**NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC)
GUIDELINE SYNTHESIS**

SCREENING FOR LIPID DISORDERS IN ADULTS

Guidelines

1. **United States Preventive Services Task Force (USPSTF)**. Screening for lipid disorders in adults: U.S. Preventive Services Task Force recommendation statement. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2008 Jun. 13 p. [17 references]
2. **Department of Veterans Affairs, Department of Defense (VA/DoD)**. VA/DoD clinical practice guideline for the management of dyslipidemia. Washington (DC): Department of Veterans Affairs, Department of Defense; 2006 Dec. 140 p.

INTRODUCTION

A direct comparison of the U.S. Preventive Services Task Force (USPSTF) and Department of Veterans Affairs, Department of Defense (VA/DoD) recommendations for lipid screening in adults is provided in the tables below. The VA/DoD guideline also provides recommendations for the management of dyslipidemia. This topic, however, is beyond the scope of this synthesis.

- Table 1 provides a quick-view glance at the primary interventions considered by each group.
- Table 2 provides a comparison of the scope of the guidelines.
- Table 3 provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis, including:
    - Whom to Screen
    - Screening Test
    - Risk Factors for CHD to be Assessed
    - Screening Frequency
- Table 4 lists the potential benefits and harms associated with the implementation of each guideline.
- Table 5 presents the rating schemes used to rate the level of evidence and/or the strength of the recommendations.

Following the content comparison tables and discussion, the areas of agreement and areas of differences among the guidelines are identified.

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

- ATP, Adult Treatment Panel

- 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
- TC, total cholesterol
- TG, triglycerides
- USPSTF, United States Preventive Services Task Force
- VA/DoD, Department of Veterans Affairs, Department of Defense

TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED ("✔" indicates topic is addressed)		
	USPSTF (2008)	**VA/DoD (2006)**
Whom to Screen	✔	✔
Screening Test	✔	✔
Risk Factors for CHD to be Assessed	✔	✔
Screening Interval	✔	✔

TABLE 2: SCOPE	
Objective	
USPSTF (2008)	• To summarize the USPSTF recommendations and supporting scientific evidence on screening for lipid disorders in adults • To update the 2001 USPSTF recommendations on screening for lipid disorders in adults
VA/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	
USPSTF (2008)	Adults aged 20 years and older who have not previously been diagnosed with dyslipidemia
VA/DoD (2006)	Adults (age 17 years or older) eligible for care in the VA/DoD health care system
Intended Users	
USPSTF (2008)	Advanced Practice Nurses Allied Health Personnel Health Care Providers Nurses Physician Assistants Physicians
VA/DoD (2006)	Advanced Practice Nurses Allied Health Personnel Dietitians Nurses Physician Assistants Physicians

TABLE 3: COMPARISON OF RECOMMENDATIONS	
Whom to Screen	
USPSTF (2008)	*Screening Men* The USPSTF strongly recommends screening men aged 35 and older for lipid disorders. **This is a grade A recommendation**. The USPSTF recommends screening men aged 20 to 35 for lipid disorders if they are at increased risk for CHD. **This is a grade B recommendation**. *Screening Women at Increased Risk* The USPSTF strongly recommends screening women aged 45 and older for lipid disorders if they are at increased risk for CHD. **This is a grade A recommendation**.

	The USPSTF recommends screening women aged 20 to 45 for lipid disorders if they are at increased risk for CHD. **This is a grade B recommendation**. *Screening of Young Men and All Women Not at Increased Risk* The USPSTF makes no recommendation for or against routine screening for lipid disorders in men aged 20 to 35, or in women aged 20 and older who are not at increased risk for CHD. **This is a grade C recommendation**. **Clinical Considerations** • An age to stop screening has not been established. Screening may be appropriate in older people who have never been screened; repeated screening is less important in older people because lipid levels are less likely to increase after age 65. However, because older adults have an increased baseline risk for coronary heart disease, they stand to gain greater absolute benefit from the treatment of dyslipidemia, compared with younger adults.
VA/DoD (2006)	Targeted lipid screening is only recommended for men $\geq$ age 35 and women $\geq$ age 45. There is evidence to support screening in younger patients when other risk factors are present. There is clinical and epidemiological evidence to continue screening until age 75 for primary prevention. There is some disagreement, however, as to the efficacy of screening beyond the age of 75. The USPSTF has not established an age at which to stop screening for primary prevention, and therefore, screening beyond age 75 should be left to clinical considerations. **Lipid Screening Criteria** a. Male age 35 or older OR female age 45 or older b. Young adults with more than one of the following: • Family history of premature CVD • Patient is smoking • Patient has or is being treated for hypertension c. Consider obtaining lipid profile for young adults with abdominal obesity **Recommendations** • 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) • 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)

