



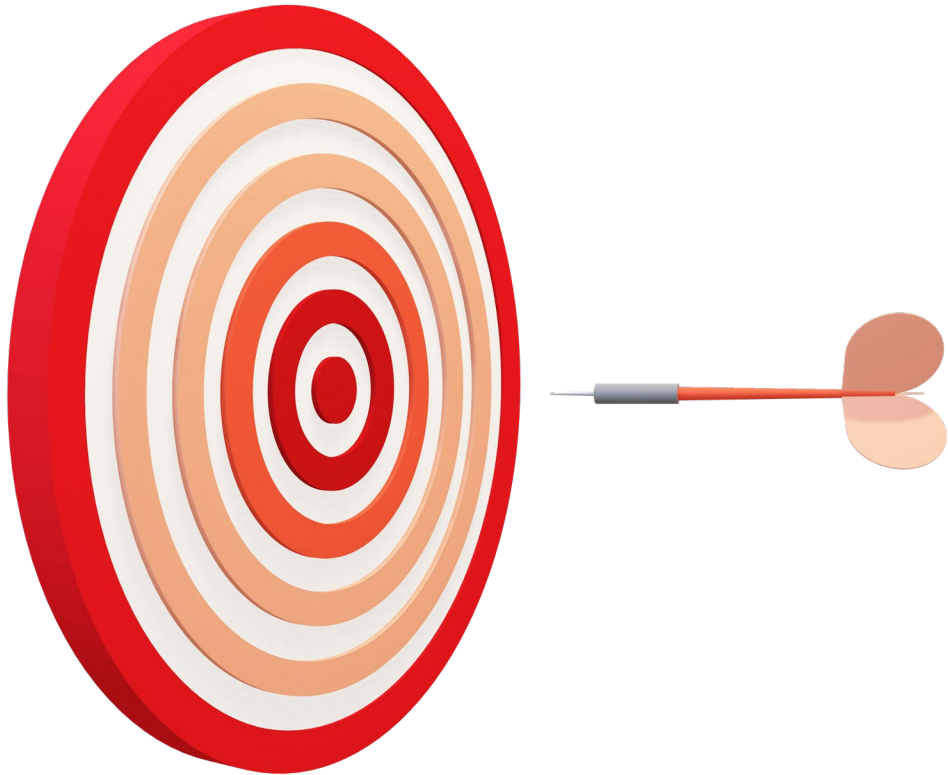
VA/DOD Clinical Practice Guideline on Lipid Management for Cardiovascular Disease Risk Reduction

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Learning Objectives



- Describe how the VA/DOD Clinical Practice Guidelines for lipid management are developed.
- Describe new calculators and biomarkers to refine risk estimates.
- List key elements of evidence-based pharmacologic treatment options for managing lipid disorders to reduce cardiovascular risk.
- Identify key non-pharmacologic strategies for lipid management, including lifestyle and behavioral interventions.
- Describe patient and family education strategies, along with relevant resources, to support effective lipid management and cardiovascular risk reduction.





