P§	.16	.002		<.001	<.001	

* Percentages (±SE) may not sum to 100 because of rounding.
† Estimated population weights ± SE presented in millions of individuals.
‡ *P* value compares percentages between the data sets.
§ *P* value compares percentages between those with and without CHD within the same data set.

the percentage unmedicated decreased from 36% (8.1 million) to 27% (6.3 million), respectively. Those with CHD dropped from 25% to 16% ($P = .033$) (Table III), and those without CHD dropped from 44% to 33% ($P = .001$). Those at high risk only because of DM trended down from 38% to 29% ($P = .069$). The percentage unmedicated with LDL-C ≥130 mg/dL was significantly lower for those with CHD than those without CHD in both surveys (25% vs 44% in 1999 to 2000; 16% vs 33% in 2001 to 2002; $P < .001$ for both) (Table III).

Discussions

This study demonstrates a national improvement in the management of elevated LDL-C in high-risk US residents from 1999-2000 to 2001-2002. Between the 2 surveys, mean LDL-C levels decreased, a higher percentage of high-risk individuals achieved LDL-C goal, and a smaller percentage of those with LDL-C ≥130 mg/dL received no cholesterol drug therapy. Although improvements occurred in the entire high-risk population, individuals with CHD demonstrated lower mean lipid levels, improved LDL-C goal achievement, and had less chance of being unmedicated with elevated LDL-C compared with high-risk individuals without CHD.

Improved treatment gap

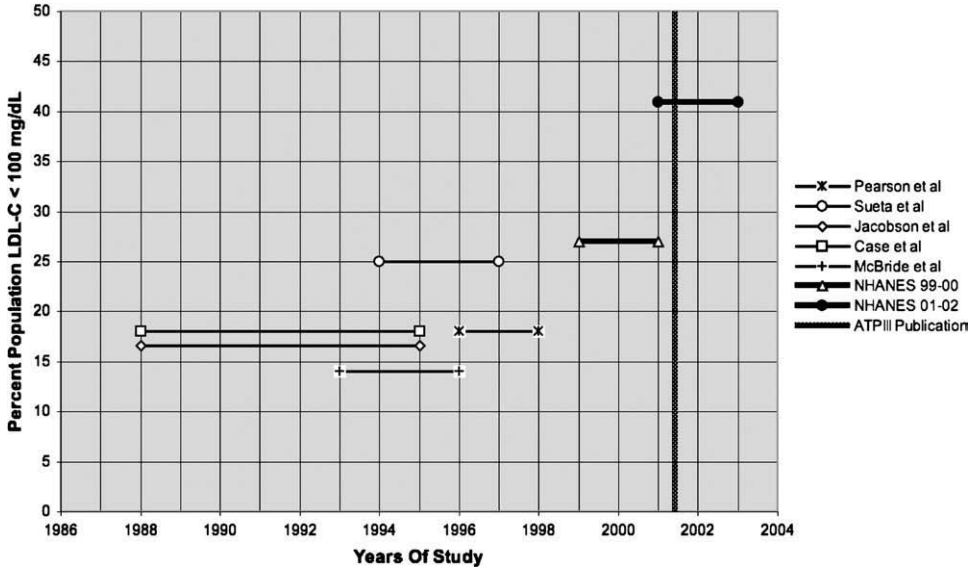
A previous analysis of the 1999 to 2000 NHANES data using ATP III criteria found that 21% of high-risk adults met LDL-C goals.[12] This aligns closely with the finding of 23% in the present study, and minor methodological variations likely account for this small difference. Goal achievement increased to 32% in the 2001 to 2002 NHANES, indicating improved control of elevated LDL-C across all high-risk individuals after the release of the ATP III guidelines.

