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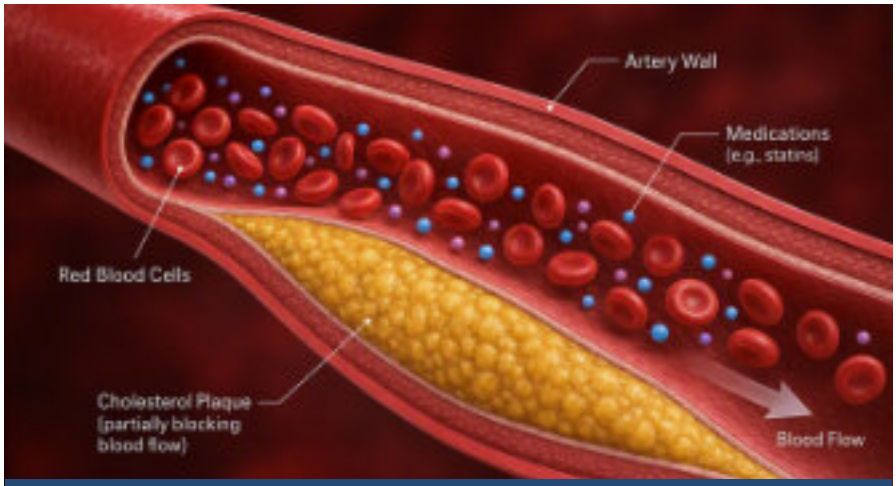

Rethinking Cholesterol: Putting the 2026 AHA/ACC Guidelines into Practice

AN ONGOING CE PROGRAM
of the University of Connecticut School of Pharmacy and Pharmaceutical Sciences

EDUCATIONAL OBJECTIVES

After completing the continuing education activity, pharmacists will be able to

- Recall lipid management goals and ASCVD risk based on comorbidities and cardiovascular disease history
- Match available lipid-lowering medications' mechanisms of action, efficacy, safety, and place in therapy
- Identify optimal lipid-management plans that combine evidence-based recommendations, patient-specific factors, and medication adherence
- Manage lipid-lowering medication regimens based on therapeutic lab monitoring and adverse effects when indicated

After completing the continuing education activity, pharmacy technicians will be able to

- Review common lipid-lowering medications and their indications
- Detect patient concerns or questions that warrant pharmacist intervention
- Describe proper storage, processing, dispensing, and counseling for lipid lowering therapies
- Optimize coverage plans to decrease barriers to medication access

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Pharmacists and pharmacy technicians are eligible to participate in this application-based activity and will receive 0.2 CEU (2 contact hours) for completing the activity, passing the post-test with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

ACPE UAN: 0009-0000-26-046-H01-P
0009-0000-26-046-H01-T

Grant funding: None
Cost: Pharmacists $7
Technicians $4
INITIAL RELEASE DATE: September 10, 2026
EXPIRATION DATE: September 10, 2029

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TARGET AUDIENCE: Pharmacists and pharmacy technicians in all practice settings

ABSTRACT: Cardiovascular disease is one of the most common causes of death in the United States. Patients with cardiovascular disease are at a significantly heightened risk for serious cardiac events such as heart attack, stroke, and sudden cardiac death. Preventing the progression of cardiovascular disease through tailored cholesterol goals, lifestyle management, and guideline-directed lipid-lowering medications is vital.

This continuing education activity highlights the 2026 update to the American Heart Association and American College of Cardiology Cholesterol Management Guidelines. The guidelines emphasize calculating 10-year cardiovascular disease risk, personalized risk calculation, reclassification with specific lipid biomarkers, and reassessment of lipid-lowering treatment—the CPR framework—to properly manage patients' cholesterol. Pharmacists and pharmacy technicians should become familiar with the updated guidelines to improve patient outcomes in the evolving field of cholesterol management.

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FACULTY DISCLOSURE: The authors have no financial relationships with an ineligible company.