Guideline Work Group

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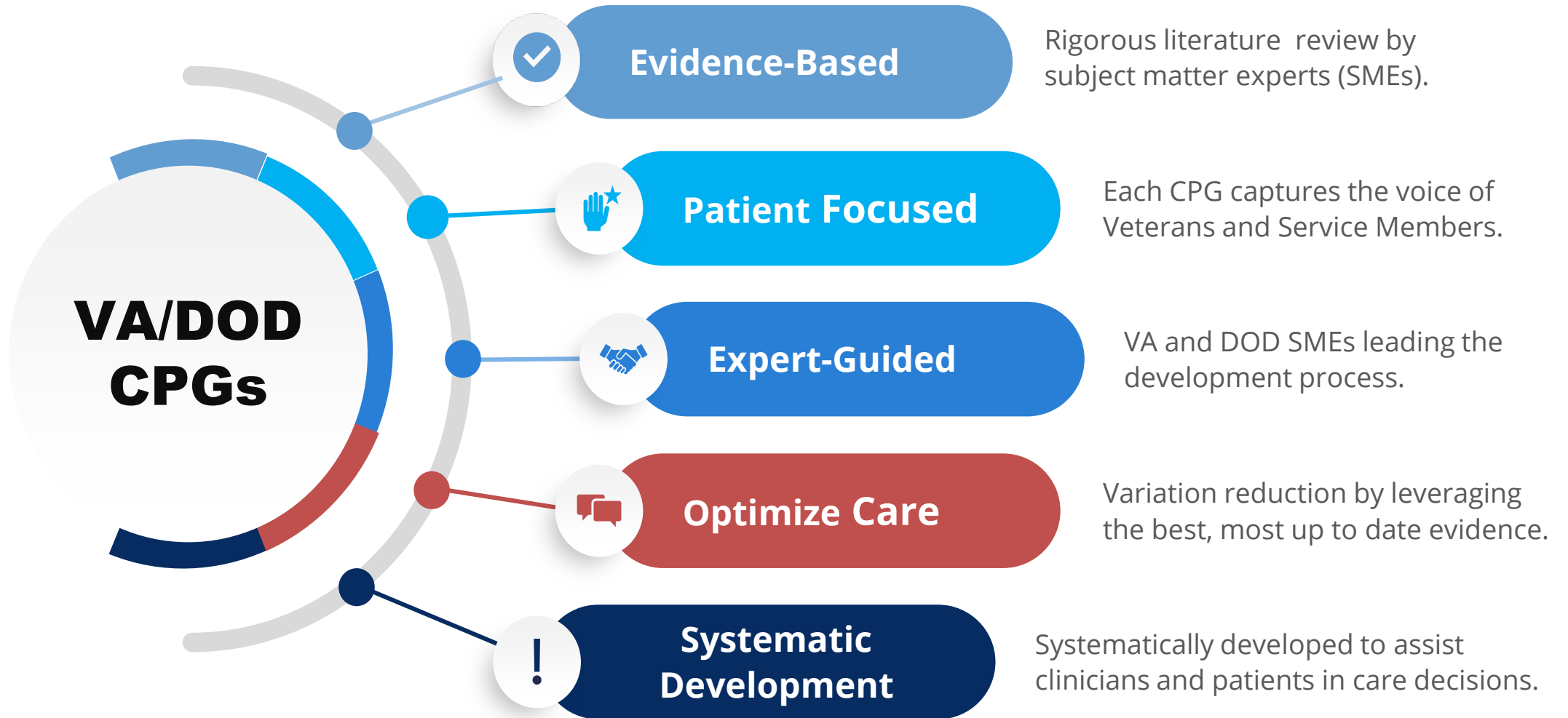
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VA/DOD Clinical Practice Guidelines





Recommendation Evidence Strength

Recommendation Wording	Evidence Strength
We recommend...	Strong evidence for
We suggest...	Weak evidence for
Neither for nor against...	Insufficient evidence
We suggest against...	Weak evidence against
We recommend against...	Strong evidence against





1. CPG *Knowledge Check!*

A Weak Recommendation means:

- a) There is no evidence to support the recommended intervention, however, clinicians think it will work
- b) The intervention may be effective, but the evidence that supports the recommendation is weak
- c) There is strong evidence to support the recommendation
- d) There is insufficient evidence to recommend for or against an intervention





1. CPG *Knowledge Check!*

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VA/DOD Clinical Practice Guideline on Lipid Management for Cardiovascular Disease Risk Reduction





Scope of the Guideline

- Audience
 - This CPG is intended for all clinicians who manage lipids for cardiovascular disease (CVD) risk reduction.
- Population
 - This CPG is intended for adults (18 years or older) with or at risk for CVD
 - Populations **excluded** from this guideline include individuals with:
 - HFrEF $\leq 35\%$
 - Limited life expectancy (<5 years)
 - ESRD with or without chronic systolic heart failure
 - Genetic lipid disorders (e.g., Homozygous/Heterozygous Familial Hypercholesterolemia, Familial Chylomicronemia Syndrome)





Update of the Lipids CPG

- Previous version of the CPG was published in 2020
- Guideline was updated with evidence published through January 15, 2025
 - 8 new recommendations added, 4 reviewed and replaced, 8 amended, and 4 carried over with no changes
- This CPG includes recommendations on the following topics:
 - Screening and Assessment of Cardiovascular Risk
 - Pharmacotherapy
 - Statin Intolerance
 - Supplements and Nutraceuticals
 - Lifestyle Interventions





Key Takeaways

- Comprehensive lifestyle medicine remains foundational for CV risk reduction.
- Moderate-intensity statins remain a core therapy for primary prevention, but other lipid-lowering medications and statin intensities may be effective.
- The PREVENT calculator is now suggested to assess risk for primary prevention.
- For primary prevention, a moderate-intensity statin is suggested for adults living with HIV.
- For patients with documented ASCVD, a high-intensity statin alone or a moderate-intensity statin combined with ezetimibe or a PCSK9 inhibitor is suggested.
- 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.





