NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

LIPID SCREENING IN THE PRIMARY PREVENTION OF CORONARY HEART DISEASE AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN ADULTS

Guidelines

1. National Heart, Lung, and Blood Institute (U.S.) (NHLBI). (1)Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2)Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. Bethesda (MD): U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung and Blood Institute; 2001. Various p. [1274 references]; Circulation 2004 Jul 13;110(2):227-39. [45 references]
2. Veterans Health Administration, Department of Defense (VHA/DoD). VA/DoD clinical practice guideline for the management of dyslipidemia. Washington (DC): Department of Veterans Affairs, Department of Defense; 2006 Dec. 140 p.

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INTRODUCTION:

A direct comparison of National Heart, Lung, and Blood Institute (NHLBI) and Veterans Health Administration, Department of Defense (VHA/DoD) recommendations for lipid screening for primary prevention of coronary heart disease (CHD) and atherosclerotic cardiovascular disease (ASCVD) in adults is provided in the tables below. The guidelines address both cholesterol testing and clinical management of high cholesterol, including primary and secondary prevention. Recommendations for clinical management and secondary prevention of dyslipidemia, however, are beyond the scope of this synthesis.

Table 1 gives a broad overview of the four guidelines. Table 2 details the recommendations for lipid screening and risk factor assessment for adults. Benefits and harms associated with screening are listed in Table 3. The supporting evidence is classified and identified with the major recommendations for VHA/DoD, and the definitions of each rating scheme are included in Table 4. Table 4 also includes references supporting specific recommendations for VHA/DoD, when applicable. Following the content comparison tables and discussion, the areas of agreement and differences among the guidelines are identified.

In formulating their recommendations, VHA/DoD drew heavily from NHLBI's *Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATPIII])* and from the 2001 U. S. Preventive Services Task Force (USPSTF) recommendations for lipid screening.

Notably, since the publication of ATP III, 5 major clinical trials of statin therapy with clinical end points have been published. These trials addressed issues that were not examined in previous clinical trials of cholesterol-lowering therapy. In 2004 the NHLBI issued an addendum to their guideline that reviews the results of these recent trials and assesses their implications for cholesterol management. Proposed modifications to the NHLBI guideline recommendations have been included in this synthesis.

Listed below are common abbreviations used within the tables and discussions:

- ATPII and ATPIII, Adult Treatment Panel II and Adult Treatment Panel III
- ASCVD, atherosclerotic cardiovascular disease
- BP, blood pressure
- CHD, coronary heart disease
- CVD, cardiovascular disease
- DM, diabetes mellitus
- HDL, high-density lipoprotein
- LDL, low-density lipoprotein
- NCEP, National Cholesterol Education Program
- NHLBI, National Heart, Lung, and Blood Institute
- RCT, randomized controlled trial
- TLC, therapeutic lifestyle changes

- TC, total cholesterol
- UMHS, University of Michigan Health Systems
- USPSTF, United States Preventive Services Task Force
- VHA/DoD, Veterans Health Administration, Department of Defense

TABLE 1: SCOPE	
Objective	
NHLBI (2001 & 2004)	• To examine the available evidence on coronary heart disease (CHD) and high blood cholesterol, especially the evidence that has emerged since the second report of the Expert Panel was published in 1993 (Second report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel II]. Bethesda [MD]: U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung and Blood Institute; 1993 Sep. 180 p.) • To update, where appropriate, the existing recommendations for management of high blood cholesterol in adults **2004 Addendum** • To review the results of five recent clinical trials and assess their implications for cholesterol management • To translate the scientific evidence into guidance that helps professionals and the public take appropriate action to reduce the risk for coronary heart disease and cardiovascular disease
VHA/DoD (2006)	• To promote reduction of cardiovascular risk via evidence-based management of dyslipidemia, thereby improving clinical outcomes • To assist primary care providers or specialists in the detection of high blood cholesterol, assessment of the global risk for CVD, determination of treatment goals and appropriate therapies, and delivery of individualized intervention • To incorporate information from several existing, national recommendations into a format that would maximally facilitate clinical decision-making
Target Population	
NHLBI (2001 & 2004)	All adults aged 20 years or older