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INTRODUCTION

For decades, lipid management focused on treating lipoprotein numbers. The 2026 guidelines instead emphasize individualized cardiovascular risk, earlier intervention, and lower low-density lipoprotein (LDL) targets for patients at highest risk. Patient Nick Smith is a 68-year-old male recently seen by the cardiologist. He currently takes several medications: metformin, empagliflozin,

metoprolol succinate, sacubitril/valsartan, rosuvastatin, and loratadine. He has a past medical history of type 2 diabetes mellitus, hyperlipidemia, hypertension, heart failure with reduced ejection fraction (38%), and seasonal allergies. He is also a current smoker with a 15-pack-year smoking history. He has no history of myocardial infarction, ischemic stroke, peripheral artery disease, or coronary revascularization. Reviewing the cardiologist's notes, his LDL-C is 91 mg/dL and his PREVENT Score is 10.2%.

Nick's prescriber reviews the new guideline and pauses. Nick has several cardiovascular risk factors, but has never had an ASCVD event. Is this primary or secondary prevention? Does he need a coronary artery calcium (CAC) scan? Does his heart failure change the classification? And is the statin dose sufficient? Rather than guess, the prescriber calls clinical pharmacist George Johnson and requests a complete lipid-management assessment.

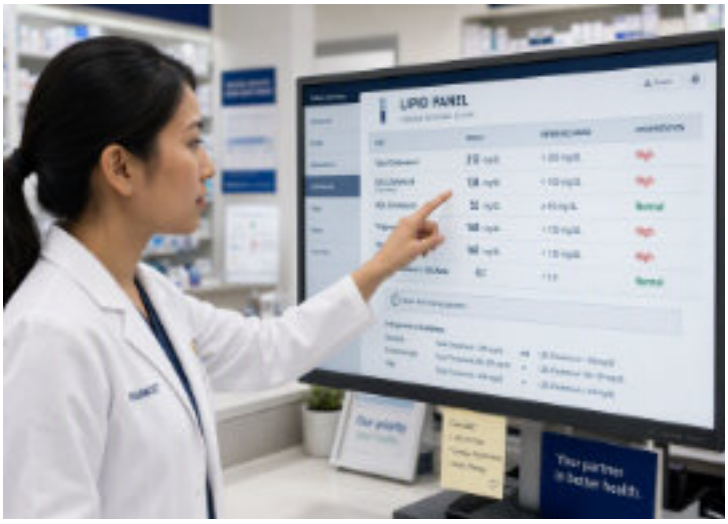
Atherosclerotic Cardiovascular Disease

Atherosclerosis, or the buildup of plaque within an artery, is a leading cause of death in the United States.[1] In 2023, cardiovascular disease caused 1 in 3 deaths nationwide.[2] As plaques grow, they progressively occlude arteries and can eventually rupture. Plaque rupture triggers local platelet-rich thrombus (clot) formation, leading to acute coronary syndromes (unstable angina or myocardial infarction [heart attack]), and sudden cardiac death. In cerebral circulation, atherosclerosis can reduce blood flow or promote thrombus formation, leading to ischemic stroke.[3]Two considerations guide lipoprotein management.[3] The first consideration is determining if patients have established atherosclerotic cardiovascular disease (ASCVD), and the second is establishing individualized lipid goals based on the patient's cardiovascular risk. This risk-based approach allows clinicians to tailor lifestyle interventions and initiate lipid-lowering therapy (LLT) to reduce the likelihood of future cardiovascular events. Strong evidence supports cholesterol management as the preferred method to reduce mortality and preventable cardiac deaths and improve quality of life.[3]

High LDL can cause catastrophic cardiovascular events and stroke later in life. Unfortunately, patients do not experience bothersome symptoms until the damage is done. New evidence suggests that higher LDL-C values starting earlier in life are strong predictors of ASCVD events in adulthood.[4] So, screening patients early and periodically, minimizing modifiable risk factors, and initiating aggressive early lipid-lowering interventions are important.[5] After an ASCVD event, secondary prevention is imperative to reduce the risk of another event.