Key Takeaways (continued)

- CAC testing is suggested to refine risk and guide management for primary prevention in some patients.
- Lp(a) testing is suggested to individualize risk assessment by identifying patients with enhanced risk when elevated.
- Icosapent ethyl in patients with ASCVD and hypertriglyceridemia (i.e., ≥ 150 mg/dL) on maximally tolerated statins is suggested.
- Bempedoic acid, ezetimibe, fibrates, or PCSK9 mAb inhibitors are suggested for patients unable to take statins.





Risk Assessment Recommendations (1-6)

#	Recommendation	Strength	Category
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

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





2. Knowledge Check!

In patients over 18 not on statin therapy and without new cardiovascular risk factors, what is the current recommendation regarding the frequency of cardiovascular disease risk assessment?

- A. Annual risk assessment is strongly recommended.
- B. Risk assessment should be done every 5 years.
- C. There is insufficient evidence to recommend a specific frequency.
- D. Risk assessment is not necessary in this population.





2. Knowledge Check!

In patients over 18 not on statin therapy and without new cardiovascular risk factors, what is the current recommendation regarding the frequency of cardiovascular disease risk assessment?

- A. Annual risk assessment is strongly recommended.
- B. Risk assessment should be done every 5 years.
- C. There is insufficient evidence to recommend a specific frequency.
- D. Risk assessment is not necessary in this population.





Treatment Recommendations (7-12)

#	Recommendation	Strength	Category
7.	For primary prevention among patients who have diabetes or 10-year cardiovascular risk $\geq 10\%$ 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
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





Treatment Recommendations (13-17)

#	Recommendation	Strength	Category
13.	For secondary prevention, we suggest treating with one of the following ^{**} : <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> • 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 (e.g., low-density lipoprotein [LDL-C] <70 mg/dL) over a fixed-dose high-intensity statin strategy.	Neither for nor against	Reviewed, New-added

^{**} Listed in alphabetical order.

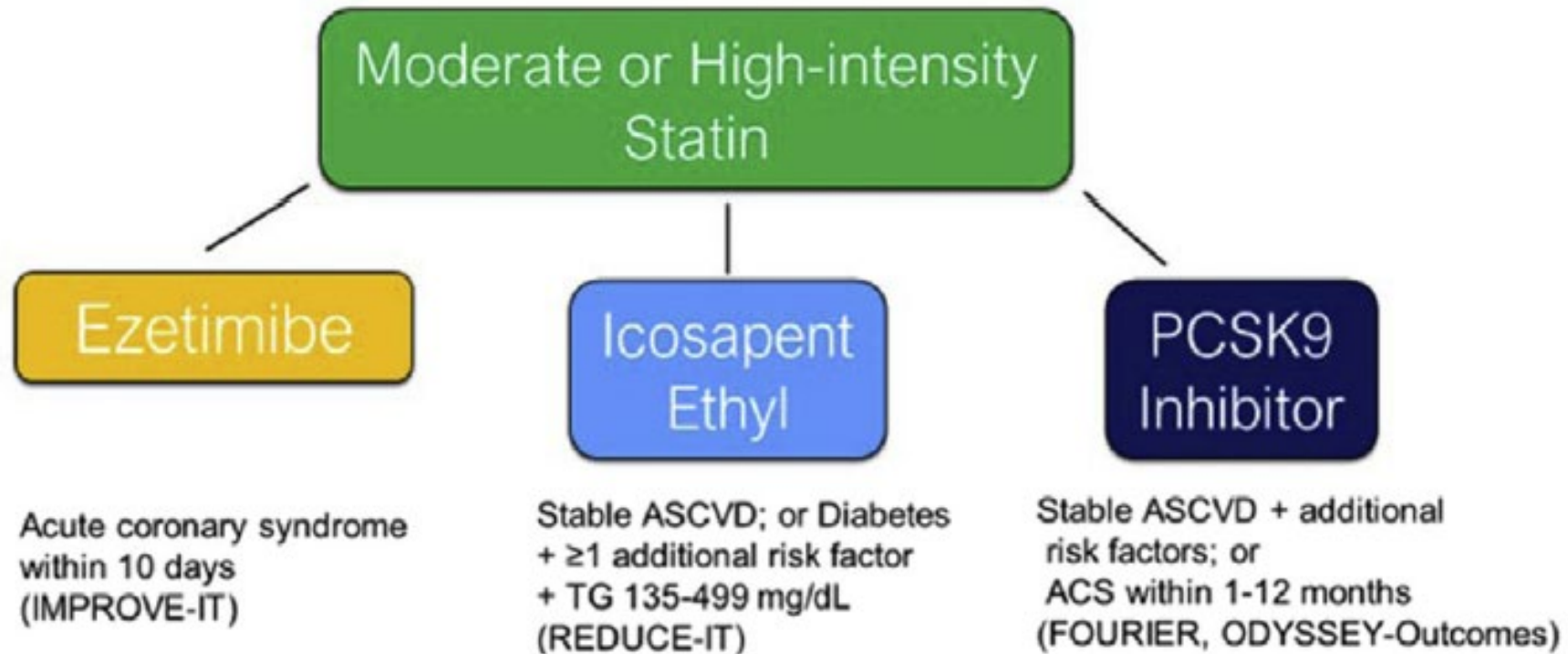
[†] Very high-risk patients defined as:

