VA/DOD Clinical Practice Guidelines

LIPID MANAGEMENT FOR CARDIOVASCULAR DISEASE RISK REDUCTION

Provider Summary

Version 5.0 | 2025

VA/DOD CLINICAL PRACTICE GUIDELINE ON LIPID MANAGEMENT FOR CARDIOVASCULAR DISEASE RISK REDUCTION

Department of Veterans Affairs
Department of Defense

Provider Summary

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical trial and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of a particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs nor TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 5.0 – 2025

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Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DOD) Evidence-Based Practice Work Group (EBPWG) was established in 2004, with a mission to use clinical and epidemiological evidence to improve population health within the Veterans Health Administration (VHA) and Military Health System (MHS) and develop clinical practice guidelines (CPGs) for the VA and DOD populations.(1) This CPG is intended to provide healthcare providers with a practical framework by which to evaluate, treat, and manage lipids, address the individual needs and preferences of patients, and improve clinical outcomes.

In 2014, the VA and DOD published a CPG for the Management of Dyslipidemia for Cardiovascular Risk Reduction (2014 VA/DOD Lipids CPG), which was based on evidence reviewed from January 2010 through February 2014. This was updated in 2020 using evidence reviewed from December 2013 through May 2019 (2020 VA/DOD Lipids CPG). Since then, a growing body of research has expanded the general knowledge and understanding of the impact of lipid management on cardiovascular (CV) risk. Consequently, an update to the 2020 VA/DOD Lipids CPG was initiated in 2024 using evidence reviewed from May 2019 through January 2025.

The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being. To that end, this CPG is intended to guide providers who care for patients along management pathways supported by evidence. These guidelines were written to emphasize the role of:

- Utilizing patient-centered care;
- Decreasing preventable complications and morbidity;
- Improving health outcomes and quality of life; and
- Using shared decision-making frameworks in patient collaboration efforts.

Scope of the CPG

This CPG is intended for use by primary care clinicians and other providers in practicing lipid management for cardiovascular disease (CVD) risk reduction.

A. Populations Included in this Guideline

This CPG is intended for adults (18 years or older) with or at risk for CVD who would benefit from lipid management and are eligible for care in the VA and DOD healthcare delivery systems. This includes Veterans and Service Members as well as their eligible adult dependents.

B. Populations Excluded from this Guideline

Populations excluded from this guideline due to a lack of evidence or a lack of demonstrated benefit (heart failure with reduced ejection fraction [HFrEF], end-stage renal disease [ESRD]) include individuals with:

- HFrEF ≤35%;
- Limited life expectancy (<5 years);
- ESRD with or without chronic systolic heart failure; and
- Genetic dyslipidemia conditions (e.g., homozygous FH [HoFH], heterozygous FH [HeFH], triglycerides >500 mg/dL, etc.)

Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as detailed in the section on Methods and Appendix A in the full 2025 VA/DOD Lipids CPG. These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications as appropriate (e.g., resource use, equity, acceptability).

A. Key Takeaways

1. Comprehensive lifestyle medicine remains foundational for CV risk reduction. The Mediterranean dietary pattern and increasing physical activity continue to be supported by evidence.
2. In addition to healthy lifestyle changes, moderate-intensity statins remain a core therapy for primary prevention, but other lipid-lowering medications and statin intensities may be effective. For primary prevention, **at least** a moderate-intensity statin is recommended in patients who have diabetes, an LDL-C >190 mg/dL, or a 10-year risk estimate of **10% or greater**.
3. Risk estimation remains essential for guiding treatment decisions. The Predicting Risk of Cardiovascular Disease Events (PREVENT) calculator is now suggested to assess risk for primary prevention. Risk calculations are the starting point for risk estimation and should be considered in the context of additional risk factors and shared decision-making.
4. For primary prevention, a moderate-intensity statin is suggested for adults living with human immunodeficiency virus (HIV) even when the 10-year risk estimate is low.
5. For patients with documented atherosclerotic CVD (ASCVD), a high-intensity statin alone or a moderate-intensity statin combined with ezetimibe or a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor is suggested.
6. For very high-risk patients with ASCVD, a more intensive approach to medication management is suggested and should include combination therapy comprised of a high-intensity statin with ezetimibe and/or a PCSK9 inhibitor.
7. Coronary artery calcium (CAC) testing is suggested to refine risk and guide management for primary prevention in some patients, especially if there is clinical uncertainty and the calculated risk is intermediate or high.
8. Lipoprotein(a) [Lp(a)] testing is suggested to individualize risk assessment by identifying patients with enhanced risk when elevated.
9. The monoclonal antibody (mAb) PCSK9 inhibitors alirocumab and evolocumab are proven to reduce CV events in patients with ASCVD, but it is still unknown if novel PCSK9 inhibiting medications such as small interfering ribonucleic acid (siRNA) therapies (e.g., inclisiran) and oral small molecules (e.g., lerodalcibep) improve clinical outcomes. Lerodalcibep was not FDA-approved at the time of this writing.
10. We suggest icosapent ethyl in patients with ASCVD and hypertriglyceridemia (i.e., ≥150 mg/dL) on maximally tolerated statins.
11. For patients unable to take statins, consider bempedoic acid, ezetimibe, fibrates, or PCSK9 mAb inhibitors.

