Implications of Cardiac Risk and Low-Density Lipoprotein Cholesterol Distributions in the United States for the Diagnosis and Treatment of Dyslipidemia

Data From National Health and Nutrition Examination Survey 1999 to 2002

Jon G. Keevil, MD; Michael W. Cullen, MD; Ronald Gangnon, PhD; Patrick E. McBride, MD, MPH; James H. Stein, MD

Background—Updated guidelines from the National Cholesterol Education Program Adult Treatment Panel III stratify patients into 5 groups of coronary heart disease (CHD) risk that determine intensity of lipid-lowering therapy. The present study assesses the distribution of low-density lipoprotein cholesterol (LDL-C) in the United States across the 5 groups of CHD risk as defined in the updated guidelines.

Methods and Results—Subjects included 7399 individuals 20 to 79 years of age in the 1999 to 2002 National Health and Nutrition Examination Survey representing 171 million individuals in the United States. CHD risk, LDL-C levels, and goal achievement were determined per Adult Treatment Panel III guidelines. CHD risk assessment incorporated a medical condition review, risk factor summation, and Framingham Risk Score calculation. Percentages were weighted to represent population estimates, and SEs were adjusted for the survey design. The distribution of individuals by CHD risk included 61.1% at lower risk, 10.6% at high risk, and 5.7% at very high risk. From Adult Treatment Panel III criteria, only 5.4% of the population was at “intermediate” risk. Two thirds (66.3%) met their Adult Treatment Panel III–defined LDL-C goal. Of those at high and very high risk, 23% and 26%, respectively, met the goal of LDL-C \( \leq 100 \text{ mg/dL} \), whereas only 3.1% and 4.6% had an LDL-C \( < 70 \text{ mg/dL} \) (or non–high-density lipoprotein C \( \leq 100 \text{ mg/dL} \)).

Conclusions—Most adult US residents are at lower 10-year CHD risk and meet risk-adjusted LDL-C goals. However, large portions of the high-risk population are undertreated. The commonly described population at intermediate risk is small. A novel method of identifying patients who might benefit from additional testing to determine their treatment strategy is provided. (Circulation. 2007;115:1363-1370.)

Key Words: cardiovascular diseases ■ cholesterol ■ guidelines ■ lipids ■ risk factors

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A recent study focused on the sizes of CHD risk groups and achievement of LDL-C goals; however, it did not address an important group of patients, those considered at “intermediate” risk.6 The size of this group is a matter of clinical and economic importance. Without an accurate understanding of the numbers of individuals in the United States at intermediate risk, policies for additional screening with new imaging or blood tests7 cannot be assessed for their impact on clinical practice and healthcare costs.

We used the 1999 to 2002 National Health and Nutrition Examination Survey (NHANES) data set to evaluate the US...
The 5 standard ATP III RFs used to risk stratify subjects include the following:

- Advanced age: Men ≥45 years; women ≥55 years.
- Low high-density lipoprotein cholesterol (HDL-C): <40 mg/dL (≥60 mg/dL counts as a negative RF).
- Hypertension: Systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medication.
- Cigarette smoking: Currently smoking every day or some days and reported having smoked ≥100 cigarettes in their lifetime.
- Family history: NHANES variable MCQ250G, family history of premature CHD in subjects reporting a heart attack or angina in grandparents, parents, or siblings <50 years of age.

Metabolic syndrome is used to subclassify those at very high risk and was present if a subject met at least 3 of the following 5 criteria:

- Waist circumference >102 cm in men or >88 cm in women. If waist circumference was not available, body mass index >30 kg/m² was substituted for this diagnostic criterion.
- Fasting triglycerides ≥150 mg/dL or random triglycerides ≥400 mg/dL.
- HDL-C <40 mg/dL in men or <50 mg/dL in women.
- Blood pressure ≥130/85 mm Hg or use of antihypertensive medication.
- Fasting glucose ≥100 mg/dL.