VHA/DoD (2006)	Adults (age 17 years or older) eligible for care in the VHA/DoD health care system
Intended Users	
NHLBI (2001 & 2004)	Advanced Practice Nurses Dietitians Nurses Patients Pharmacists Physician Assistants Physicians Public Health Departments
VHA/DoD (2006)	Advanced Practice Nurses Allied Health Personnel Dietitians Nurses Physician Assistants Physicians
Screening and Risk Assessment Interventions Considered	
NHLBI (2001 & 2004)	• Fasting lipoprotein profiles (TC, LDL-cholesterol, HDL-cholesterol, and triglyceride) • Identification of major risk factors as well as life-habit and emerging risk factors • Estimation of 10-year CHD risk with Framingham scoring
VHA/DoD (2006)	• Patient history and assessment of risk factors for cardiovascular disease, including estimation of 10-year CHD risk with Framingham scoring • Measurement of TC and HDL or TC, HDL, TG, and LDL • Fasting lipid profile, including LDL

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR LIPID SCREENING IN THE PRIMARY PREVENTION OF CORONARY HEART DISEASE AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE	
Who Should Be Screened?	
NHLBI (2001 & 2004)	• Screening should begin at age 20, at the first appropriate opportunity presented by a visit to a physician (case finding), in

	both men and women.
VHA/DoD (2006)	• Fasting lipid profile testing should be obtained in all men age 35 and older and women age 45 years or older every 5 years. **[A]** (Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report [NCEP ATP-III], 2002; U.S. Preventive Services Task Force [USPSTF], 2001) • Fasting lipid profile testing should be obtained in individuals with a family history or clinical evidence of familial hyperlipidemia. **[A]** (NCEP ATP-III, 2002) • Fasting lipid profile testing in young adults may be considered depending upon the association with other risk factors. Younger adults (men younger than age 35 and women age 45 or younger) should be screened for lipid disorders if they have one or more of the following risk factors: family history of premature CVD, hypertension (or under treatment for hypertension), or smoking. **[B]** (NCEP ATP-III, 2002; Pignone et al., 2001; USPSTF, 2001; "A multicenter comparative trial," 1993) • A lipid profile should be obtained for individuals with abdominal obesity (waist circumference >40 inches in men and >35 inches in women) to aid in assessment of metabolic syndrome. **[B]** (NCEP ATP-III, 2002) • All persons with average or below average risk for atherosclerotic events should be screened for dyslipidemia every five years. **[I]** (Working Group Consensus) • Elderly patients age 75 or older should be screened if they have multiple CVD risk factors, or a history of CVD and good quality of life with no other major life-limiting diseases. **[I]** (Working Group Consensus)
What Type of Screening Test Should Be Used?	
NHLBI (2001 & 2004)	• A fasting lipoprotein profile is recommended, including major blood lipid fractions (i.e., total cholesterol, LDL-cholesterol, HDL -cholesterol, and triglycerides). • If the testing opportunity is nonfasting, only the values for TC and HDL will be usable. In such a case, if total cholesterol is $\geq$200 mg/dL or HDL is <40 mg/dL, a follow-up lipoprotein profile is needed for appropriate management based on LDL.
VHA/DoD (2006)	Lipid levels are preferably obtained in a fasting state. However, if the testing opportunity is nonfasting, only the values for TC and HDL will be usable. In otherwise low-risk person (0 to 1 risk factor), further testing is not required if the HDL-C level is >40 mg/dL and TC is <200 mg/dL. For persons with multiple (2+) risk factors, LDL-

	C levels are needed as a guide to clinical management. • A complete fasting lipid profile should be obtained in an individual with other risk factors for coronary disease. **[A]** (USPSTF, 2001) • Clinical decisions should be based upon lipid profiles done 1 to 8 weeks apart (fasting) with an LDL-C or TC difference of <30 mg/dL. **[I]** (Working Group Consensus) • Lipid profiles should not be obtained within 8 weeks of acute hospitalization, surgery, trauma, or infection unless they are obtained within 12 to 24 hours of the event to ensure accuracy. **[I]** (Working Group Consensus) • Lipid profiles should not be measured in pregnant women until three to four months post partum. **[I]** (Working Group Consensus) <u>Lipid Screening Test</u> • Ensure test is obtained in fasting state (9 to 14 hour fast) • TC, TG, and HDL-C are measured directly • LDL-C is calculated; therefore, TG level should be considered (If TG >400 mg/dL, try to reduce with diet and exercise, or consider direct measurement of LDL-C)
What Other Important Risk Factors for CHD Should Be Assessed?	