12. In 2020, we recommended against routinely ordering a lipid panel more frequently than every 10 years for primary prevention in patients not on statin therapy (2020 Recommendation 2), as well as against routinely monitoring lipid levels in patients taking statins (2020 Recommendation 22). This updated CPG removes these recommendations.

B. Evidence-Based Clinical Practice Recommendations with Strength and Category

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Screening and Assessment of Cardiovascular Risk		1.	For cardiovascular risk assessment in primary prevention, we suggest the PREVENT risk assessment tool.	Weak for	Reviewed, New-replaced
		2.	For primary prevention, in patients over 18 and not on statin therapy who have not developed new cardiovascular risk factors (e.g., diabetes, hypertension, tobacco use), there is insufficient evidence to recommend for or against a specific frequency for cardiovascular disease risk assessment.	Neither for nor against	Reviewed, New-added
		3.	For primary prevention, in patients identified with intermediate to high risk*, we suggest coronary artery calcium testing to improve the accuracy of risk assessment when deemed to affect clinical decision-making.	Weak for	Reviewed, New-added
		4.	For patients with low risk, we suggest against the routine use of coronary artery calcium testing.	Weak against	Reviewed, Not changed
		5.	We suggest measuring lipoprotein(a) [Lp(a)] to identify patients with enhanced risk.	Weak for	Reviewed, New-added
		6.	There is insufficient evidence to recommend for or against the routine use of ankle brachial index (ABI), apolipoprotein B (ApoB), polygenic risk scores (PRS), carotid plaque/total carotid plaque area (TPA), and high-sensitivity C-reactive protein (hs-CRP) for estimating cardiovascular risk.	Neither for nor against	Reviewed, Amended
Pharmacotherapy	***Primary Prevention***	7.	For primary prevention among patients who have diabetes or 10-year cardiovascular risk ≥10% or low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL, we recommend using **at least** a moderate-intensity statin.	Strong for	Reviewed, Amended
		8.	For primary prevention among patients without diabetes who have low-density lipoprotein cholesterol (LDL-C) <190 mg/dL and a 10-year cardiovascular risk between approximately 5% to less than 10%, we suggest using a moderate-intensity statin.	Weak for	Reviewed, Amended
		9.	For primary prevention, there is insufficient evidence to recommend for or against icosapent ethyl in patients on statin therapy with persistently elevated fasting triglycerides ≥150 mg/dL.	Neither for nor against	Reviewed, Amended
		10.	For primary prevention in patients with human immunodeficiency virus (HIV), we suggest a moderate-intensity statin that has a low risk of interactions with antiretroviral therapy, even when 10-year risk estimates are low (i.e., <5%).	Weak for	Reviewed, New-added