**Framingham Risk Score**

The FRS is a standard method to assess cardiovascular risk. Seven components are used to estimate the 10-year risk of CHD events (heart attack or CHD death). The mathematical functions used were provided by the Framingham study by personal communication (L.M. Sullivan, PhD, and R.B. D’Agostino, Sr, PhD, written communication, 2002).

**Definitions of Risk Levels**

Subjects were classified into risk levels using the ATP III guidelines:

- Very high risk: Subjects with CHD and ≥1 of the following: DM, cigarette smoking, the metabolic syndrome, and/or ≥3 ATP III RFs.
- High risk: Subjects with CHD, peripheral vascular disease, cerebrovascular disease, and/or DM or with ≥2 ATP III RFs and 10-year FRS >20%. This group excludes those with the combinations above defined as very high risk.
- Moderately high risk: Subjects with no high-risk diagnoses, ≥2 ATP III RFs, and FRS of 10% to 20%. This group is commonly referred to as intermediate risk.
Low-density lipoprotein cholesterol (LDL-C) and non–high-density lipoprotein cholesterol (non–HDL-C) levels for use as goals and thresholds for initiating therapy.2 These goals and thresholds match the cut points for the 6 LDL-C and non–HDL-C values for use as goals and thresholds for initiating therapy.2 These goals and thresholds match the cut points for the 6

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>LDL-C [or Non-HDL-C] Levels (mg/dL) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70 [mg/dL]</td>
<td>0.5±0.2 (0.3%±0.2%)</td>
</tr>
<tr>
<td>70–99 [mg/dL]</td>
<td>2.1±0.5 (1.2%±0.3%)</td>
</tr>
<tr>
<td>100–129 [mg/dL]</td>
<td>3.2±1.6 (1.9%±0.4%)</td>
</tr>
<tr>
<td>130–159 [mg/dL]</td>
<td>2.3±0.4 (1.3%±0.3%)</td>
</tr>
<tr>
<td>160–189 [mg/dL]</td>
<td>0.8±0.3 (0.5%±0.2%)</td>
</tr>
<tr>
<td>210–229 [mg/dL]</td>
<td>0.9±0.4 (0.5%±0.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>9.8±1.4 (5.7%±0.7%)</td>
</tr>
</tbody>
</table>

Figure 1. Estimated distributions (±95% CI) are given in millions of individuals. Percentages (±95% CI) are in terms of the 171 million adults in the study population. Heavy black lines represent the ATP III LDL-C or non–HDL-C goals for individuals at each risk level. Green cells contain subjects for whom cholesterol change is unnecessary; yellow cells, subjects for whom change should be considered; and red cells, subjects for whom cholesterol change is necessary (see text). *Non–HDL-C was used for goal achievement in subjects fasting <8.5 hours, missing fasting time, missing triglycerides data, or with triglycerides >400 mg/dL.

- **Moderate risk**: Subjects with no high-risk diagnoses, ≥2 ATP III RFs, and an FRS <10%. 
- **Lower risk**: Subjects with no high-risk diagnoses and <2 ATP III RFs.

**LDL-C and Non–HDL-C Calculation and Goal Assignment**

For the subjects (n=4560; population, 105.8 million; 61.9%) with a fasting cholesterol panel and triglycerides <400 mg/dL, LDL-C was calculated from the Friedewald equation.13 They were stratified by LDL-C into 1 of 6 groups: <70, 70 to 99, 100 to 129, 130 to 159, 160 to 189, and ≥190 mg/dL (Figure 1). For subjects with laboratory fasting times <8.5 hours (n=2712),14 triglycerides >400 mg/dL (n=116), or missing fasting time (n=10) or triglyceride data (n=1), the secondary goal of non–HDL-C was calculated. Subjects were stratified into the same 6 groups by the use of thresholds corresponding to the respective ATP III goals for non–HDL-C (30 mg/dL higher than the respective LDL-C goals at each risk level).2

The ATP III update uses the risk levels to define LDL-C (or non–HDL-C) values for use as goals and thresholds for initiating therapy.2 These goals and thresholds match the cut points for the 6 LDL-C (or non–HDL-C) groups (Figure 1 and Table 2).