The improved treatment gap after the release of the ATP III guidelines becomes most apparent when considering studies of those with CHD for a 15-year time span (Figure 1). Analysis of NHANES III from 1988 to 1994 showed that 17% to 18% of individuals with CHD met the LDL-C goal of ≤100 mg/dL.[13,14] A survey of practice patterns among primary care physicians from 1993 to 1995 found that 14% of patients with cardiovascular disease had an LDL-C <100 mg/dL.[15] A retrospective chart audit of outpatient visits in a managed care setting from 1994 to 1996 found that 25% of 20,878 patients with coronary artery disease had a documented LDL-C ≤100 mg/dL.[7] The L-Tap study evaluated 4,888 patients with dyslipidemia from 1996 to 1997, and of the 1460 patients with CHD, 18% achieved their LDL-C target of ≤100 mg/dL.[6] The present study found that 27% of high-risk individuals with CHD in 1999 to 2000 achieved LDL-C goal of <100 mg/dL. This measure increases markedly in the 2001 to 2002 survey to 41%. National improvements in the treatment gap indicate both a positive clinical response to the ATP III guidelines and a recent acceleration of goal achievement in the management of elevated LDL-C.[3]

Treatment gap in those with DM

Numerous studies have documented the presence of a treatment gap in patients with DM and dyslipidemia. For example, a study of a regional managed care database from 1996 to 1998 found that 16% of 6,586 patients with diabetes achieved their LDL-C goal.[16] In 2001 to 2002, 44% of diabetic patients taking statins in a managed care diabetic practice reached their LDL-C goal of <100 mg/dL.[17] A population-based Scottish study examining records from 2000 to 2001 found that only approximately one third of diabetic patients with macrovascular disease took lipid-lowering medications.[18] Though studies measure different parameters, they show

Figure 1



Low-density lipoprotein cholesterol goal achievement of patients with CHD over time. Figure plots the results of 5 previous studies of various high-risk populations with CHD and the percentage achievement of the goal of LDL-C <100 mg/dL. The 2 bars to the right represent the 2 NHANES groups from the present evaluation.

suboptimal control of elevated LDL-C in persons with diabetes. With the elevation of DM to the status of CHD risk equivalent in the ATP III guideline, treatment rates of those with diabetes could have been expected to improve. For those at high risk with DM as their only CHD risk equivalent condition, a smaller rise in LDL-C goal achievement was not statistically significant (26% vs 32.%, $P = .152$) (Table III). Thus, despite the recent emphasis on the treatment of dyslipidemia in those with diabetes,[18] this study supports that individuals with DM remain in need of improved LDL-C management.

Comparing unmedicated subjects exceeding treatment threshold

As a marker of clinical management, we evaluated the high-risk population above the recommended treatment threshold[1] (LDL-C ≥130 mg/dL) who were not taking cholesterol-lowering medications. This group is most clearly outside the ATP III guideline recommendations and represents a clean comparison across surveys. The group is viewed as a percentage of the entire high-risk population because it is not possible to separate subjects with LDL-C ≥130 mg/dL before therapy who are now treated to below that threshold. In 1999 to 2000, the percentage of all high-risk individuals exceeding the treatment threshold and not taking lipid-lowering medications was 36%. This group dropped to 27% in 2001 to 2002 ($P < .001$) (Table III). Again, these data illustrate improved management of elevated LDL-C in high-risk patients associated with the ATP III guideline release.

Improvements in those with CHD versus CHD risk equivalent conditions

Although improvements are seen between the 2 surveys, these changes are larger in those at high risk with CHD compared with those at high risk due to CHD risk equivalent conditions across all 3 measures studied. Across the 2 surveys, subjects with CHD lowered their LDL-C from 123 ± 3 to 112 ± 4 mg/dL ($P = .01$). All high-risk subjects without CHD also dropped their mean LDL-C but from 133 ± 3 to 126 ± 2 ($P = .03$). Subjects with DM as their only high-risk diagnosis trended down with intermediate values from 125 ± 3 to 119 ± 2 ($P = .06$).