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Pharmacotherapy (cont.)		11.	In patients with an indication for statin therapy and elevated baseline aspartate aminotransferase (AST) or alanine transaminase (ALT) less than 3-times the upper limit of normal, we suggest using statins as indicated.	Weak for	Reviewed, New-added
		12.	For primary or secondary prevention, we suggest against adding fibrates to statins.	Weak against	Reviewed, Not changed
	Secondary Prevention	13.	For secondary prevention, we suggest treating with one of the following**: • High-intensity statin • Moderate-intensity statin with ezetimibe • Moderate-intensity statin with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor.	Weak for	Reviewed, New-replaced
		14.	For secondary prevention in very high-risk patients†, we suggest a combination therapy of one of the following: • High-intensity or maximally tolerated statin with ezetimibe • High-intensity or maximally tolerated statin with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor • High-intensity or maximally tolerated statin with ezetimibe and PCSK9 inhibitor.	Weak for	Reviewed, New-replaced
		15.	For patients who achieve a very low low-density lipoprotein value (LDL-C <30 mg/dL) with therapy, we suggest continuing treatment.	Weak for	Reviewed, New-added
		16.	For secondary prevention, we suggest icosapent ethyl in patients on statin therapy with persistently elevated fasting triglycerides ≥150 mg/dL.	Weak for	Reviewed, Amended
		17.	For secondary prevention, there is insufficient evidence to recommend a treat-to-target strategy (low-density lipoprotein [LDL-C] <70 mg/dL) over a fixed-dose high-intensity statin strategy.	Neither for nor against	Reviewed, New-added
Statin Intolerance		18.	For patients who cannot tolerate a statin, we suggest a washout period followed by a re-challenge with the same or a different statin or lower dose, and if that fails, a trial of intermittent (nondaily) dosing.	Weak for	Reviewed, Not changed
		19.	For primary and secondary prevention in patients unable to take a statin, we suggest one of the following non-statins: bempedoic acid, ezetimibe, fibrates, or proprotein convertase subtilisin/kexin type 9 monoclonal antibody (PCSK9 mAb) inhibitors.	Weak for	Reviewed, New-added
Supplements and Nutraceuticals		20.	There is insufficient evidence to recommend for or against the use of fiber, garlic, ginger, green tea, and red yeast rice supplements to reduce cardiovascular risks.	Neither for nor against	Not reviewed, Not changed
		21.	For primary or secondary prevention, we suggest against the use of omega-3 fatty acids as a dietary supplement or any omega-3 formulation other than icosapent ethyl.	Weak against	Reviewed, Amended

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Lifestyle Interventions		22.	For primary and secondary prevention of cardiovascular disease, we suggest a Mediterranean diet.	Weak for	Reviewed, New-replaced
		23.	For primary and secondary prevention, we suggest increasing regular aerobic physical activity that maximizes what the patient is willing and able to achieve.	Weak for	Not reviewed, Amended
		24.	We recommend a structured, exercise-based cardiac rehabilitation program for patients with recent occurrence of coronary heart disease (i.e., myocardial infarction, diagnosis of coronary artery disease, coronary artery bypass grafting, or percutaneous coronary intervention).	Strong for	Not reviewed, Amended

[a] For additional information, please refer to **Determining Recommendation Strength and Direction** in the full CPG.

[b] For additional information, please refer to **Recommendation Categorization** in the full CPG

* Read narrative discussion for the definition of intermediate to high risk.

** Listed in alphabetical order.

† Very high-risk patients defined as:

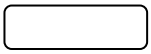
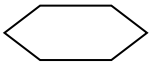
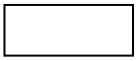
- MI or ACS in the past 12 months on lipid-lowering therapy;
- Recurrent ACS, MI, or atherosclerotic CVA on lipid-lowering therapy; or
- ASCVD and LDL-C ≥70 mg/dL on lipid-lowering therapy.