Because LDL-C levels are associated with some variation or uncertainty in treatment recommendations, we developed a novel method to clarify risk based on need for treatment change, For example, among patients with CHD with LDL-C between 70 and 99 mg/dL, therapy is described as “optional” or “reasonable.15 To address this ambiguity, for each risk level, LDL-C (and non–HDL-C) levels are defined as “change unnecessary” if below the range of recommendations, “change necessary” if above levels requiring drug therapy, and “consider change” when between these 2 levels.

**Statistical Analysis**

Subject data were downloaded from http://www.cdc.gov/nchs/nhanes.htm and imported into Microsoft Excel (version 11.2 for Macintosh, Microsoft Corp, Redmond, Wash). Separate fields were developed for each data point and clinical decision to model a virtual prevention clinic addressing each individual subject. Subjects were stratified by risk level and substratified by LDL-C or non–HDL-C levels, and total individuals were computed in each category. Population totals and percentages were calculated from the full sample 4-year mobile-examination-center weight for each subject, which represents unbiased population estimates.16

The entire NHANES 1999 to 2002 mobile-examination-center data set includes 19,759 subjects with a combined weight representing 278.7 million individuals. Restricting analysis to individuals 20 to 79 years of age resulted in the selection of 8747 subjects representing 190.4 million US residents. After all exclusions, 7399 subjects made up the study sample, with a population weight of 278.7 million individuals representing 190.4 million US residents. After all exclusions, 7399 subjects made up the study sample, with a population weight of 171.0 ± 10.6 million individuals (Table 1). The data set then was imported into SAS version 9.1 (SAS Institute, Cary, NC) to calculate SEs adjusted for the complex survey design. Data are presented as population weight±half-width of the 95% confidence interval. Percentages were calculated using the denominator of 171.0 million (the study population after exclusions).

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**TABLE 2. LDL-C Goals and Thresholds for Intervention**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Category Definition</th>
<th>LDL-C Goal*</th>
<th>Initiate TLC*</th>
<th>Initiate Drug Therapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high</td>
<td>Any 1 of CHD, CVD, or PVD, plus smoking, DM, metabolic syndrome, or ≥3 major RFs</td>
<td>&lt;70 mg/dL</td>
<td>≥70 mg/dL</td>
<td>≥70 mg/dL</td>
</tr>
<tr>
<td>High</td>
<td>CHD, PVD, CVD, DM or ≥2 RFs and FRS &gt;20%</td>
<td>&lt;100 mg/dL (optional†) &lt;70 mg/dL</td>
<td>≥100 mg/dL</td>
<td>≥100 mg/dL (consider &lt;100 mg/dL)</td>
</tr>
<tr>
<td>Moderately high</td>
<td>≥2 RFs and FRS of 10%–20%</td>
<td>&lt;130 mg/dL (optional †) &lt;100 mg/dL</td>
<td>≥130 mg/dL</td>
<td>≥130 mg/dL (consider 100–129 mg/dL)</td>
</tr>
<tr>
<td>Moderate</td>
<td>≥2 RFs and FRS &lt;10%</td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>≥160 mg/dL</td>
</tr>
<tr>
<td>Low</td>
<td>≥2 RFs</td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>≥190 mg/dL (consider 160–189 mg/dL)</td>
</tr>
</tbody>
</table>

TLC indicates therapeutic lifestyle change; CVD, cerebrovascular disease; and PVD, peripheral vascular disease.