In addition, in 1999 to 2000, the percentage at goal (LDL-C< 100 mg/dL) was not significantly different between those with and without CHD (27% vs 20%, $P = .16$). However, the difference became significant in 2001 to 2002 (41% vs 26%, $P = .002$), driven by a robust improvement in goal achievement for those with CHD (27-41%, $P = .02$). The change in the percentage at goal was not significant for those at high risk without CHD (20-26%, $P = .07$) or for those with only DM (26-32%, $P = .15$) (Table III).

Finally, those with CHD were markedly less likely to be unmedicated with an LDL-C ≥130 mg/dL (dropping from 25% to 16%) compared with those with CHD risk equivalent conditions (dropping from 44% to 33%)

(Table III). That only 16% of individuals with CHD in the 2001 to 2002 NHANES exceed the LDL-C treatment threshold and do not take lipid-lowering medications suggests that most patients with CHD either met goal or were at least partially treated.

It appears that the changes in clinical management were more substantial among those without CHD. Interestingly, at the time of ATP III publication, not all of the proposed high-risk equivalent conditions had been supported by strong clinical trial data. Clinicians appear to have been slower to change their practice patterns for these less well-supported definitions of high risk.[19]

Factors related to improved compliance

The national improvement in mean LDL-C levels and goal achievement occurred in the context of educational efforts associated with the release of the ATP III guidelines in May 2001. New data and system changes likely had impact as well. Multiple large trials published between 1998 to 2002 supported more aggressive lipid lowering in primary[20] and secondary prevention,[21] including elderly[22] and female[23] subgroups. Treating patients with diabetes and/or lower than traditional LDL-C was also supported.[23,24] In addition, studies in managed care settings showed higher rates of compliance compared with national studies at the same period (Figure 1).[7] It is likely that publicity from the ATP III guidelines, scientific advances, and managed care penetration all combined to improve recognition and treatment of elevated LDL-C levels in high-risk populations.

Limitations

Limitations to this study include those inherent to the NHANES data set, such as statistical modeling, selection bias of subjects, and data release lags.[2] For example, the NHANES does not include the incarcerated or institutionalized populations of the United States. The NHANES data from interviews and questionnaires are subject to misunderstanding and recall bias. The current investigation analyzes data that are now several years old consistent with other studies of NHANES data.[3,4,12]

Some variables within NHANES do not precisely match those in the ATP III guidelines. The NHANES reports a positive family history of CHD as a heart attack or angina afflicting a parent, grandparent, or sibling younger than 50 years without sex distinction, whereas ATP III recognizes family history as a risk factor if CHD afflicts a male first-degree relative younger than 55 years or a female first-degree relative younger than 65 years.[1] The ATP III includes stroke as a marker of CHD risk equivalent, but the NHANES does not distinguish between hemorrhagic and embolic, leading to possible overestimation of stroke as a contributor to CHD risk. The NHANES does not include a test for aortic aneurysms or question a history of aortic surgery. Claudication was not used as a marker of PVD. Both could lead to possible underestimation of those afflicted with PVD.

Because these data represent single measurements for each individual NHANES subject, assessing treatment effects becomes difficult. It is impossible to know pretreatment cholesterol levels for those on medications and, thus, to address the clinical effectiveness of the treatment. Medication use relied on subject self-report and did not confirm with pharmacy records or give information regarding medicine class or dose. Consequently, we restricted our analysis of treatment rates to those with LDL-C $\geq$130 mg/dL, the treatment threshold at that time.

Future directions

In 2004, an update to the ATP III guidelines based on the release of 5 clinical trials modified lipid treatment goals.[19] This update added a "very high-risk" category and recommended lower LDL-C goals in the higher risk populations. One study used the 4-year 1999 to 2002 NHANES to assess the expected repercussions of these updates on goal achievement and medication requirements.[25] Ongoing collection and dissemination of the cyclic NHANES data will allow for additional assessment of national cholesterol management associated with the guideline updates.