Screening Test

USPSTF (2008)	**Clinical Considerations** • The preferred screening tests for dyslipidemia are TC and HDL-C on non-fasting or fasting samples. There is currently insufficient evidence of the benefit of including TG as a part of the initial tests used to screen routinely for dyslipidemia. Abnormal screening test results should be confirmed by a repeated sample on a separate occasion, and the average of both results should be used for risk assessment. • Measuring TC alone is acceptable for screening if available laboratory services cannot provide reliable measurements of HDL-C; measuring both TC and HDL-C is more sensitive and specific for assessing CHD risk than measuring TC alone. In conjunction with HDL-C, the addition of either LDL-C or TC would provide comparable information, but measuring LDL-C requires a fasting sample and is more expensive. Direct LDL-C testing, which does not require a fasting sample measurement, is now available; however, calculated LDL (TC minus HDL minus TG/5) is the validated measurement used in trials for risk assessment and treatment decisions. In patients with dyslipidemia identified by screening, complete lipoprotein analysis is useful.

VA/DoD (2006)	**Obtain a Fasting Lipid Profile** 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. *Lipid Screening Test* • 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 **Recommendations** • 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) In the previous VA/DoD guideline for dyslipidemia (1999), initial classification for primary prevention was based on measurement of TC and HDL-C. This guideline recommends measurement of LDL-C for screening purposes. This measurement requires a fasting lipid analysis that includes TC, HDL-C, TG and estimation of LDL-C.
Risk Factors for CHD to Be Assessed	

USPSTF (2008)	**Clinical Considerations**
	
	• Increased risk, for the purposes of this recommendation, is defined by the presence of any one of the risk factors listed below. The greatest risk for CHD is conferred by a combination of multiple listed factors. While the USPSTF did not use a specific numerical risk to bound this recommendation, the framework used by the USPSTF in making these recommendations relies on a 10-year risk of cardiovascular events:
	    • Diabetes
	    • Previous personal history of CHD or non-coronary atherosclerosis (e.g., abdominal aortic aneurysm,

	peripheral artery disease, carotid artery stenosis) • A family history of cardiovascular disease before age 50 in male relatives or age 60 in female relatives • Tobacco use • Hypertension • Obesity (body mass index [BMI] >30)

VA/DoD (2006)	**Assess Risk Factors for Cardiovascular Disease**
	
	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 $\geq$age 45 and females $\geq$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 $\geq$140 mmHg or diastolic BP $\geq$90 mmHg confirmed on more than one occasion, or current therapy with anti-hypertensive medications)
	   e. Diabetes mellitus (elevated fasting blood sugar [$\geq$126 mg/dL], or a random blood sugar [$\geq$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 $\geq$30), waist circumference measurement should be obtained to assist in the diagnosis of metabolic syndrome.

	Screening Frequency
USPSTF (2008)	**Clinical Considerations** • The optimal interval for screening is uncertain. On the basis of other guidelines and expert opinion, reasonable options include every 5 years, shorter intervals for people who have lipid levels close to those warranting therapy, and longer intervals for those not at increased risk who have had repeatedly normal lipid levels.
VA/DoD (2006)	**Repeat Dyslipidemia Evaluation in 1 to 5 Years** • 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 4: BENEFITS/HARMS OF LIPID SCREENING	
Benefits	
USPSTF (2008)	**Benefits of Detection and Early Treatment** There is good evidence that lipid-lowering drug therapy substantially decreases the incidence of coronary heart disease in persons with abnormal lipids. The absolute benefits of lipid-lowering treatment depend on a person's underlying risk for coronary heart disease. Men