*When non–HDL-C is used to determine goal achievement, levels are 30 mg/dL higher than the respective LDL-C goal at each risk level.
†ATP III update uses “optional”; secondary prevention guidelines use “reasonable.”15
Results

Distribution of CHD Risk

Subject distribution across the 5 risk levels includes 61.1% at lower risk and 17.2% at moderate risk. Only 5.4% are at moderately high risk (often referred to as intermediate risk), 10.6% are at high risk, and the remaining 5.7% are at very high risk (Figure 1, right column). Of the 171 million individuals, 5.3% are in the lowest group (LDL-C ≤70 mg/dL or non–HDL-C ≤100 mg/dL), and 5.7% are in the highest (LDL-C ≥190 mg/dL or non–HDL-C ≥220 mg/dL). The largest stratum (32.3%) is LDL-C 100 to 129 mg/dL (or non–HDL-C 130 to 159 mg/dL) (Figure 1).

At least 1 high-risk criterion is required for inclusion in the high- and very high-risk categories. Table 3 presents both the number of individuals who meet each criterion and the number for whom that criterion is the only definition of high-risk status. Of the 28.0 million US residents at high or very high risk, nearly half (48.2%) have DM, and 33.7% have DM alone. CHD is present in only 34.6% of the high- and very high-risk groups (Table 3). Multiple RFs and an FRS ≥20% is present in 20.9%, whereas peripheral vascular disease (13.8%) and cerebrovascular disease (12.4%) are less common.

CHD Risk and Cholesterol Goals

Stratifying the 5 risk categories by the 6 LDL-C and non–HDL-C levels creates a 30-cell matrix (Figures 1 and 2). All subjects fit into a cell. Applying the LDL-C goals from ATP III (Table 2) shows that 66.3/1.9% (113.4 ± 7.8 million) are at or below goal, whereas 33.7/1.9% (57.6 ± 5.1 million) are above goal.

The population can be divided into 3 clinical groups based on the necessity of LDL-C reduction as follows:

- Change unnecessary: This group (green in Figures 1 and 2) includes 107.7/1.4 million (63.0/1.6%) who meet even the most aggressive goals for their risk category.
- Change necessary: This group (red in Figures 1 and 2) includes 37.3/3.8 million (21.8/1.6%) who require change in their LDL-C (or non–HDL-C) levels because they are above more conservative thresholds for lifestyle changes and drug therapy.

Table 3. Prevalence of Conditions Leading to High-Risk Status

<table>
<thead>
<tr>
<th>High-Risk Condition</th>
<th>DM (95% CI)</th>
<th>CHD (95% CI)</th>
<th>PVD (95% CI)</th>
<th>CVD (95% CI)</th>
<th>FRS ≥20% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total individuals with condition</td>
<td>13.5 ± 1.5 (48.2)</td>
<td>9.7 ± 1.5 (34.6)</td>
<td>3.9 ± 0.5 (13.8)</td>
<td>3.5 ± 0.8 (12.4)</td>
<td>3.9 ± 0.5 (20.9)</td>
</tr>
<tr>
<td>High-risk status defined by this condition alone</td>
<td>9.5 ± 1.5 (33.7)</td>
<td>5.3 ± 0.8 (18.8)</td>
<td>2.0 ± 0.3 (7.1)</td>
<td>1.4 ± 0.5 (5.1)</td>
<td>3.4 ± 0.7 (12.1)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 2.

Five conditions define inclusion in the high- and/or very high-risk categories. For each of the 5, the total number of high-risk individuals with the condition and the number of individuals for whom this is the only condition defining high risk are presented. Estimated distributions (±95% confidence interval) are given in millions of individuals. Percentages are of the 28.0 million individuals in the study population at high or very high risk. Percentages do not equal 100% because of overlap of multiple conditions.
• Consider change: This group (yellow in Figures 1 and 2) has LDL-C between aggressive and conservative treatment recommendations and numbers 26.0±2.8 million (15.2±1.2%), a figure that includes 10.1±1.7 million from the lower-risk group.

Discussion
The risk assessment process defined by ATP III includes identification of high-risk medical conditions, enumeration of major RFs, and calculation of the FRS when appropriate. Cholesterol goals are linked to estimates of absolute CHD risk. Therefore, making individualized LDL-C treatment recommendations requires consideration of both CHD risk and the LDL-C level. The matrix in Figure 1 provides several insights into the risk assessment process.