Algorithm

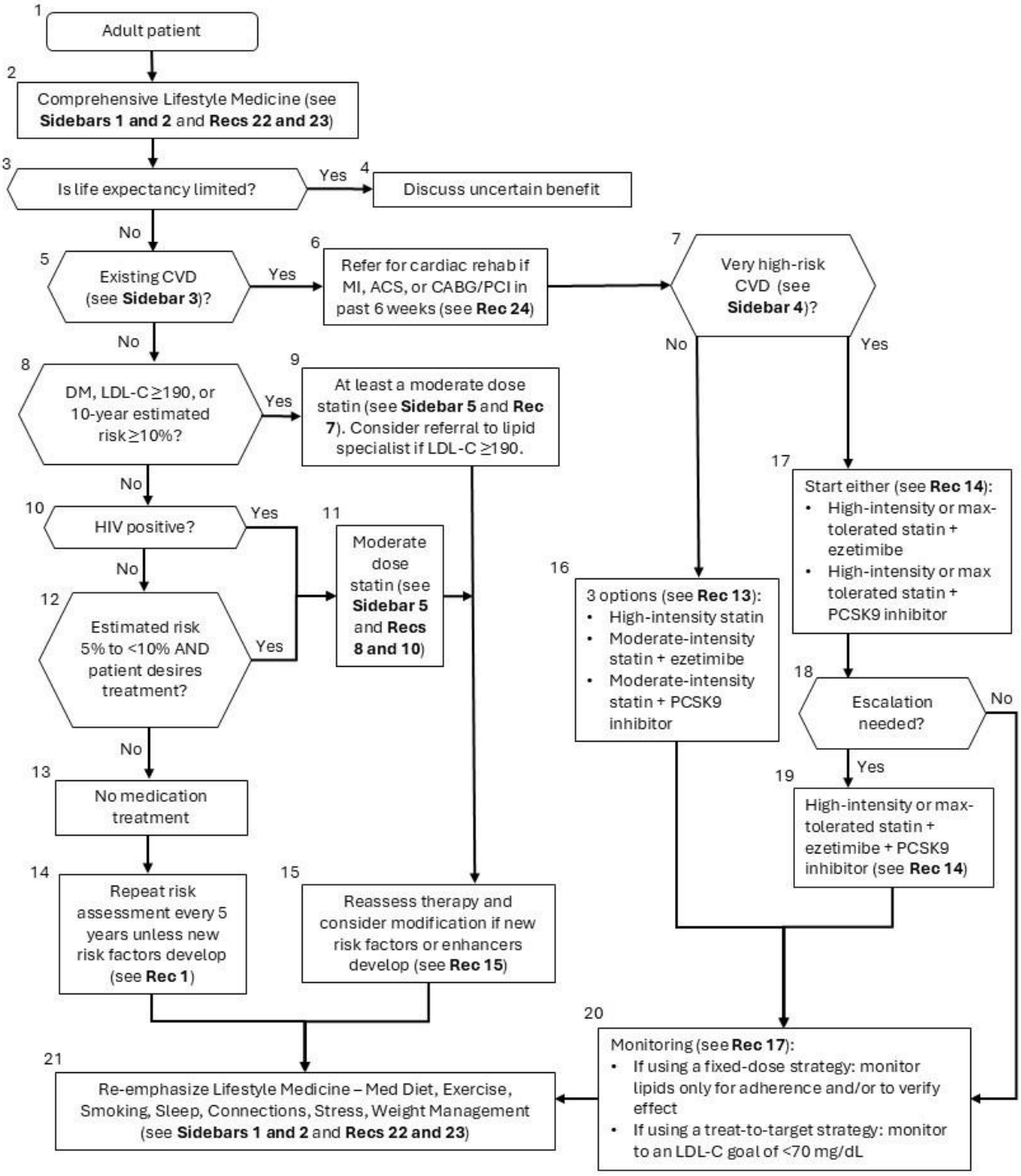
This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in lipid management to reduce CVD risk. This algorithm format represents a simplified flow of the management of patients with or at risk for CVD and who would benefit from lipid management, helping to foster efficient decision making by providers. It includes:

- An ordered sequence of steps of care;
- Recommended observations and examinations;
- Decisions to be considered; and
- Actions to be taken.

The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(2) Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered "Yes" or "No".
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm

Management Algorithm*



*Values for estimated risk are based on the PREVENT risk assessment tool.

Abbreviations: ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; CVD: cardiovascular disease; DM: diabetes mellitus; HIV: human immunodeficiency virus; LDL-C: low-density lipoprotein cholesterol; LFTs: liver function tests; Med: Mediterranean; MI: myocardial infarction; PCI: percutaneous coronary intervention; PCSK9: proprotein convertase subtilisin/kexin type 9; Rec: Recommendation; ULN: upper limit of normal

Sidebar 1: Comprehensive Lifestyle Medicine

- Increase physical activity (aerobic and resistance exercise) that maximizes what the patient is willing and able to achieve
    - The stated goals of minutes per week are 150 minutes of moderate-intensity physical activity OR 75 minutes of vigorous-intensity physical activity OR an equivalent combination.
- Choose a healthy dietary pattern (e.g., Mediterranean diet)
- Sleep 7-8 hours/night
- Socialize: forge and embrace social connections
- Quit using tobacco and nicotine
- Minimize alcohol consumption
- Manage stress
- Address overweight and obesity (see VA/DOD Obesity and Overweight CPG)