	over the age of 35 and women over the age of 45 who are at increased risk will realize a substantial benefit from treatment; younger adults with multiple risk factors for coronary disease, including dyslipidemia, will realize a moderate benefit from treatment; and younger men and women without risk factors for coronary heart disease will realize a small benefit from treatment, as seen in the risk reduction in 10-year CHD event rate.
VA/DoD (2006)	Dyslipidemia is a major risk factor for coronary heart disease and atherosclerotic cardiovascular disease and its subsequent morbidity and mortality. Lipid-related interventions, including lifestyle modifications, such as diet and exercise, and drug therapy can reduce the risk of atherosclerotic cardiovascular disease in patients with high cholesterol.
Harms	
USPSTF (2008)	**Harms of Detection and Early Treatment** There is good evidence that the harms from screening and treatment are small and include possible labeling and the adverse effects associated with lipid-lowering therapy (e.g., rhabdomyolysis).
VaA/DoD (2006)	No screening related harms are provided.

TABLE 5: EVIDENCE AND RECOMMENDATION RATING SCHEMES	
USPSTF (2008)	**Definitions**: The U.S. Preventive Services Task Force (USPSTF) grades its **recommendations** according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms). **A** The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians provide [the service] to eligible patients. (The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.) **B** The USPSTF recommends that clinicians provide [the service] to

eligible patients. (The USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits outweigh harms.)

C

The USPSTF makes no recommendation for or against routine provision of [the service]. (The US Preventive Services Task Force found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms it too close to justify a general recommendation.)

D

The USPSTF recommends against routinely providing [the service] to asymptomatic patients. (The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.)

I

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. (Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.)

The USPSTF grades the **quality of the overall evidence** for a service on a 3-point scale (good, fair, or poor).

Good

Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes.

Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

| VA/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

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GUIDELINE CONTENT COMPARISON

The United States Preventive Services Task Force (USPSTF) and the Department of Veterans Affairs, Department of Defense (VA/DoD) present recommendations for screening for high lipid disorders in adults. The VA/DoD guideline also contains recommendations for the management of dyslipidemia. This topic, however, is beyond the scope of this synthesis.

The guidelines describe the clinical evidence and give explicit reasoning for their recommendations.

Areas of Agreement

Whom to Screen

Men

Both groups recommend that all men aged 35 and older, regardless of risk level, should be screened for lipid disorders. There is also agreement that men younger than 35 at increased risk for CHD should be screened. With regard to average risk men younger than 35, USPSTF makes no recommendation for or against routine screening. VA/DoD does not provide a recommendation for routine screening in this population.

Women

Both groups agree that all women at increased risk of CHD should be screened.

Refer to Areas of Differences below for discussion of screening in women at average risk of CHD.

<u>Older Adults</u>

USPSTF states that an age to stop screening has not been established. VA/DoD refers to USPSTF, noting that USPSTF has not established an age at which to stop screening for primary prevention, and therefore, screening beyond age 75 should be left to clinical considerations.

Screening Frequency

Recommendations regarding screening frequency are similar. USPSTF states that the optimal interval for screening is uncertain, but that reasonable options include every 5 years, with shorter intervals for people who have lipid levels close to warranting therapy, and longer intervals at those not at increased risk who have had repeatedly normal lipid levels. VA/DoD similarly notes that patients with average or below average risk should be screened every 5 years, and patients with risk factors should be screened more frequently. VA/DoD explicitly recommends annual screening for middle aged adults (men > age 35; women > age 45) if CVD risk factors exist.

Areas of Difference

Whom to Screen

<u>Women</u>

While both groups recommend screening of all women at increased risk of CHD, VA/DoD also recommends routine screening of women older than 45 at average risk. USPSTF makes no recommendation for or against routine screening in women who are not at increased risk for CHD.

Screening Tests

Recommendations regarding which screening tests should be performed differ. According to USPSTF, the preferred screening tests are TC and HDL-C on fasting or non-fasting samples. They add that there is currently insufficient evidence of the benefit of including TG as a part of the initial tests used to screen routinely for dyslipidemia. VA/DoD, in contrast to USPSTF, recommends screening on a fasting sample for TG (in order to calculate LDL-C) in addition to TC and HDL-C. VA/DoD notes that, in recommending measurement of LDL-C for screening purposes, its current recommendation differs from its previous (1999) statement.

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. This synthesis was revised in November 2008 to remove NHLBI

recommendations and to add USPSTF recommendations. This synthesis was verified by USPSTF on December 29, 2008.

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