High-and Very High-Risk Individuals
There are 18.1 million individuals at high risk and 9.8 million at very high risk. Restricting to those with known CHD (including angina) identifies only 35% (9.7 million) of the 2 highest-risk groups. Hard CHD alone would identify only 29% (8.0 of 28.0 million).

ATP III expanded the definition of high risk to include “CHD-equivalent” conditions, nearly tripling its size. The diagnosis of DM is made in 13.5 million, 34% of whom are at high risk by this diagnosis alone. High risk is uniquely defined in 3.4 million because of ≥2 RFs and an FRS >20%, 2.0 million because of a low ankle brachial index, and 1.4 million because of stroke history. These findings have important implications for clinics that assess cardiac risk. Failure to routinely measure ankle brachial indices, calculate FRS, or recognize patients in the very high-risk category may lead clinicians to underestimate cardiac risk in up to 11.1 of 28.0 million high- and very high-risk individuals.

Current cholesterol treatment guidelines maintain the LDL-C goal of <100 mg/dL and define LDL-C <70 mg/dL as optional or reasonable, with particular emphasis on those at very high risk. Only 4.6% of very high-risk and 3.1% of high-risk individuals have LDL-C <70 mg/dL. For these 2 groups, 75.8% (21.1 million) have LDL-C ≥100 mg/dL and are not meeting the more conservative cholesterol goals (Figure 1).

Not all authors or groups define the very high-risk group similarly. A recent national survey observed that 75% of patients with cardiovascular disease were at very high risk. They defined “multiple major RFs” as ≥2 compared with ≥3 in the present study. Repeating their analysis with a 3-RF threshold, we find that 67.3% of US residents with known cardiovascular disease are at very high risk. Defining “multiple RFs” as ≥2 RFs increases the same measure to 82.4%. Better clarity of very high-risk definition may be needed to improve the utility of such comparisons.

Lower Risk
The next step in ATP III risk assessment is counting RFs and assigning those with <2 to the lower-risk category. We found that 61.1% (104.5±6.7 million) were at lower risk. These individuals have an LDL-C goal of <160 mg/dL; 86% (90.3±5.9 million) achieved it.

When the RF count establishes lower-risk status, clinicians must not reflexively assume that lipid treatment remains unnecessary. Of US residents, 4.1±0.8 million lower-risk individuals have LDL-C >190 mg/dL (or non-HDL-C ≥220 mg/dL) for whom guidelines recommend medical therapy. An additional 10.1±1.7 million are above the LDL-C goal of 160 mg/dL and are candidates for lifestyle modifications and consideration of medical therapy. This combined group is larger than the moderately high- or very high-risk groups.

Omitting HDL-C ≥60 mg/dL as a negative RF moves 8.0±1.0% (8.3±1.2 million) out of the lower-risk group, 7.2±1.2 million become moderate risk, and 1.1±0.3 million become moderately high risk on the basis of the FRS. Accordingly, 3.6±0.6 million (3.5±0.5% of the initial lower-risk group) receive a new LDL-C goal with this omission.

A broader question about the lower-risk group is how to assess the relative importance of RF counting versus the FRS. Although ATP III does not require it, assessing the FRS in all 104.5 million individuals at lower risk by RFs identifies 9.4±1.6 million with an FRS >6% (a threshold some suggest should trigger additional testing). A previous analysis demonstrated that calculating the FRS before RF evaluation (an option in ATP III) reclassified the risk of >6 million individuals in the lower-risk group.