NHLBI (2001 & 2004)	• Assessment of major risk factors* (exclusive of LDL-cholesterol) that modify LDL goals is recommended. Factors to assess include:
	  • Cigarette smoking
	  • Hypertension
	  • Low HDL-cholesterol (<40 mg/dL)**
	  • Family history of premature CHD
	  • Age (men $\geq$45 years, women $\geq$55years)
	
	*Diabetes is regarded as a CHD risk equivalent.
	
	**HDL cholesterol $\geq$60 mg/dL counts as a "negative" risk factor; its presence removes 1 risk factor from the total count
	
	• A 10-year risk assessment using Framingham scoring in persons identified to have multiple (2+) risk factors is recommended in order to identify individuals whose short-term (10-year) risk warrants consideration of intensive treatment.
	• In addition, assessment of life-habit risk factors and emerging risk factors is recommended. The former include obesity, physical inactivity, and atherogenic diet; the later consist of lipoprotein (a), homocysteine, prothrombotic and proinflammatory factors, impaired fasting glucose, and evidence

	of subclinical atherosclerotic disease. **2004 Addendum** • Lifestyle-related risk factors include obesity, physical inactivity, elevated triglycerides, low HDL-C, or metabolic syndrome.
VHA/DoD (2006)	1. Patients screened for dyslipidemia should be assessed for risk factors for CVD. Assessment should include, but not be limited to, the following: a. Age (males ≥age 45 and females ≥age 55) b. Family history of premature coronary artery disease; definite myocardial infarction (MI) or sudden death before age 55 in father or other male first-degree relative, or before age 65 in mother or other female first-degree relative c. Current tobacco use/cigarette smoking (or within the last month) d. Hypertension (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg confirmed on more than one occasion, or current therapy with anti-hypertensive medications) e. Diabetes mellitus (elevated fasting blood sugar [≥126 mg/dL], or a random blood sugar [≥200 mg/dL] confirmed on more than one occasion, an abnormal glucose tolerance test or current therapy with anti-diabetic medications) f. Level of HDL-C (less than 40 mg/dL confirmed on more than one occasion) 2. In obese patients (body mass index ≥30), waist circumference measurement should be obtained to assist in the diagnosis of metabolic syndrome. **10-Year Risk Score for CVD** • A global 10-year risk for CVD should be calculated to assess the short-term (10-year) absolute risk of a CVD event. **[A]** (Grover, Coupal, & Hu, 1998; Grover et al., 2000; Grundy et al., 2004) • The Framingham Risk Calculator should be used, as it is the most commonly used and readily available calculator validated in numerous populations. **[I]** (Grundy et al., 1999; Sheridan, Pignone, & Mulrow, 2003; Wilson et al., 1998) http://hin.nhlbi.nih.gov/atpiii/calculator.asp?usertype=prof • Other risk markers or measure of atherosclerotic burden may be useful to adjust the risk category, if they have been validated to have independent prognostic value. **[C]** (Ford et al., 1998; Greenland et al., 2000 & 2004; O'Donnel, 2004; Pearson et al., 2003; Pletcher et al., 2004; Ridker, 2001)

How Should Serum Lipid Concentrations Be Classified in Terms of Risk?	
NHLBI (2001 & 2004)	**ATP III Classification of LDL, Total, and HDL-Cholesterol (mg/dL)** • **LDL-cholesterol — (primary target of therapy)** <100 Optimal 100 to 129 Near Optimal/Above Optimal 130 to 159 Borderline High 160 to 189 High ≥190 Very high • **Total cholesterol** <200 Desirable 200 to 239 Borderline High ≥240 High • **HDL-cholesterol** <40 Low ≥60 High
VHA/DoD (2006)	• Classify serum lipid levels based on degree of elevation of LDL, TG, or low HDL. **[C]** (NCEP ATP-III, 2002) • Total Cholesterol (mg/dL) (mmol/L) <200 (<5.2) Normal 200 to 239 (5.2 to 6.1) Borderline High ≥240 (≥6.2) High • LDL-C (mg/dL) (mmol/L) <100 (<2.6) Normal 100 to 129 (2.6 to 3.3) Above, near optimal 130 to 159 (3.4 to 4.0) Borderline High 160 to 189 (4.1 to 4.8) High ≥190 (≥4.9) Very High • HDL-C (mg/dL) (mmol/L) <40 (<1.0) Low ≥60 (≥1.6) High • Triglycerides (mg/dL) (mmol/L) <150 mg/dL (<1.7) Normal 150 to 199 mg/dL (1.7 to 2.2) Borderline High 200 to 499 mg/dL (2.3 to 5.6) High ≥500 mg/dL (≥5.6) Very High
What Is the Significance of the Lipid Screening Results for Future Management Decisions?	
NHLBI (2001 & 2004)	• If an initial nonfasting test reveals a total cholesterol >200 mg/dL or an HDL <40mg/dL, a follow-up lipoprotein profile is needed for appropriate management based on LDL. • Any person with elevated LDL-cholesterol or other form of hyperlipidemia should undergo clinical or laboratory assessment