- 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.





Adjunctive Therapies for ASCVD Risk Reduction in High- or Very-high-risk Statin-treated Patients Supported by RCT Evidence



Orringer CE, Jacobson TA, Maki KC. "National Lipid Association Scientific Statement on the use of icosapent ethyl in statin-treated patients with elevated triglycerides and high or very-high ASCVD risk." J Clin Lipidol. 2019 Nov-Dec;13(6):860-872. PMID: 31787586





Additional Recommendations (18-24)

#	Recommendation	Strength	Category
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
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
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





3. *Knowledge Check!*

All the following are suggested treatment options for secondary prevention except:

- A. High intensity statin monotherapy
- B. Moderate intensity statin monotherapy
- C. Combination of moderate intensity statin and ezetimibe
- D. Combination of moderate intensity statin and PCSK9i





3. *Knowledge Check!*

All the following are suggested treatment options for secondary prevention except:

- A. High intensity statin monotherapy
- B. Moderate intensity statin monotherapy
- C. Combination of moderate intensity statin and ezetimibe
- D. Combination of moderate intensity statin and PCSK9i





Case Study - Initial

You're seeing a 56 y/o male for a follow up exam. He doesn't have any new concerns, so you consider his CV risk.

- PMH: HTN (chlorthalidone), BPH (tamsulosin), gout (allopurinol).
 - No history of CAD, ischemic stroke, DM or PVD.
- FH: Father had a “heart attack in his 70’s.”
- Vitals: BP130/70 and BMI 29.
- Labs: TC 170, TG 260, HDL 38, and LDL is 126. eGFR 100

Questions:

1. Does he need medications? If so, which ones?
2. If meds are indicated and he is hesitant, what else?
3. If statin intolerant?
4. Lifestyle?