Intermediate Risk and Use of the FRS
Without updated numbers that carefully apply guideline-based risk stratification criteria, there have been widely varying and potentially misleading estimates of the number of individuals at intermediate risk, and guidelines recommending additional tests to assist with risk assessment have incorporated these estimates. The ATP III guidelines do not define an intermediate-risk group, but some have defined it as subjects without high-risk conditions but with ≥2 RFs and an FRS of 10% to 20%. This matches the ATP III moderately high-risk group. Although 1 report estimated that this group was 40% of the US population and others have quoted this estimate, our study found just 5.4% at moderately high risk. This finding suggests that previous reports overestimated the number of patients considered to be at intermediate risk. Low-risk patients were defined in 1 article as having “a low-risk FRS [<6%] and no major RFs outside the desirable range.” These authors estimated this group to be 35% of the population. We applied these criteria to our data set and found only 11.8 million subjects (6.9%) at low risk by this definition. Subtracting the 17.9% of individuals at high or very high risk would imply that the remaining 75.2% are at intermediate risk, >10-fold the size of the moderately high-risk group in our analysis. Thus, the size of this group is very sensitive to RF number and definitions.

For the purpose of considering additional testing, a recent consensus conference expanded the definition of intermediate risk to include an FRS of 6% to 20%. This definition change alone approximately doubled the size of the intermediate-risk group to 10.0±0.8% (17.1±2.0 million), which still is below previous estimates.
After high-risk subjects have been assigned by medical conditions and lower-risk subjects by RFs, ATP III recommends assessment by the FRS. Although some recent reports\(^{19,21}\) equate the entire risk assessment process with the FRS by linking risk categories to the FRS, they are not the same. In our study, after separating subjects with high-risk conditions and those at lower risk by RFs, only \(24.5 \pm 1.6\%\) (41.9 \(\pm\) 4.6 million) required FRS to determine their risk status. Only \(15.0 \pm 2.3\%\) of the high-risk group and none of the very high-risk group use the FRS for risk assignment. This suggests that the FRS alone should not be considered a substitute for the other components of the risk assessment process.

**Finding a Focused Group for Consideration of Additional Testing**

A growing body of literature addresses how new imaging and blood tests may improve risk prediction.\(^7,22,23\) Subjects at moderately high (intermediate) risk often are described as those in greatest need of additional testing.\(^7,22,23\) However, many in this risk group need no further evaluation to make clear decisions about LDL-C treatment (Figure 1). Subjects with LDL-C \(\geq 130\) mg/dL (70.5 \(\pm\) 4.4\% of the moderately high-risk group) exceed thresholds for both lifestyle changes and drug therapy. Another 0.6 \(\pm\) 0.3 million (7.5 \(\pm\) 3.3\% of moderately high group) are below the more aggressive threshold of 100 mg/dL and thus do not require further LDL-C reduction. Only 2.1 \(\pm\) 0.5 million (22.0 \(\pm\) 4.3\% of the moderately high-risk group, 1.2 \(\pm\) 0.3\% of the population) have LDL-C of 100 to 129 mg/dL. Although this subset may benefit from further diagnostic information, it is small.

Others who may benefit from additional evaluation include high-risk patients with LDL-C 70 to 99 mg/dL who do not receive clear treatment recommendations from the guidelines. In addition, some lower- and moderate-risk patients have thresholds for initiating drug therapy that are 30 mg/dL higher than their LDL-C goals, creating a clinical scenario in which the goal is not met but medications may not be clearly indicated. For example, a 60-year-old woman with no other RFs and an LDL-C of 185 mg/dL may pose a difficult decision for the clinician because she is estimated to be at lower risk but with a high LDL-C. This may not be a rare clinical scenario because 10.1 \(\pm\) 1.7 million US residents fit this narrow definition.

For additional testing, we suggest a novel method of selection based on the following 3 categories:

- **Change unnecessary:** For these 107.7 million individuals (63.2\%), additional testing is unlikely to change treatment recommendations (green in Figures 1 and 2).
- **Consider change:** This group of 26.0 million (15.2\%) is most likely to benefit from additional testing that might reassign subjects into other risk groups (yellow in Figures 1 and 2).
- **Change necessary:** These 37.3 million individuals (21.8\%) should initiate therapeutic interventions without additional testing (red in Figures 1 and 2). There may be situations in which the initial therapy brings subjects into the “consider change” level.