to rule out secondary dyslipidemia before initiation of lipid-lowering therapy. Causes of secondary dyslipidemia include diabetes, hypothyroidism, obstructive liver disease, chronic renal failure, and certain drugs (e.g., progestins, anabolic steroids, corticosteroids).

- Framingham projections of 10-year absolute CHD risk are used to identify certain patients with multiple (2+) risk factors for more intensive treatment.
- Patients who are identified with multiple metabolic risk factors (metabolic syndrome) are candidates for intensified therapeutic lifestyle changes.
- ATP III identifies three categories of risk that modify the goals and modalities of LDL-lowering therapy (see also relevant changes noted in the 2004 addendum presented below).
    - CHD and CHD risk equivalents: LDL goal <100 mg/dL
    - Multiple (2+) risk factors: LDL goal <130 mg/dL
    - Zero to one risk factor: LDL goal <160 mg/dL
- LDL goals in primary prevention depend on a person's absolute risk for CHD (i.e., the probability of having a CHD event in the short term or the long term)—the higher the risk, the lower the goal. Therapeutic lifestyle changes are the foundation of clinical primary prevention. Nonetheless, some persons at higher risk because of high or very high LDL cholesterol levels or because of multiple risk factors are candidates for LDL-lowering drugs. Recent primary prevention trials show that LDL-lowering drugs reduce risk for major coronary events and coronary death even in the short term (see also relevant changes noted in the 2004 addendum presented below).

2004 Addendum

The ATP III goals and cutpoints for therapeutic lifestyle changes and drug therapy in different risk categories, and proposed modifications in the treatment algorithm for LDL cholesterol based on evidence from recent clinical trials, are presented below. Essential modifications are highlighted in the footnotes and summary that follow.

Risk Category: *High risk*: CHD[1] or CHD risk equivalents[2] (10-year risk >20%)

- **LDL-C Goal**: [6]
- **Initiate TLC**: >100 mg/dL[8]
- **Consider Drug Therapy[9]**: >100 mg/dL10 ([9]

Risk Category: *Moderately high risk*: 2+ risk factors[3] (10-year risk 10% to 20%)[4]

- **LDL-C Goal**: [7]
- **Initiate TLC**: >130 mg/dL[8]
- **Consider Drug Therapy[9]**: >130 mg/dL (100 to 129 mg/dL:

consider drug options)[11]

Risk Category: Moderate risk: 2+ risk factors[3] (10-year risk <10%)[4]

- **LDL-C Goal**:
- **Initiate TLC**: >130 mg/dL
- **Consider Drug Therapy[9]**: >160 mg/dL

Risk Category: Lower risk: 0 to 1 risk factor[5]

- **LDL-C Goal**:
- **Initiate TLC**: >160 mg/dL
- Consider Drug Therapy[9]: >190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

[1]Coronary heart disease (CHD) includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia.

[2]CHD risk equivalents include clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease [transient ischemic attacks or stroke of carotid origin or >50% obstruction of a carotid artery]), diabetes, and 2+ risk factors with 10-year risk for hard CHD >20%.

[3]Risk factors include cigarette smoking, hypertension (BP >140/90 mm Hg or on antihypertensive medication), low high-density lipoprotein (HDL) cholesterol (45 years; women >55 years).

[4]Electronic 10-year risk calculators are available at www.nhlbi.nih.gov/guidelines/cholesterol.

[5]Almost all people with zero or 1 risk factor have a 10-year risk

[6]Very high risk favors the optional LDL-C goal of

[7]Optional LDL-C goal

[8]Any person at high risk or moderately high risk who has lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglyceride, low HDL-C, or metabolic syndrome) is a candidate for therapeutic lifestyle changes to modify these risk factors regardless of LDL-C level.

[9]When LDL-lowering drug therapy is employed, it is advised that intensity of therapy be sufficient to achieve at least a 30% to

	40% reduction in LDL-C levels.
	