Sidebar 2: Mediterranean and Other Cardioprotective Diets

Emphasize	Limit
Fruits and vegetables	Added sugar
Whole grains	Sugar-sweetened beverages
Seafood (primarily fatty fish)	Sodium
Skinless poultry	Highly processed foods
Tree nuts, seeds, peanuts, nut butters	Refined carbohydrates
Beans and legumes	Saturated fats
Non-tropical vegetable oils (olive, canola, avocado, etc.)	Tropical vegetable oils (coconut, palm, etc.)
Low-fat dairy products (milk, cheese)	High-fat and processed meats
	Alcoholic beverages

Sidebar 3: ASCVD (Secondary Prevention)

- MI or ACS
- CABG/PCI
- Stable CAD
- CVA/TIA due to atherosclerosis
- PAD
- Does **not** include asymptomatic atherosclerosis on imaging (e.g., CCTA, CAC, catheterization)

Abbreviations: ACS: acute coronary syndrome; ASCVD: atherosclerotic cardiovascular disease; CABG: coronary artery bypass grafting; CAC: coronary artery calcium; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CVA: cerebrovascular accident; MI: myocardial infarction; PAD: peripheral arterial disease; PCI: percutaneous coronary intervention; TIA: transient ischemic attack

Sidebar 4: Very High-Risk CVD Patients

- MI or ACS in past 12 months on lipid-lowering therapy; or
- Recurrent ACS, MI, or atherosclerotic CVA on lipid-lowering therapy; or
- ASCVD and LDL-C ≥70 mg/dL on lipid-lowering therapy

Abbreviations: ACS: acute coronary syndrome; ASCVD: atherosclerotic cardiovascular disease; CVA: cerebrovascular accident; CVD: cardiovascular disease; dL: deciliter; LDL: low-density lipoprotein; mg: milligram; MI: myocardial infarction

Sidebar 5: Statin Intensity

Generic Name	Moderate Intensity	High Intensity
Rosuvastatin	5 – 10 mg	20 – 40 mg
Atorvastatin	10 – 20 mg	40 – 80 mg
Fluvastatin	80 mg (XL) or 40 mg BID	N/A
Lovastatin	40 – 80 mg	N/A
Pitavastatin	1 – 4 mg	N/A
Pravastatin	40 – 80 mg	N/A
Simvastatin	20 – 40 mg	N/A

Intensified patient care (e.g., phone calls, emails, patient education, drug regimen simplification) may improve adherence to lipid-lowering medications.

Abbreviations: BID: twice per day; mg: milligrams; N/A: not applicable; XL: sustained release

Sidebar 6: For Statin Intolerance*

1. Washout period (e.g., 1 month) followed by the same or a different statin; continue other lipid-lowering therapy
2. Lower dose or nondaily dosing (e.g., every other day or 2-3 days per week) of statin (see **Recommendation 18**)
3. Consider initiating bempedoic acid, ezetimibe, fibrates, or PCSK9 mAb inhibitors in patients unable to take a statin (see **Recommendation 19**)

*Other groups have described in more detail additional management strategies for statin intolerance; for example: Management of Statin Intolerance Clinician Factsheet IB 10-1695.

Abbreviations: mAb: monoclonal antibody; PCSK9: proprotein convertase subtilisin/kexin type 9

Sidebar 7: Novel Risk Markers

- Suggest checking Lp(a) to identify intrinsic enhanced risk (see **Recommendation 5**)
- Not recommended to routinely measure CAC in patients with low risk (see **Recommendation 4**)
- Suggest CAC measurement in patients with intermediate to high risk who question the need for therapy (see **Recommendation 3**)
- The routine measurement of hs-CRP, ApoB, PRS, TPA, or ABI is not useful to refine risk (see **Recommendation 6**)

Abbreviations: ABI: ankle brachial index; ApoB: apolipoprotein B; CAC: coronary artery calcium; hs-CRP: high-sensitivity C-reactive protein; PRS: polygenic risk scores; TPA: total carotid plaque area

Sidebar 8: Elevated Triglycerides for Secondary CVD Prevention

- Consider secondary causes of elevated triglycerides*
- If triglycerides are persistently elevated (≥150 mg/dL) despite maximally tolerated statin, then consider icosapent ethyl 2 g BID (see **Recommendation 16**)
- Modify diet

*Secondary causes defined as co-occurring conditions, alcohol intake, and medications that can contribute to elevated triglycerides (e.g., hormones, immune-related, beta blockers, thiazide/loop diuretics, bile acid sequestrants, atypical antipsychotics, isotretinoin).