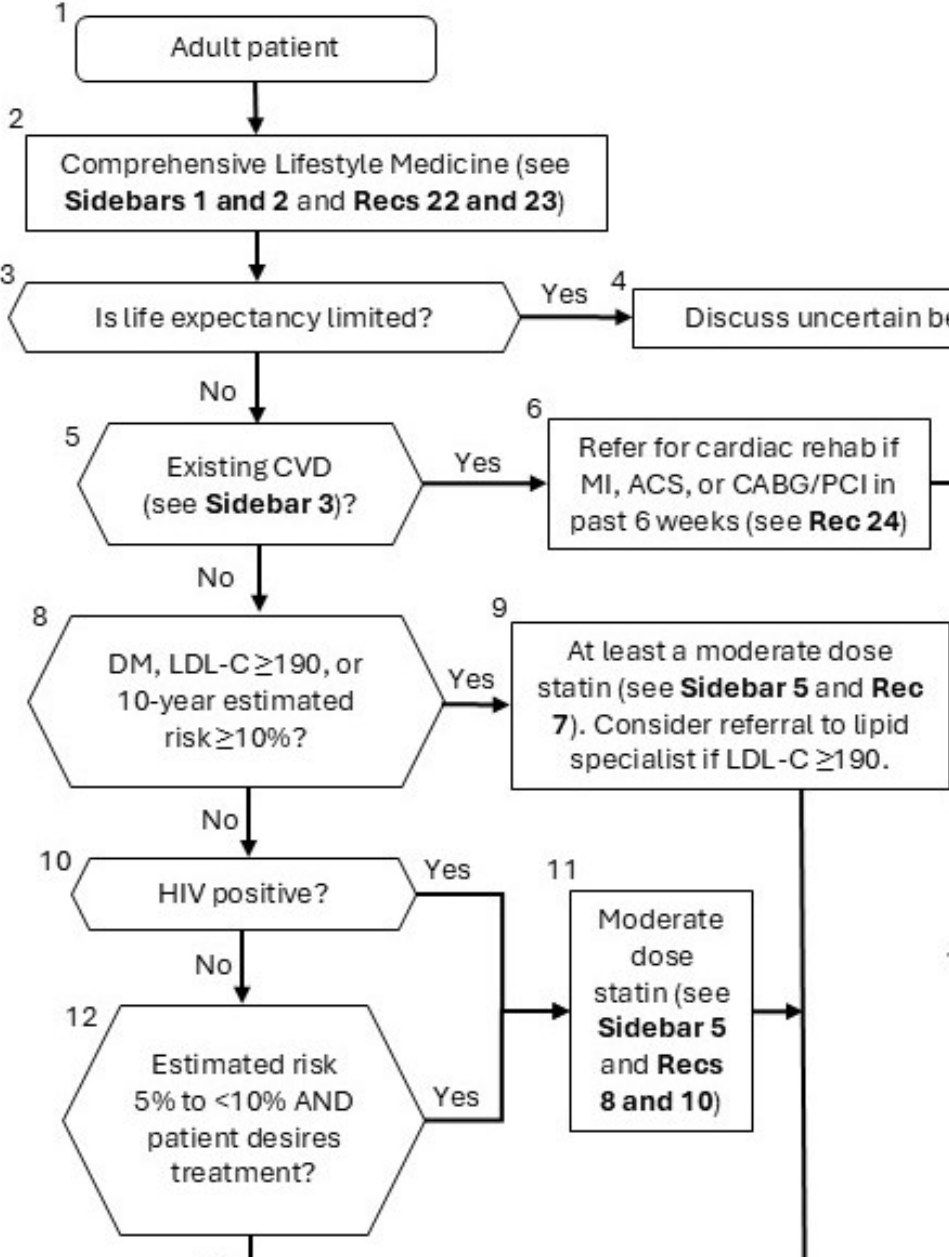


Case Study – Initial Response

- Risk Calculator – PREVENT (10-year risk 10.14%, 6.84% if non-smoker)
- Treatment by 10-year Risk
 - 10% or greater – Recommended, at least moderate statin
 - 5-10% - Suggests moderate statin
- High risk, but resistant
 - Consider Coronary Artery Calcium scoring – Useful in clarifying only intermediate to high risk
 - Lp(a) reasonable but most useful if calculated risk is low – can show inherent elevated risk
- Statin side effects?
 - Evidence – RCTs where restart same or different statin blinded have great results
 - Alternatives for intolerance – washout and restart statin, lower dose/interval, alternative med
 - Alternative medications – bempedoic acid, ezetimibe, fibrates, PCSK9i
- Lifestyle – Always, see Sidebar 1 (2 slides ahead)



Management Algorithm (Primary Prevention)





Algorithm – Sidebars

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)





Case Study – Follow up

Our 56 y/o male follows up after admission for chest pain 3 weeks later.