	[10]If baseline LDL-C is
	
	[11]For moderately high-risk persons, when LDL-C level is 100 to 129 mg/dL, at baseline or on lifestyle therapy, initiation of an LDL-lowering drug to achieve an LDL-C level
	
	Summary of Modifications
	
	• Therapeutic lifestyle changes (TLC) remain an essential modality in clinical management. TLC has the potential to reduce cardiovascular risk through several mechanisms beyond LDL lowering.
	• In high-risk persons, the recommended LDL-C goal is
	  • An LDL-C goal of
	  • If LDL-C is >100 mg/dL, an LDL-lowering drug is indicated simultaneously with lifestyle changes.
	  • If baseline LDL-C is
	  • If a high-risk person has high triglycerides or low HDL-C, consideration can be given to combining a fibrate or nicotinic acid with an LDL-lowering drug. When triglycerides are >200 mg/dL, non-HDL-C is a secondary target of therapy, with a goal 30 mg/dL higher than the identified LDL-C goal.
	• For moderately high-risk persons (2+ risk factors and 10-year risk 10% to 20%), the recommended LDL-C goal is
	• Any person at high risk or moderately high risk who has lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglyceride, low HDL-C, or metabolic syndrome) is a candidate for TLC to modify these risk factors regardless of LDL-C level.
	• When LDL-lowering drug therapy is employed in high-risk or moderately high-risk persons, it is advised that intensity of therapy be sufficient to achieve at least a 30% to 40% reduction in LDL-C levels.
	• For people in lower-risk categories, recent clinical trials do not modify the goals and cutpoints of therapy.

VHA/DoD (2006)	• Patients with LDL $\geq$130 mg/dL, HDL <40 mg/dL, or TG >200 mg/dL should be assessed for further management of dyslipidemia. **[C]** (NCEP ATP-III, 2002) • Goals of lipid lowering therapy should be tailored to risk level and based upon the balance between benefits, risks, and patient preferences. **[C]** (27th Bethesda Conference, 1996; Grundy et al., 2004) • Adults with abnormal lipid profiles (dyslipidemia) should be assessed for secondary causes, familial disorders, and other underlying conditions that may influence lipid levels. **[I]** (NCEP ATP-III, 2002; Stone, Blum, & Winslow, 1997; Stone & Blum,

	2002) **Non-Pharmacologic Therapy** • TLC should be recommended for ALL patients with dyslipidemia, regardless of risk or baseline LDL-C level. [C] **Goals of Therapy for Primary Prevention** • LDL-C should be lowered to <100 mg/dL for patients with high 10-year risk >20 percent. **[B]** (Sever et al., 2003; Heart Protection Study Collaborative Group, 2002; "Screening experience and baseline characteristic in the West of Scotland Coronary Prevention Study," 1995) • LDL-C should be lowered to <130 mg/dL for patients with intermediate 10-year risk (15 to 20 percent). **[B]** (Downs et al., 1998) • LDL-C should be lowered to <130 mg/dL for patients with intermediate 10-year risk (10 to 14 percent). **[C]** (NCEP ATP-III, 2002) • LDL-C should be lowered to <160 mg/dL for patients with low 10-year risk. **[I]** (Working Group Consensus) • LDL-C reduction of 30 to 40 percent from baseline may be considered an alternative therapeutic strategy for patients who cannot meet the above goal **Drug Therapy for Primary Prevention** • Drug therapy should be initiated for high-risk patients (>20%) if baseline LDL is ≥130 mg/dL. [B] (Downs et al., 1998; Sever et al., 2003; "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study," 1995) • Drug therapy is optional to consider in high-risk patients (>20%) if baseline LDL is 100 to 129 mg/dL. **[B]** (Heart Protection Study Collaborative Group, 2002) • Drug therapy may be offered to patients with high-intermediate risk (15 to 20 percent) if baseline LDL is ≥130 mg/dL. **[B]** (Downs et al., 1998; Sever et al., 2003; "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study," 1995) • Drug therapy may be offered to patients with low-intermediate risk (10 to 14 percent) if baseline LDL is ≥160 mg/dL. **[C]** (NCEP ATP-III, 2002) • Drug therapy may be offered to low-risk patients (<10 percent) if baseline LDL is ≥190 mg/dL. **[I]** (NCEP ATP-III, 2002)
How Frequently Should Patients Be Screened?	
NHLBI	• Screening is recommended every 5 years unless more frequent

(2001 & 2004)	testing is warranted.
	• Follow-up lipoprotein analysis should be carried out according to the following schedule:
	  • In patients with 2+ risk factors whose LDL levels are observed at <130 mg/dL, lipoprotein analysis should be repeated ≤2 years;
	  • In patients with 0 to 1 risk factors whose LDL levels are observed at 130 to 159 mg/dL, lipoprotein analysis should be repeated ≤2 years,
	  • In patients with 0 to 1 risk factors whose LDL levels are observed at <130 mg/dL, lipoprotein analysis should be repeated ≤5 years.