Cholesterol Screening Blueprint

When clinicians examine lipid panels for patients, they need to use standardized methods for measuring lipoprotein levels.[3] Total cholesterol is the sum of high-density lipoprotein (HDL, also called the good cholesterol), LDL, and the very-low-density lipoprotein (VLDL) component of triglyceride (TG) levels.[6] The



2026 American College of Cardiology/American Heart Association (ACC/AHA) guidelines define high total cholesterol as levels greater than 200 mg/dL. LDL is considered high above 100 mg/dL. HDL should remain above 40 mg/dL in men and 50 mg/dL in women. Non–HDL is calculated by subtracting HDL from total cholesterol or adding together the LDL and VLDL, with values above 130 mg/dL considered high. Non-HDL is important in determining other lipoproteins besides LDL that can contribute to atherosclerosis.

The guidelines also recommend measuring lipoprotein(a), a cholesterol-carrying lipoprotein, at least once. Its normal levels are less than 75 nmol/L with intermediate levels between 75 and 125 nmol/L. Levels above 125 nmol/L independently increase the risk for ASCVD.[7] Genetics heavily influences lipoprotein(a) levels, and levels remain relatively unchanged after age 5, meaning testing once is often sufficient.[8]

LDL-C measurements may underestimate the number of circulating atherogenic particles. In patients who are taking lipid-lowering therapy (LLT) and have high TG levels, cardiometabolic disease, or diabetes despite LDL-C at goal, apolipoprotein B (ApoB) is useful to determine if therapeutic intensification is warranted.[3,9,10] ApoB is the main structural protein found in LDL, VLDL, intermediate-density lipoprotein (IDL), and lipoprotein(a) particles. Elevated ApoB at therapeutic LDL levels suggests persistent atherogenic particle burden that may increase residual ASCVD risk. Many patients with diabetes who have normal cholesterol levels also have elevated ApoB concentrations.[11] ApoB is a useful adjunct to traditional lipid measurements to determine if clinicians should intensify LLT.[3]

TGs should be below 150 mg/dL.[3] While high TG levels contribute to ASCVD risk, LDL is the primary lipid target for risk reduction. However, TG levels above 500 mg/dL increase the risk of pancreatitis. Lipoprotein and TG thresholds may change based on a patient's cardiovascular risk factors and history, meaning interventions may be appropriate even when lipid values fall below these cutoffs.[3]

Between 2017 and 2020, nearly 90 million adults aged 20 or older had elevated total cholesterol (200 mg/dL or greater).[12] Increasing age, comorbidities, and established ASCVD are factors that call for increased screening frequency. Additionally, one in five adolescents had an LDL above 130 mg/dL.[13] Pediatricians should screen children between the ages of 9 and 11 at least once, and again between the ages of 17 and 21.[12] Children with obesity or diabetes may need more frequent screening. Diabetes, heart failure, hypertension, current or former smoking history, or consistently high LDL levels warrant more frequent testing. Clinicians should order lipid panels for patients with established ASCVD every 4 to 12 weeks after initiating or titrating LLT, and then every 6 to 12 months thereafter.[3]

PAUSE AND PONDER: Can LDL values be too low?

Defining ASCVD, Calculating PREVENT Scoring, and Personalizing Primary Prevention Goals

Determining if patients are at risk for ASCVD (and the level of risk) or have experienced an ASCVD event is critical. Whether or not a patient has established ASCVD greatly impacts their risk for future cardiovascular events, and their treatment goals. In short, the best predictor of a future event is a past event in this case.

Because atherosclerosis affects the body systemically, clinical ASCVD can manifest in the heart and in other vascular areas.[3] Locally, ASCVD can result in myocardial infarction (ST-segment elevation [STEMI] and non-ST-segment elevation [NSTEMI]), unstable angina, or the need for arterial revascularization, such as bypass or stents. Ischemic stroke or a transient ischemic attack (TIA) can result if clots embolize and travel to the brain. Finally, plaque buildup in lower extremity arteries leads to peripheral artery disease (PAD). Heart failure, hypertension, and atrial fibrillation do not, by themselves, constitute clinical ASCVD. Patients with these conditions who have no established ASCVD and should not receive lipid-lowering therapy for secondary prevention.