- Ordered medications by mail-in pharmacy – hadn't arrived yet.
- Diagnosis was NSTEMI, received 2 drug-eluting stents
- New medications: ASA 81 mg, clopidogrel 75 mg, atorvastatin 20 mg
- Peak troponin was 21 ng/ml, echocardiogram shows no wall motion abnormalities

Questions:

1. Should we change medications?
2. What else should we do?



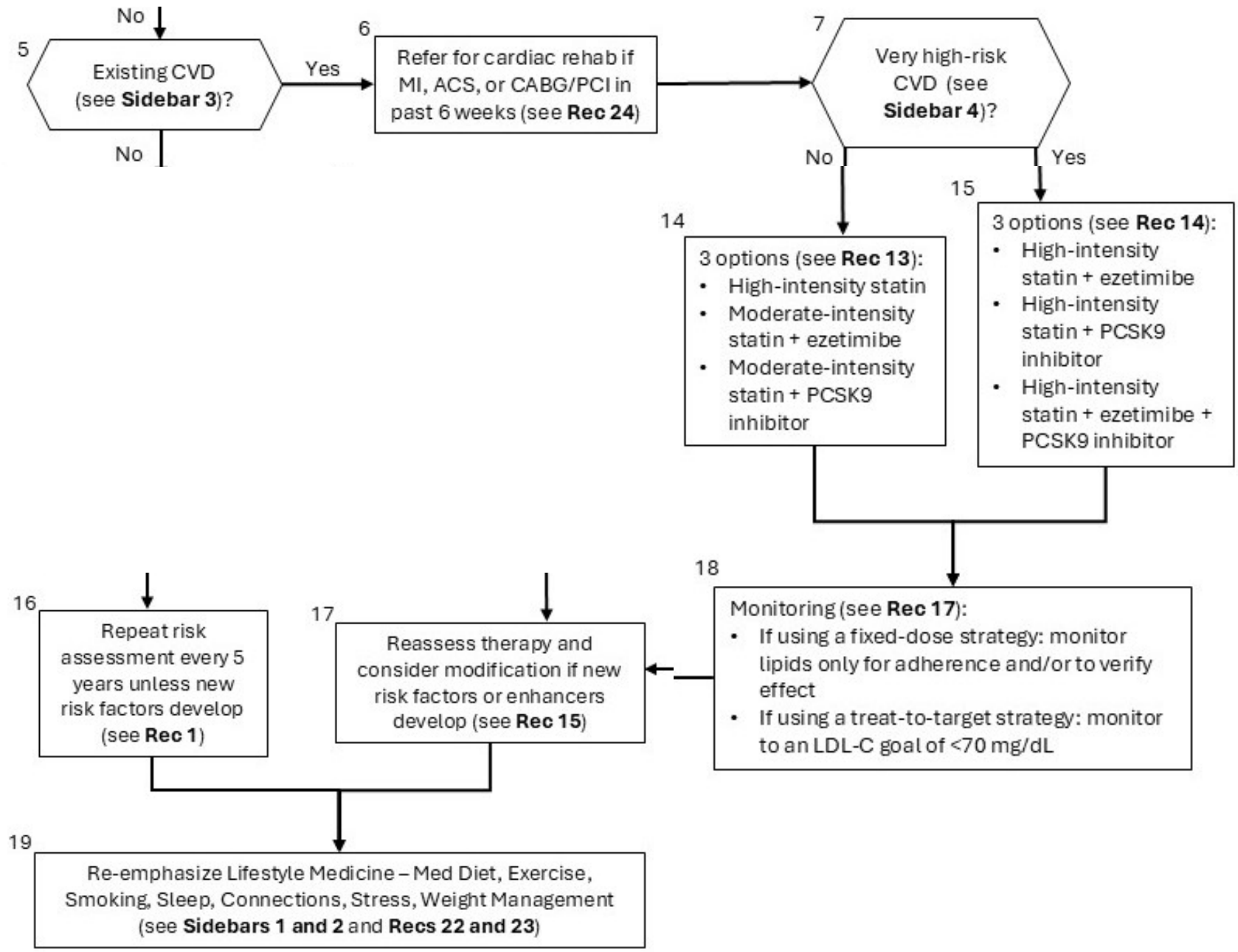


Case Study – Follow Up

- Medications for Secondary Prevention – 3 options
 1. High-intensity statin (e.g. atorvastatin 40-80 mg)
 2. Moderate-intensity statin AND ezetimibe
 3. Moderate-intensity statin AND PCSK9i
- Consult – Cardiac Rehabilitation
 - NNT of 31 to reduce 10-year cardiovascular mortality
 - Only structured programs have this advantage
- Consult Cardiology, if not already done



Management Algorithm (Secondary Prevention)





Algorithm – Sidebars

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)
<ul style="list-style-type: none"> • 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)





Algorithm – Sidebars

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 \geq 70 mg/dL on lipid-lowering therapy

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





Algorithm – Sidebars

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**)

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**)

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).