VHA/DoD (2006)	• Patients with average or below average risk for atherosclerotic events should be screened for dyslipidemia every five years. **[B]** (NCEP ATP-III, 2002; "A multicenter comparative trial," 1993) • If the initial dyslipidemia screening reveals TC >200 mg/dL, or fasting LDL-C >130 mg/dL or HDL-C <40 mg/dL, but LDL-C level is under the recommended goal level based upon cardiovascular risk, the patient will be at low-risk for lipid-related events over a one to two-year period and thus, should be reevaluated for dyslipidemia in one to two years. **Recommended Screening Schedules for Dyslipidemia** *For young adults (men <age 35; women <age 45)* • Every 5 years when no CVD risk factors are present • More often, if family history of premature CVD exists (definite myocardial infarction or sudden death before 55 years of age in father or other male first-degree relative or before age 65 in mother or other female first-degree relative) *For middle-aged adults (men ≥age 35; women ≥age 45)* • Every 5 years, when no CVD risk factors are present • Annually, if CVD risk factors exist (hypertension, smoking, family history of premature CVD) *For elderly patients up to age 75 years* • Every 5 years when no CVD risk factors are present • More often if CVD risk factors exist *For elderly patients >age 75* • Evaluate if patient has multiple CVD risk factors, established CVD, or a history of revascularization procedures and good

	quality of life with no other major life-limiting diseases.

TABLE 3: BENEFITS/HARMS OF LIPID SCREENING	
Benefits of Lipid Screening	
NHLBI (2001 & 2004)	By adopting the clinical high-risk CHD prevention strategy, individuals at significantly increased risk are identified and treated, thus reducing the individual's risk for CHD and reducing the overall burden of CHD. The clinical high-risk strategy and the population strategy, which seeks to lower average blood cholesterol levels in the whole population by promoting changes in dietary patterns and physical activity levels, are complementary. Both strategies are incorporated into the National Cholesterol Education Program and together reduce the societal burden of CHD. **2004 Addendum** Since the publication of ATP III, 5 major clinical trials of statin therapy have confirmed the benefit of cholesterol-lowering therapy in high-risk patients and support the ATP III treatment goal of low-density lipoprotein cholesterol (LDL-C)
VHA/DoD (2006)	Lipid-related risk factors for ASCVD include high levels of total cholesterol or LDL-C) and low levels of HDL-C). Other risk factors include age, male sex, high blood pressure, tobacco use, diabetes mellitus, and family history of premature coronary heart disease. Because the range of CVD 10-year absolute risk is wide, targeted screening for patients at high absolute risk to develop CVD is recommended. All adults—regardless of age—with a history of CVD should undergo lipoprotein screening. For asymptomatic individuals (i.e., for primary prevention), available evidence supports cholesterol screening only if other characteristics place them at high-risk. Targeted screening to identify these risk factors will allow for lipid-related interventions to reduce the risk of ASVCD.
Harms of Screening	
NHLBI (2001 & 2004)	Not stated
VHA/DoD (2006)	Not stated

TABLE 4: EVIDENCE AND RECOMMENDATION RATING SCHEMES	
NHLBI (2001 & 2004)	**Type of Evidence:** A. Major randomized controlled trials B. Smaller randomized controlled trials and meta-analyses of other clinical trials C. Observational and metabolic studies D. Clinical experience **Strength of Evidence:** 1. Very strong evidence 2. Moderately strong evidence 3. Strong trend
VHA/DoD (2006)	**Strength of the Recommendations** **A**: A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.* **B**: A recommendation that clinicians provide (the service) to eligible patients. *At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.* **C**: No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.* **D**: Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.* **I**: The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, or poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

	Net Benefit of the Intervention			
Quality of Evidence	**Substantial**	**Moderate**	**Small**	**Zero or Negative**
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

Quality of Evidence

I: At least one properly done randomized controlled trial

II-1: Well designed controlled trails without randomization

II-2: Well designed cohort or case-control analytic study, preferably from more than one source

II-3: Multiple time series evidence with/without intervention; dramatic results of uncontrolled experiment

III: Opinion of respected authorities, descriptive studies, case reports, and expert committees

Overall Quality

Good: High grade evidence (I or II-1) directly linked to health outcome

Fair: High grade evidence (I or II-1) linked to intermediate outcome; or moderate grade evidence (II-2 or II-3) directly linked to health outcome

Poor: Level III evidence or no linkage of evidence to health outcome.