Before clinicians can establish an individualized LDL-C target, they must first calculate the patient's Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) score.[14] For patients aged 30 to 79 with an LDL-C of 70 to 189 mg/dL, the PREVENT score gauges patients' 10- and 30-year ASCVD risk to determine optimal LDL-C targets and whether LLT is warranted. (The AHA provides an online calculator here: https://professional.heart.org/en/guidelines-and-statements/prevent-calculator.) The scoring system estimates an individual's percentage risk of cardiovascular disease using age, systolic blood pressure, total cholesterol, HDL, estimated glomerular filtration rate, and body mass index (BMI).[14] These factors guide LLT initiation. Clinicians can also input comorbidities such as diabetes, current smoking, or patients' current use of lipid-lowering or antihypertensive medications. The scoring system breaks patients into four categories.[3]

- Low-risk patients have a 10-year risk of less than 3%.
- In borderline-risk patients who have a 3% to less than 5% risk, clinicians should discuss the risks versus benefits of initiating LLT with the patient.
- For intermediate-risk patients (5% to less than 10%), LLT is indicated, with moderate-high intensity statins preferred.
- High-risk patients with a 10% or greater PREVENT score should start a high-intensity statin or optimize LLT with other medications.

In patients who have not experienced an ASCVD event, primary prevention strategies focus on reducing cardiovascular risk using less intensive interventions with higher LDL treatment thresholds. Primary prevention targets also depend on patient-specific risk factors. Risk factors include

- Age 65 years or older
- Chronic kidney disease
- Current smoker
- Diabetes
- Heart failure
- Heterozygous familial hypercholesterolemia
- Hypertension
- LDL value above 100 mg/dL despite optimized LLT

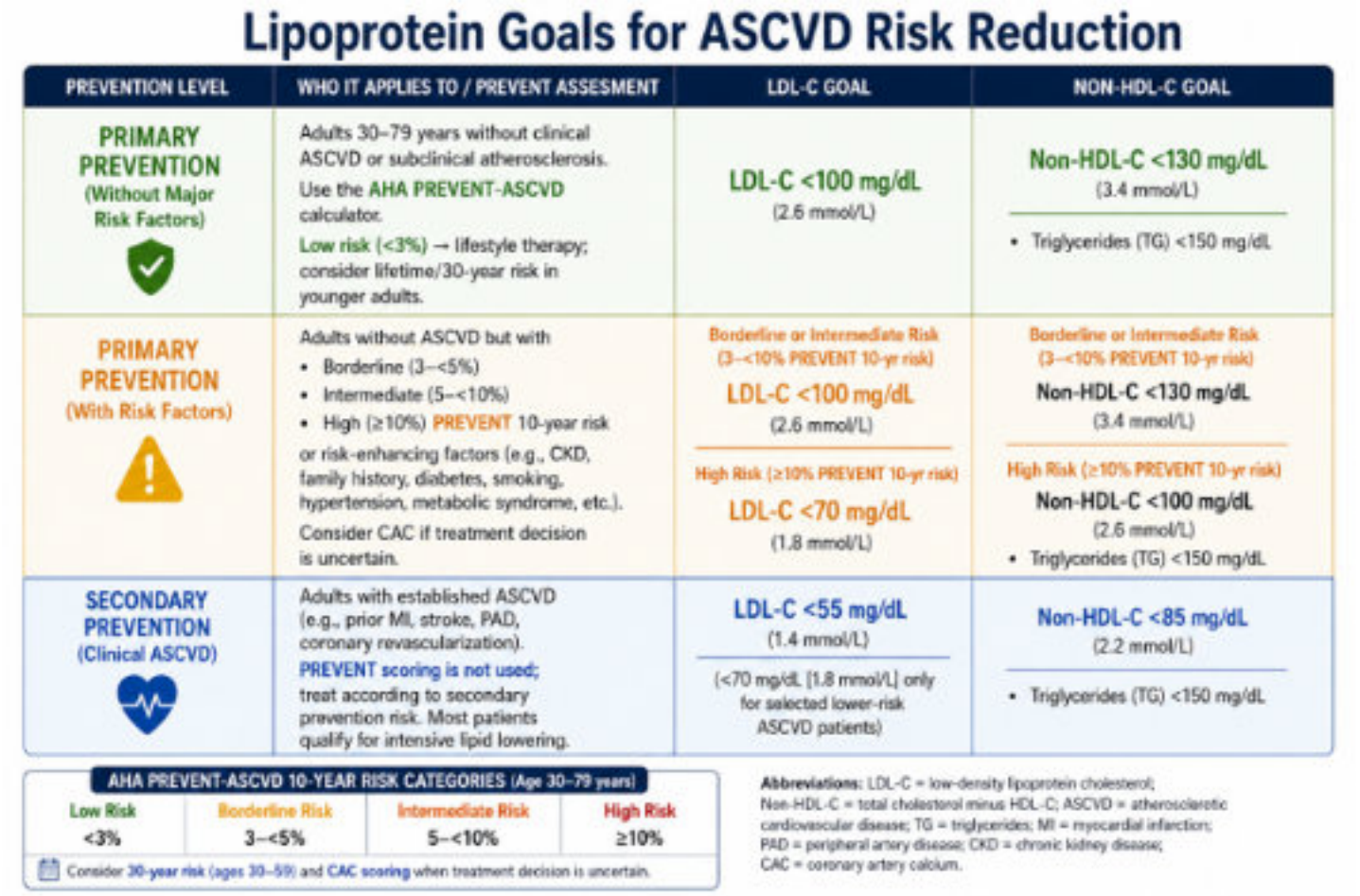
For patients who do not have these risk factors, an LDL goal of below 100 mg/dL is adequate to reduce their risk of ASCVD. For patients at high risk for ASCVD (PREVENT score 10% or higher), clinicians should target an LDL goal of below 70 mg/dL.[3] Prior guidelines favored less stringent goals for primary prevention, but lower LDL levels have been consistently linked to decreased ASCVD risk.