Summary and clinical recommendations

This study uses 2 phases of the NHANES to demonstrate national improvements in the recognition and treatment of LDL-C in high-risk populations from 1999-2000 to 2001-2002. It is the first to compare LDL-C goal achievement before and after release of the ATP III guidelines. These advancements are likely secondary to both a positive clinical response to the ATP III guidelines and augmentation of larger multifactorial trends. They offer 3 major points for practicing clinicians caring for patients at high cardiovascular risk.

(1) Decreasing LDL-C levels and increasing goal achievement offer encouragement to clinicians and patients as these efforts continue.
(2) The LDL-C goal achievement demonstrates a marked improvement at the time of ATP III publication compared with studies across the previous 13 years.
(3) Improvements were concentrated in subjects with CHD. Limited improvement in cholesterol management of those without CHD supports the need to identify and treat this population more effectively.

References

1. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III). JAMA 2001;285:2486-97.

2. NHANES Analytic guidelines June 2004. The National Health and Nutrition Examination Survey. National Center for Health Statistics, Centers for Disease Control and Prevention. Hyattsville, MD. Available at http://www.cdc.gov/nchs/data/nhanes_general_guidelines_june_04.pdf. Last accessed May 2008.
3. Carroll MD, Lacher DA, Sorlie PD, et al. Trends in serum lipids and lipoproteins of adults, 1960-2002. JAMA 2005;294:1773-81.
4. Ford ES, Mokdad AH, Giles WH, et al. Serum total cholesterol concentrations and awareness, treatment, and control of hypercholesterolemia among U.S. adults: Findings from the National Health and Nutrition Examination Survey, 1999 to 2000. Circulation 2003; 107:2185-9.
5. Hoerger TJ, Bala MV, Bray JW, et al. Treatment patterns and distribution of low-density lipoprotein cholesterol levels in treatment-eligible United States adults. Am J Cardiol 1998;82:61-5.
6. Pearson TA, Laurora I, Chu H, et al. The lipid treatment assessment project (L-TAP): A multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Arch Int Med 2000;160: 459-67.
7. Sueta CA, Chowdhury M, Boccuzzi SJ, et al. Analysis of the degree of undertreatment of hyperlipidemia and congestive heart failure secondary to coronary artery disease. Am J Cardiol 1999;83: 1303-7.
8. National Health and Nutrition Examination Survey questionnaire, examination protocol and laboratory protocol. Hyattsville (Md): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 1999-2000 & 2001-2002. Available at http://www.cdc.gov/nchs/about/major/nhanes/questexam01_02.htm. Last accessed May 5, 2008.
9. Keevil JG. Online risk and cholesterol goal calculator. Available at https://www.heartdecision.org. Last accessed November 8, 2007.
10. National Heart, Lung and Blood Institute (NHLBI) Risk assessment tool for estimating your 10-year risk of having a heart attack. http://hp2010.nhlbihin.net/atpiii/calculator.asp. Last accessed February 14, 2008.
11. Fedder DO, Koro CE, L'italien GJ. New National Cholesterol Education Program III guidelines for primary prevention lipid-lowering drug therapy: Projected impact on the size, sex, and age distribution of the treatment-eligible population. Circulation 2002;105:152-6.
12. Klingman D, Williams SA, Benner JS, et al. Gauging the treatment gap in dyslipidemia: Findings from the 1999-2000 National Health and Nutrition Examination Survey. Am Heart J 2005;150:595-601.
13. Jacobson TA, Griffiths GG, Varas C, et al. Impact of evidence-based "clinical judgment" on the number of American adults requiring lipid-lowering therapy based on updated NHANES III data. Arch Int Med 2000;160:1361-9.
14. Case CC, Jacobson TA, Roberts S, et al. Management of persons with high risk of coronary heart disease but low serum, low-density lipoprotein cholesterol. Am J Cardiol 2003;91:1134-6.
15. McBride P, Schrott HG, Plane MB, et al. Primary care practice adherence to National Cholesterol Education Program guidelines for patients with coronary heart disease. Arch Int Med 1998;158:1238-44.
16. Straka RJ, Taheri R, Cooper SL, et al. Assessment of hypercholesterolemia control in a managed care organization. Pharmacotherapy 2001;21:818-27.
17. Parris ES, Lawrence DB, Mohn LA, et al. Adherence to statin therapy and LDL cholesterol goal attainment by patients with diabetes and dyslipidemia. Diabetes Care 2005;28:595-9.
18. James P, Tan HH, MacAlpine R, et al. Treatment gap in the use of lipid-lowering drug therapy in diabetes; a population-based study. Diabetes Medicine 2004;21:1108-12.
19. Grundy SM, Cleeman JI, Merz CNB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation 2004;110:227-39.
20. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). JAMA 1998;279: 1615-22.
21. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study group. N Engl J Med 1998;339: 1349-57.
22. Lewis SJ, Moye LA, Sacks FM, et al. Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) Trial. Ann Intern Med 1998;129:681-9.
23. Collins R, Armitage J, Parish S, et al. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomized placebo-controlled trial. Heart Protection Study Collaborative Group. Lancet 2002;360:7-22.
24. Goldberg RB, Mellies MJ, Sacks FM, et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: Subgroup analyses in the Cholesterol and Recurrent Events (CARE) Trial. Circulation 1998;98:2513-9.
25. Persell SD, Lloyd-Jones DM, Baker DW. Implications of changing National Cholesterol Education Program goals for the treatment and control of hypercholesterolemia. J Gen Intern Med 2006;21:171-6.