Abbreviations: BID: twice per day; CVD: cardiovascular disease; dL: deciliter; g: gram; mg: milliliter

Pharmacotherapy

Table 1. Summary of Pharmacologic Agents*

Consult agency formulary for availability

Drug Class	Drug	Dose	Mean % LDL Reduction+	Major Drug Interactions	Adverse Drug Reactions	Notes
Statins	Atorvastatin	10 – 80 mg once daily	Moderate-dose intensity: 30 to <50% High-dose intensity: ≥50%	Since statins vary in their metabolic pathway, refer to product labeling for drug-drug interactions and use in special populations (e.g., Asian patients) regarding statin dosage guidance and dose limits.	Risk for myalgia, myopathy and, very rarely, rhabdomyolysis. Other risks include new onset diabetes (primarily with higher doses), LFT elevation, and asymptomatic CK elevation.	• First line therapy for primary or secondary prevention of CVD. • True statin intolerance is uncommon. Evaluation of previous statin use, and retrial should be strongly considered to reduce CV risk (except for patients with life-threatening adverse events, e.g., rhabdomyolysis). Intermittent dosing regimen may be considered (see **Recommendation 18**). • Statins, particularly longer-acting statins (e.g., rosuvastatin, atorvastatin), may be taken any time of day.
	Rosuvastatin	5 – 40 mg once daily				
	Simvastatin	5 – 40 mg once daily				
	Lovastatin	20 – 80 mg once daily	High-intensity statins: Atorvastatin 40-80 mg Rosuvastatin 20-40 mg			
	Pravastatin	10 – 80 mg once daily				
	Fluvastatin	20 – 80 mg per day				
	Pitavastatin	1 – 4 mg once daily				
Cholesterol absorption inhibitors	Ezetimibe	10 mg once daily	Monotherapy: 18-20% Combined with statins: additional 12-15% (up to 20%)	Increased incidence of transaminase elevation >3x ULN when combined with statins vs. statins alone (1.3% vs. 0.4%, respectively)	Generally well tolerated	• Benefit for reducing non-fatal CV events in secondary prevention when added to statins (IMPROVE-IT Trial). • Available as a combination product with simvastatin.

Drug Class	Drug	Dose	Mean % LDL Reduction+	Major Drug Interactions	Adverse Drug Reactions	Notes
PCSK9 inhibitors (Monoclonal Antibody or mAb)	Alirocumab	75 mg once every 2 weeks *OR* 300 mg once every 4 weeks Max: 150 mg every 2 weeks	50 to >60%	No known significant interactions.	Generally well tolerated. Injection site reactions (3-7%) reported more often than placebo in clinical trials. Other adverse reactions with PCSK9 inhibitors were similar to placebo.	• Benefit for reducing non-fatal CV events in secondary prevention when added to maximally tolerated statin +/- ezetimibe (ODYSSEY Outcomes and FOURIER trials). • Self-administered as SQ injection.
	Evolocumab	140 mg once every 2 weeks *OR* 420 mg once monthly				
Adenosine triphosphate-citrate lyase inhibitor	Bempedoic acid	180 mg once daily	Monotherapy: 21-23% Combined with statins: 12-17% Combined with ezetimibe: 36%	Avoid concomitant use with >20 mg simvastatin or >40 mg pravastatin.	In CLEAR Outcomes, the following adverse events occurred more often with bempedoic acid vs. placebo, respectively: LFT elevation: 4.5 vs. 3% Renal impairment: 11.5 vs. 8.6% Tendon rupture: 1.2 vs. 0.9% Hyperuricemia: 10.9 vs. 5.6% Gout: 3.1 vs. 2.1% Cholelithiasis: 2.2 vs. 1.2% Caution should be used in patients who might be at greater risk for these events.	• Benefit in reducing CV events in patients with statin intolerance (In the CLEAR Outcomes trial, 30% of patients did not have established CVD but were at high risk). • Available as a combination product with ezetimibe 10 mg.