Personalizing Secondary Prevention of ASCVD

In patients with established ASCVD, the new ACC/AHA guidelines recommend aggressive lipid management—these patients are at the highest risk of additional ASCVD events. Secondary prevention targets also depend on defining patients as very high risk for another ASCVD event or not. Very high risk is defined as

- 2 or more previous major ASCVD events, or
- 1 major ASCVD event and 2 or more high-risk conditions (defined in primary prevention)

Figure 1. Cholesterol Targets for Primary and Secondary Prevention of ASCVD



The target for those at very high risk is an LDL of less than 55 mg/dL.[3] The guidelines also indicate that an LDL goal of less than 70 mg/dL is acceptable for patients without high-risk factors for another ASCVD event. However, most patients require lower LDL targets. Evidence suggests that there is no clear lower LDL threshold at which LDL reduction harms patients. The Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) and Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) trials demonstrated that patients with LDL-C values below 30 mg/dL experienced the lowest rates of cardiovascular events without an increase in adverse safety outcomes.[15,16] So, clinicians can intensify LLT to achieve very low LDL levels without increasing safety concerns.

For all patients, a TG level of below 150 mg/dL is optimal, but slight elevations contribute less to ASCVD risk than LDL-C elevations do. **Figure 1** depicts primary and secondary prevention cholesterol goals.

George begins by confirming that Nick has no established ASCVD. Although diabetes, hypertension, HFrEF, and smoking increase his cardiovascular risk, none converts his treatment to secondary prevention. So, Nick is receiving LLT for primary prevention. A PREVENT score of 10.2% puts him in the high-risk category, for which the LDL goal is below 70 mg/dL.

Special Population Lipid Targets

Many patients' concurrent conditions influence recommended lipid goals. For example, primary ASCVD prevention for adults with diabetes has an LDL goal of below 100, or below 70 in the presence of high-risk factors or a PREVENT score of 5% or higher.[21] Diabetes significantly increases the risk of ASCVD, warranting early guideline-directed risk assessment and lipid-lowering interventions by clinicians.[22] Chronic kidney disease, heart failure, and HIV also warrant early LDL lowering, targeting levels under 100 mg/dL if patients have no additional risk factors and under 70 mg/dL in higher-risk patients.[3]

Patients older than 75 may require individualized lipid management rather than strict adherence to LDL targets. LLT still reduces the risk of major cardiovascular events, but data are limited on lower lipid levels for patients in this age group.[23] While LLT is safe and effective in this population, evidence supporting very low LDL targets is more limited. Poor functional status, frailty, and polypharmacy put these patients at an increased risk for adverse effects and potential injury. Clinician-based decision-making is essential to weigh the cardiovascular benefits of stringent lipid targets against the potential negative impact on patients' quality of life.[24] In patients with limited life expectancy, the risk of a major cardiovascular event is low. So, if patients experience negative effects from aggressive lipid management, clinicians should consider less intensive management.