Net Effect of Intervention

Substantial:

- More than a small relative impact on a frequent condition with a substantial burden of suffering, *or*
- A large impact on an infrequent condition with a significant impact on the individual patient level

Moderate:

- A small relative impact on a frequent condition with a substantial burden of suffering, *or*
- A moderate impact on an infrequent condition with a significant impact on the individual patient level

Small:

- A negligible relative impact on a frequent condition with a substantial burden of suffering, *or*
- A small impact on an infrequent condition with a significant impact on the individual patient level

Zero or Negative:

- Negative impact on patients, *or*
- No relative impact on either a frequent condition with a substantial burden of suffering, *or*
- An infrequent condition with a significant impact on the individual patient level

References Supporting the Recommendations

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GUIDELINE CONTENT COMPARISON

The National Heart, Lung, and Blood Institute (NHLBI) and the Veterans Health Administration, Department of Defense (VHA/DoD) present recommendations for screening for high cholesterol among adults for primary prevention of CHD and ASCVD. The guidelines also contain recommendations for clinical management of

high blood cholesterol and secondary prevention in patients with existing CHD or ASCVD; these topics, however, are beyond the scope of this synthesis.

The guidelines describe the clinical evidence and give explicit reasoning for their recommendations. VHA/DoD presents its guideline in algorithmic form, with accompanying objectives, direct recommendations, and discussions that expand on the statements found in each box of the algorithm. A review of the evidence is included in the discussions, and a more detailed comprehensive summary of major recent studies is also provided in the appendices of the guideline. The NHLBI guideline and addendum contain both detailed discussions of the clinical evidence and summary algorithms. NHLBI provides graded evidence statements in the original guideline document. Both guidelines grade the evidence supporting their recommendations using a pre-specified rating scheme.

Areas of Agreement

Which Screening Tests Should Be Used?

There is agreement between the guidelines that initial screening should be a fasting lipid profile, which includes measurement of TC, TG, HDL-C, and LDL-C (direct or calculated), in preference to the nonfasting tests.

Serum Lipid Concentrations and Risk

The classification scheme of total, LDL-C and HDL-C levels used by VHA/DoD is derived from, and thus in agreement with, the NHLBI ATP II/ATP III guidelines. A total cholesterol concentration <200 mg/dL represents a "normal" or "desirable" blood cholesterol level; a concentration between 200 and 239 mg/dL is "borderline high," and $\geq$240 mg/dL is "high." Critical values for LDL-C are 130 to 159 mg/dL (borderline high) and $\geq$160 mg/dL (high-risk). HDL-cholesterol levels are considered optimal at $\geq$60 mg/dL, while HDL-C levels below 40 mg/dL will place patients at high risk for CHD. ATP III specifically states that "low" HDL-cholesterol should be defined as <40 mg/dL because this is a better measure of depressed HDL than <35 mg/dL.

Significance of Lipid Screening Results and Future Management Decisions

There is general agreement between both guideline groups that any further management decisions should be based on CHD risk assessment as well as results of lipid screening. The core set of risk factors (excluding LDL-cholesterol) for CHD includes advanced age, hypertension, obesity, family history of CHD, cigarette smoking, diabetes mellitus type II, and low HDL-cholesterol levels. Both NHLBI and VHA/DoD go a step beyond simple counting of risk factors by recommending use of Framingham projections of 10-year absolute CHD risk to identify certain patients with $\geq$2 risk factors for more intensive treatment. The use of the Framingham model in risk assessment is a change from the previous (1999) version of the VHA/DoD guideline. Both guidelines also recommend that secondary causes of dyslipidemia, such as diabetes mellitus, obstructive liver disease, hypothyroidism, use of certain drugs, and ethanol use, need to be investigated and addressed before initiation of lipid-lowering therapy.