Drug Class	Drug	Dose	Mean % LDL Reduction+	Major Drug Interactions	Adverse Drug Reactions	Notes
Icosapent Ethyl	Icosapent ethyl	2 g twice daily with meals	N/A	May enhance antiplatelet and anticoagulation effects. Use caution with concomitant agents that increase risk of bleeding.	Arthralgia (2.3%), oropharyngeal pain, peripheral edema, constipation, gout, and atrial fibrillation. Potential for allergic reactions in patients with fish allergy.	• Benefit for reduction of CV mortality and morbidity in patients treated for secondary prevention on statins with persistently elevated TG (>150 mg/dL); evidence is limited to one RCT (REDUCE-IT Trial). • Experts have suggested a confirmatory trial be completed to confirm the results since the mineral oil placebo arm in the REDUCE-IT trial led to increases in LDL-C and inflammatory markers (e.g., hs-CRP) which may have amplified the magnitude of the findings. • Hospitalization for atrial fibrillation or flutter was statistically higher with icosapent and a non-significant trend towards a higher incidence of hospitalization for serious bleeding events was also observed.

Drug Class	Drug	Dose	Mean % LDL Reduction+	Major Drug Interactions	Adverse Drug Reactions	Notes
Small Interfering RNA (siRNA) agent	Inclisiran	284 mg once, at 3 months, and then every 6 months	40% to >50%	No known interactions	Injection site reactions (2% placebo vs. 8% inclisiran), arthralgia (4% placebo vs. 5% inclisiran), bronchitis (3% placebo vs. 4 % inclisiran)	• Ongoing outcomes trials: ORION 4: secondary prevention trial, potential for results in 2026 VICTORION-1 PREVENT: primary prevention trial; expected after 2027 VICTORION-2 PREVENT: secondary prevention trial; expected completion date is 2027 • Should be reserved for patients who cannot use a PCSK9 mAb inhibitor. • Do not use in combination with PCSK9 mAb inhibitor. • Administered SQ by a healthcare professional.

* Refer to product labeling for more information regarding use restrictions, dose modification, dosing in special populations (e.g., renal or liver impairment, advanced age, pregnancy, etc.), drug-drug interactions, and adverse events.

+ Mean percent LDL-C lowering are estimates, individual response may vary.

Abbreviations: CK: creatine kinase; CV: cardiovascular; CVD: cardiovascular disease; dL: deciliter; gm: grams; DM: diabetes mellitus; hs-CRP: high-sensitivity C-reactive protein; LDL-C: low density lipoprotein cholesterol; LFT: liver function test; mAb: monoclonal antibody; mg: milligrams; PCSK9: proprotein convertase subtilisin/kexin type 9; RCT: randomized controlled trial; SQ: subcutaneous, TG: triglyceride; ULN: upper limit of the normal range

Lifestyle Medicine Interventions

Lifestyle interventions, including a healthy diet and adequate physical activity, play a pivotal role in CV risk reduction in persons with and without CVD.(3-5)

A. Physical Activity

Increasing the level of physical activity can be done with limited resources and can prove beneficial in the management of lipid profiles.(5,6) Large-scale epidemiological studies consistently demonstrate that routine physical activity increases HDL-C levels and decreases CV risk.(7-10) These benefits accrue from aerobic activity, resistance exercise, or a combination of both.(3,6)

Modes of aerobic activity can include walking, running, gardening, cycling, swimming, in-person or virtual exercise classes, or nearly any movement that increases respiratory rate. Regular aerobic activity is recommended for both primary and secondary prevention of CVD.(10) Cardiovascular risk reduction has been observed in routine aerobic activity with decreases in TC, TG, LDL-C, and very-low LDL-C, and an increase in HDL-C.(6,10) A total of 150 minutes of moderate intensity, 75 minutes of vigorous intensity physical activity, or an equivalent combination of the two intensities per week is associated with a reduction in CV mortality by 21%-91% and all-cause mortality by 19%-70%.(10,11)