SIDEBAR: When to Reclassify with Coronary Artery Calcium (CAC) Scoring?[17,18]

Coronary Artery Calcium (CAC) refers to calcium deposits within the heart's arterial walls. This noninvasive imaging test performed with a noncontrast cardiac scan is specific to atherosclerotic plaques, meaning it is a precise way to detect early cardiovascular disease. CAC at any level indicates subclinical coronary atherosclerosis, but it does not transform the patient into someone with clinical ASCVD or automatically place everyone into the same treatment category. CAC is principally a selective risk-reclassification tool when the treatment decision remains uncertain.

Coronary artery calcium (CAC) is specific to atherosclerotic plaques and strongly predicts ASCVD risk. It can help refine risk estimates. In adults without established ASCVD who have a borderline or intermediate 10-year PREVENT-ASCVD risk (3% to less than 10%), CAC measurement may be considered when uncertainty remains about whether to initiate lipid-lowering therapy. CAC also guides treatment in asymptomatic men aged 40 years and older and women aged 45 years and older previously not receiving LLT. In patients with CAC scores greater than 0 Agatston Units (AU; a score that reflects both the area and density of calcified plaque in the coronary arteries) who are at borderline risk, clinicians should initiate LLT.

Interestingly, elite endurance athletes can have increased CAC scores without significant risk for atherosclerosis.[19],[20] However, increased plaque calcification may serve a cardioprotective role, as calcified plaques are more stable and less likely to rupture and cause thrombosis than lipid-rich, vulnerable plaques. Further research is needed to clarify this association. Athletes with elevated CAC scores should not stop exercising, as exercise is cardioprotective.[20]

The prescriber asks if a CAC scan would reclassify Nick's ASCVD risk. George explains that a scan is unlikely to change how Nick is treated. Nick's PREVENT score, age, and concurrent conditions are clear indications for LLT. A CAC scan is useful if providers are uncertain about initiating LLT, not if patients are already indicated.

In pregnant patients, cholesterol targets increase with each trimester of gestation. Maternal lipid levels progressively increase as the fetus grows, with triglycerides demonstrating the largest increase. Consequently, standard lipid goals are not applicable to this population, so the need for LLT is clinician-guided and only warranted in very high-risk individuals.[25]

Current evidence has not established a lower LDL threshold at which treatment becomes harmful. Patients at very high ASCVD risk may benefit from LDL levels below 30 mg/dL, provided therapy is clinically indicated, tolerated, and monitored. All clinicians need to remember that "lower is better" does not mean "lower everyone's cholesterol levels indiscriminately."

PAUSE AND PONDER: Which lipid-lowering medications bypass hepatic metabolism and may offer advantages in select patients with hepatic or renal dysfunction?