This categorization scheme combines the full risk assessment process (medical condition review, RF summation, and FRS calculation) with LDL-C levels and may provide better guidance for individualized treatment and need for additional testing.

**Study Limitations**

NHANES data are collected by examination, laboratory testing, and interview and therefore are subject to sampling and nonsampling errors. Interview data based on self-report are subject to recall bias and misunderstanding of questions. Additionally, NHANES does not include the incarcerated or institutionalized populations of the United States.\(^{24}\)

Some of the NHANES variables do not precisely match those in the ATP III guidelines or clinical practice. For instance, NHANES reports family history of CHD as a parent or grandparent <50 years of age without gender distinction, whereas ATP III recognizes family history as an RF if CHD afflicts a male first-degree relative <55 years of age or a female first-degree relative <65 years of age.\(^1\) We diagnosed DM from a single glucose sample with different thresholds based on the fasting time. A second sample and/or a glucose tolerance test were not available. We included stroke as a CHD risk equivalent. Some subjects with stroke match the ATP III criteria of “symptomatic carotid disease,” but others likely experienced hemorrhagic or cardioembolic strokes with less well-defined correlation to future cardiac risk. Thus, the risk in the 1.4 \(\pm\) 0.5 million individuals (0.8 \(\pm\) 0.3\%) designated high on the basis of a history of a stroke alone may be overestimated. No test for aortic aneurysm or history of aortic surgery is included in NHANES, so some CHD risk–equivalent subjects may be unrecognized. Our definition of CHD included 48 subjects representing 1.0 \(\pm\) 0.4 million individuals (0.6 \(\pm\) 0.2\%) for whom angina was the only high-risk diagnosis. Risk in this small subset may be overestimated by this softer end point.

No data identifying recent acute coronary syndrome are present, likely resulting in some subjects being classified as high risk instead of very high risk. Furthermore, the definition of the very high-risk group in ATP III is vague because it includes, for example, “multiple” and “severe” RFs without explicitly defining these terms.\(^2\)

For subjects with short fasting times or triglycerides >400 mg/dL, we calculated non–HDL-C. Subjects then were assigned to the LDL-C level associated with the corresponding non–HDL-C goal (30 mg/dL higher). This approach follows the ATP III recommendation of using the non–HDL-C goal in this situation.\(^1\) The NHANES data set does not provide information on fibrate or niacin use, so some subjects might not qualify for the latest metabolic syndrome criteria.\(^{25}\)

Finally, the present study includes 4 years from NHANES, which represent a sample of the country from a fixed range in time. More recent data may be slightly different.

Despite these limitations, the estimates provided here are similar to those independently published by a research group from another institution.\(^6\) In addition to providing significantly more detail on the number of Americans in the different cardiovascular risk groups and their treatment status by LDL-C goals, the present study adds unique information...
describing how patients at high and very high risk qualified for these designations. In addition, this discussion focuses specifically on the number of patients at intermediate risk, the implications of this designation for additional testing, and the implications of errors in risk stratification.

Conclusions
The present study offers important information to policy makers and those needing estimates of the size of the at-risk population based on the presence of CHD, RFs, and LDL-C levels. This study also provides 3 additions to the understanding of cardiovascular risk assessment: (1) assessment of CHD risk in the entire US population, (2) stratification of CHD risk by levels of LDL-C, and (3) identification of clinical groups oriented around the necessity of reducing LDL-C. This study underscores the importance of a complete clinical evaluation to accurately identify high-risk subjects rather than using only the FRS.

The majority of the population (61%) is at lower risk as defined by current guidelines. A significant percentage (34%) of individuals from all risk levels has not met LDL-C goals. The commonly described group of patients at intermediate risk (5.4%) is much smaller than previously estimated and contains few subjects for whom treatment recommendations are not clear. A novel strategy for identifying patients who may benefit most from additional testing is provided.

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References
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