4. *Knowledge Check!*

Which of the following treatment options is recommended for secondary prevention of cardiovascular disease?

- A. Low-intensity statin therapy only
- B. High-intensity statin therapy
- C. Moderate-intensity statin therapy without any additional agents
- D. Lifestyle modification alone without pharmacologic therapy





4. *Knowledge Check!*

Which of the following treatment options is recommended for secondary prevention of cardiovascular disease?

- A. Low-intensity statin therapy only
- B. High-intensity statin therapy
- C. Moderate-intensity statin therapy without any additional agents
- D. Lifestyle modification alone without pharmacologic therapy





Questions and Open Discussion





VA/DOD CPG Resources Available

- Full Clinical Practice Guidelines
- Clinician Summary
- Clinical Support Tools
- Webinar(s)
- Patient-facing Education



<http://www.healthquality.va.gov>

VA/DOD CLINICAL PRACTICE GUIDELINES
Lipid Management for Cardiovascular Disease Risk Reduction
Management Algorithm*

Sidebars:

- 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 7.5 hours/night
 - Socialize, forge and embrace social connections
 - Quit using tobacco and nicotine
 - Minimize alcohol consumption
 - Manage stress
 - Address overweight and obesity
- 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	Tropical vegetable oils
Low-fat dairy (cheese)	
- Sidebar 3: ASCVD (Secondary Prevention)**
 - MI or ACS
 - CAG/PCI
 - Stable CAD
 - CVA/TIA due to atherosclerosis
 - PAD
 - Does **not** include asymptomatic atherosclerosis on imaging (e.g., CCTA, CAC, catheterization)
- 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
- Sidebar 5: Statin Intensity**

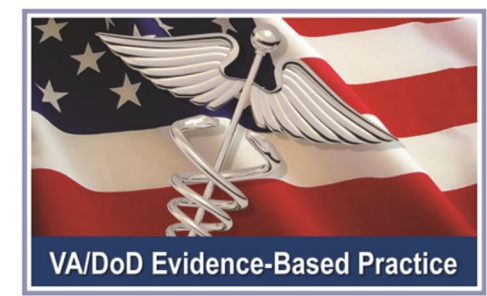
Generic Name	Moderate Intensity	High Intensity
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Atorvastatin	10 – 20 mg	40 – 80 mg
Fluvastatin	80 mg (XL) or 40 mg BID	N/A
Lovastatin	40 – 80 mg	N/A
Pitavastatin	1 – 4 mg	N/A
- Sidebar 6: For Statin Intolerance****
 - Washout period (e.g., 1 month) followed by the same or a different statin; continue other lipid-lowering therapy
 - Lower dose or non-daily dosing (e.g., every other day or 2-3 days per week) of statin (see Recommendation 1B)
 - Consider initiating bempedoic acid, ezetimibe, fibrates, or PCSK9 mAb inhibitors in patients unable to take a statin (see Recommendation 1C)
- 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)
- Sidebar 8: Elevated Triglycerides for Secondary CVD**
 - 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 1E)
 - Modify diet

Abbreviations: ABI: ankle brachial index; ApoB: apolipoprotein B; ACS: acute coronary syndrome; ASCVD: atherosclerotic cardiovascular disease; BID: twice per day; CABG: coronary artery bypass grafting; CAC: coronary artery calcium; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CVA: cerebrovascular accident; CVD: cardiovascular disease; dx: diagnosis; DM: diabetes mellitus; g: gram; hs-CRP: high-sensitivity C-reactive protein; LDL-C: low-density lipoprotein cholesterol; JCO: joint commission; mg: milligram; MI: myocardial infarction; mAb: monoclonal antibody; mg/dL: milligram per deciliter; N/A: not applicable; PCSK9: proprotein convertase subtilisin/kexin type 9; PREVENT: Primary Prevention of Cardiovascular Disease Events; PRS: polygenic risk scores; TPA: total carotid plaque area; XL: sustained

*Values for estimated risk are based on the PREVENT risk assessment tool.
**Other groups: intolerance Clin

VA/DOD Clinical Practice Guidelines

LIPID MANAGEMENT FOR CARDIOVASCULAR DISEASE RISK REDUCTION



VA/DoD Evidence-Based Practice

Provider Summary

Version 5.0 | 2025