The authors would like to thank Marla Johnson for her assistance with the preparation of this manuscript.

Appendix A. National Health and Nutrition Examination Survey variables

NHANES item ID	Content
Demographics	
SEQN	Respondent sequence number
RIDAGEYR	Age at screening
RIAGENDR	Sex
RIDSTATR	Interview/examination status
WTMEC2YR	Full sample of 2-y of MEC examination weight
RIDPREG	Pregnancy status
Medical history *	
MCQ160C †	History of coronary artery disease
MCQ160D †	History of angina/angina pectoris
MCQ160E †	History of a myocardial infarction
MCQ160F †	History of a stroke/CVA
MCQ250G ‡	Family history of early coronary artery disease
SEQ020 (1999-2000)	Cancer chemotherapy in past or future 4 wk
SMQ020	Lifetime smoking history of at least 100 cigarettes

(*continued on next page*)

(*continued*)

NHANES item ID	Content
SMQ040	Currently smoking cigarettes
DIQ010 †	History of DM
DIQ050	Currently taking insulin
DIQ070	Currently taking diabetic pills/oral hypoglycemic agents
BPQ050A	Currently taking prescription blood pressure medications
BPQ100D	Currently taking medications to lower cholesterol
Physical examination	
BPXSAR	Systolic blood pressure; average of 3-4 measurements (mm Hg)
BPXDAR (1999-2000) SBXDAR (2001-2002)	Diastolic blood pressure, average of 3-4 measurements (mm Hg)

(*continued*)

NHANES item ID	Content
LEXLABPI	Left ankle brachial pressure index
LEXRABPI	Right ankle brachial pressure index
Laboratory evaluation	
LBXTC	Total cholesterol (mg/dL)
LBDHDL	HDLC (mg/dL)
LBXSTR	Triglycerides (mg/dL)

CVA, cerebrovascular accident.
NHANES historical variables relied on self-reports of the individual subjects or their questionnaire proxies.
NHANES medical history questions asked if the subject had ever been told by a health professional that they have or had the condition in question.
NHANES asked the family history of early coronary artery disease question as follows: "Including living and deceased, were any of biological that is, blood relatives including grandparents, parents, brothers, sisters ever told by a health professional that they had a heart attack or angina before the age of 50?"