The two guidelines differ somewhat in their LDL goals for patients in the various risk groups. With the 2004 addendum, NHLBI modified their recommendations for initiation of TLC and drug therapy. This is discussed further under areas of disagreement.

Screening Frequency

The guidelines advocate repeated screening at least once every five years in persons with no or low risk factors for CHD. Depending on the results of the initial lipid screen, testing may occur more frequently. In addition, testing should occur more often in persons whose TC approaches a threshold for initiating treatment.

HDL-Cholesterol

While both groups included in this synthesis recognize that low HDL-C is a strong independent predictor of CHD, neither of them specifically recommends treating low HDL-C nor do they specify a goal for raising HDL. NHLBI reports there is insufficient evidence to specify such a goal and also notes the lack of available drugs for treating low HDL-C. Both NHLBI and VHA/DoD instead focus on LDL-cholesterol as the primary target of therapy.

Areas of Difference

Who Should Be Screened?

Who should be screened for dyslipidemia is the major area of disagreement between the two guideline groups. NHLBI recommends lipid screening for all individuals starting at 20 years of age, based on evidence that CHD disease develops in a continuous fashion, often beginning in the early twenties. They also argue that early awareness may encourage healthy behaviors. Furthermore, waiting until age 35 in men and age 45 in women may result in missed opportunities for early intervention. VHA/DoD, on the other hand, does not recommend screening before age 35 for men and before age 45 for women unless the individuals have one or more risk factors for CHD or a history suggestive of familial hyperlipidemia. VHA/DoD presents evidence that the short-term risk for developing CHD is low in these groups, even among those with an elevated cholesterol level, and the potential benefits of cholesterol reduction are small and thus not cost-effective. Neither of the guidelines identified randomized clinical trials that provided direct evidence on the effects of cholesterol reduction in these age groups.

NHLBI does not indicate an upper age limit for lipid screening and maintains that age alone should not be reason to withhold the benefits of cholesterol lowering. VHA/DoD, on the other hand, suggests an upper age limit of 75 years for testing, based on a lack of benefit of treatment in this age group.

Significance of Lipid Screening Results and Future Management Decisions

Recent statin trials have provided new information on benefits of LDL-lowering therapy applied to persons in categories in which ATP III could not make definitive recommendations about drug therapy. To this point, the 2004 NHLBI guideline

addendum has issued modified LDL-C goals and cutpoints for initiation of therapeutic lifestyle changes and drug therapy. These changes include the expansion of risk categories from 3 to 4 defined as:

- High Risk: CHD or CHD risk equivalents (10-year risk >20%)
- Moderately High Risk: 2+ risk factors (10-year risk 10% to 20%)
- Moderate Risk: 2+ risk factors (10-year risk <10%)
- Lower Risk: 0-1 risk factor

TLC is recommended in high-risk patients whenever the LDL-C level is >100 mg/dL. Furthermore, any person at high risk who has lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglycerides, low HDL-C, or metabolic syndrome) is a candidate for TLC to modify these risk factors regardless of LDL-C level. As before, whenever the baseline LDL-C concentration is >130 mg/dL, simultaneous initiation of an LDL-lowering drug and dietary therapy is recommended. If LDL-C is 100 to 129 mg/dL, the same now holds. If baseline LDL-C is

For patients at moderately high risk (10-year risk 10% to 20%), the LDL-C goal remains 130 mg/dL. Again, any person at moderately high risk who has lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglycerides, low HDL-C, or metabolic syndrome) is a candidate for TLC to modify these risk factors regardless of LDL-C level. If the LDL-C concentration is >130 mg/dL after TLC, consideration should be given to initiating an LDL-lowering drug, to achieve and sustain the LDL-C goal of

The lipid goals and therapies for primary prevention recommended by VHA/DoD parallel those of the NHLBI guidelines in most respects. The major difference is that VHA/DoD states that an LDL-C reduction of 30 to 40% from baseline may be considered an alternative therapeutic strategy in patients unable to meet the prescribed goals. VHA/DoD's rationale is that in patients with a high LDL at baseline, the full risk-benefit of combination drug therapy or high-dose statin therapy is unknown, particularly in patients with comorbid diseases or those taking concomitant drugs. They cite data from meta-analyses of major statin randomized controlled trials to support this option.

This Synthesis was prepared by NGC on July 28, 2000. It was reviewed by the guideline developers as of October 10, 2000. It has been modified a number of times. The most recent version updates the VHA/DoD guidelines.

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