Aerobic activity is also foundational in cardiac rehabilitation programs and is strongly recommended for reducing morbidity and mortality for persons who had a recent occurrence of CHD (i.e., MI, diagnosis of CAD, CABG, or PCI).(10,12)

Resistance exercise can be performed using free weights, bands, weight machines, and body weight resisted exercises. This form of exercise promotes adaptations of muscles, commonly noted in hypertrophy, and an increase in metabolism. Resistance exercise favorably changes the lipid profile by elevating HDL-C. A 2024 SR and meta-analysis reported that combined aerobic and resistance exercise is most favorable in dyslipidemia management for those without CVD, as compared to resistance or aerobic activity alone. The lipid profiles improved when participation in resistance, aerobic, or combined training occurred at a median frequency of 3 bouts per week and a duration of 3 weeks or more.(6)

Engaging in routine physical activity has been shown to be safe for most individuals. Exercise at light to moderate levels, such walking or gardening, is associated with a low risk of musculoskeletal injury and unwanted CV events. Moreover, a gradual increase in activity overtime, especially in low level or inactive individuals, provides additional risk reduction. Adults may successfully adopt a more active lifestyle when there are identified benefits that have personal value to the individual. These may include health benefits associated with physical activity, the opportunity to enjoy recreational activities in a social setting, improved personal appearance or energy, the ability to help a friend or family member be more active, and a greater opportunity to live independently in the community for older adults Following the identification of personal benefits, setting goals connected to those personal benefits and having a graduated approach to physical activity can assist in helping adults become and stay physically active.(13)

B. Diet

Table 2. Patient Education on the Mediterranean and Other Cardioprotective Diets

Eat More	Eat Less
• Fruits and vegetables • Whole grains • Seafood (primarily fatty fish) • Skinless poultry • Tree nuts, seeds, peanuts, nut butters • Beans and legumes • Non-tropical vegetable oils (olive, canola, avocado, etc.) • Low-fat dairy products (milk, cheese)	• Added sugar • Sugar-sweetened beverages • Sodium • Highly processed foods • Refined carbohydrates • Saturated fats • Tropical vegetable oils (coconut, palm, etc.) • High-fat and processed meats • Alcoholic beverages

While a new U.S. Surgeon General advisory risk was issued sharing how alcohol increases cancer risk, it is generally understood that red wine, in limited amounts, is healthy for the heart and can reduce CV risk. Resveratrol, a polyphenolic antioxidant compound, is thought to be the compound specifically found in red wine and red grape juice that is known to contribute to CV risk reduction. Providers should consider the risk of recommending alcohol to individual patients.

Guideline Work Group

Organization	Names*
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Methods

The 2025 Lipids CPG is an update to the 2020 VA/DOD Lipids CPG. The methodology used in developing the 2025 CPG follows the *Guideline for Guidelines*, an internal document of the VA/DOD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DOD CPGs.(14) The *Guideline for Guidelines* is available at http://www.healthquality.va.gov/policy/index.asp. A full description of this guideline's methodology is available at https://www.healthquality.va.gov/guidelines/cd/lipids/.

Patient-Centered Care

VA and DOD encourage providers to be sensitive to demographic, cultural, and other differences that affect patients' values, needs, and preferences, aimed at treating the condition while also optimizing the individual's overall health and well-being. Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(15,16) A whole health approach (https:/www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and well-being goals. Clear communication is essential and should be supported by evidence-based information tailored to each patient's needs. Guideline recommendations should be applied in a holistic approach to care that is patient-centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. The focus is using an individual's risk factors and event history to guide the various treatment and management strategies among patients at risk for CVD morbidity and mortality.

Shared Decision-Making

This CPG encourages providers to practice shared decision-making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(17) Shared decision-making is emphasized in *Crossing the Quality Chasm,* an Institute of Medicine IOM (now NAM) report, in 2001 (18) and is a core component of a patient-centered, whole health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, possible outcomes, and levels and/or settings of care, especially where patient heterogeneity in weighing risks and benefits might exist. The VA and DOD have embraced shared decision-making. Providers are encouraged to use shared decision-making to individualize treatment goals and plans based on patient capabilities, needs, values, and preferences.

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Access to the full guideline and additional resources are available at the following link:
https://www.healthquality.va.gov/guidelines/CD/lipids