Lifestyle Interventions

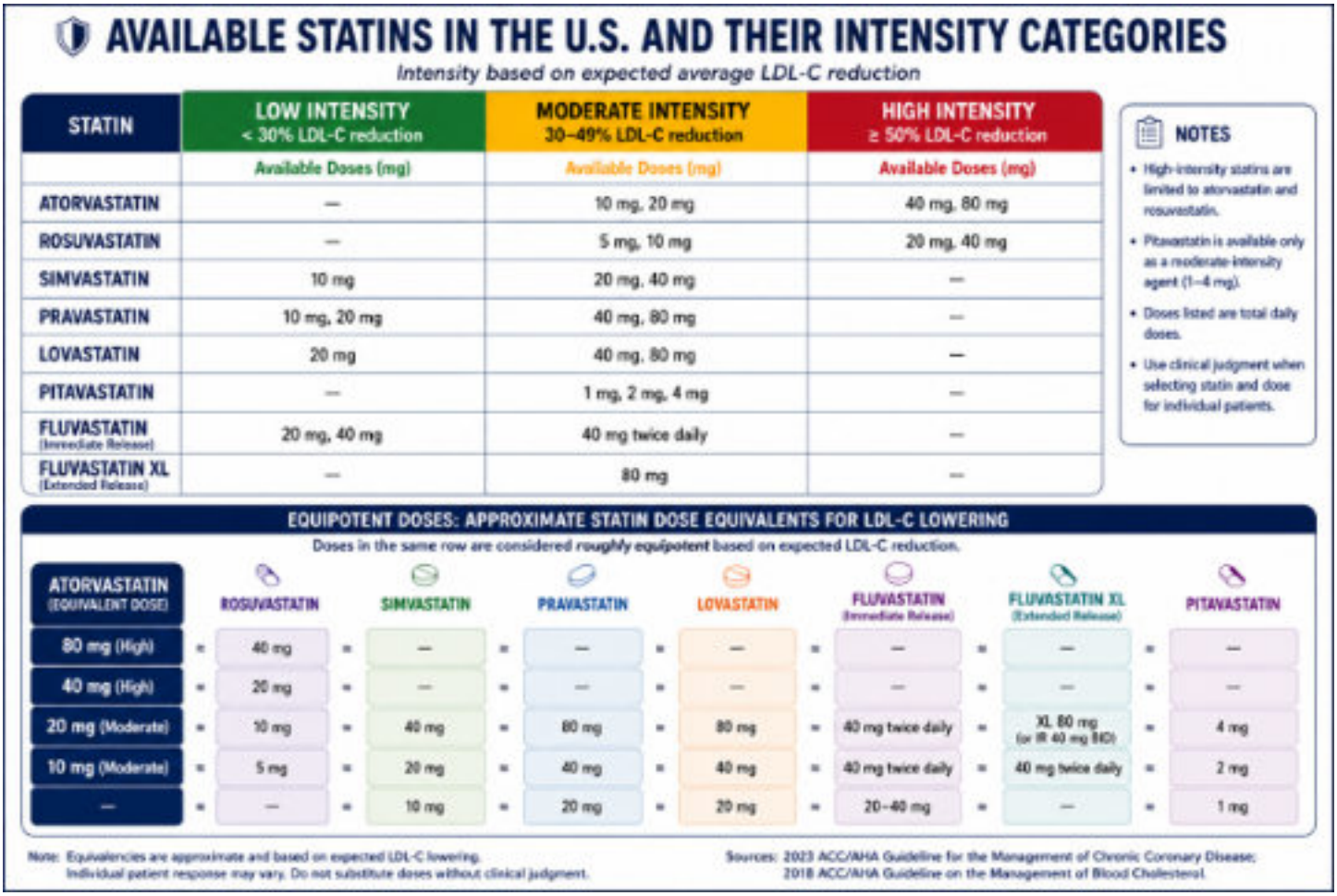
Multimodal lifestyle modifications are the backbone of any lipid-lowering regimen, and prescribers should initiate them in all patients who meet the criteria for intervention.[3] Dietary modifications emphasize consumption of fruits, vegetables, legumes, whole grains, fiber, and foods with low saturated fats and high mono- and poly-unsaturated fats. To examine the optimal diet to lower LDL, researchers compared the Mediterranean diet to a vegan diet.[26] At 16 weeks, patients on a vegan diet decreased their LDL by an average of 15 mg/dL, while the Mediterranean diet failed to show a statistically significant decrease. These data are limited by small sample size—only 62 participants—so more data is needed.[26] However, many patients prefer diets that include meat and meat products, rendering vegan diets unsustainable. Any nutritional intervention that lowers LDL and weight is beneficial, provided patients adhere to the diet indefinitely. When coupled with other lifestyle modifications, dietary modifications can lower LDL and reduce the risk of developing ASCVD. Triglyceride-lowering diets decrease added sugars, refined carbohydrates, saturated fats, and alcohol—these modifications can lower TG levels by over 70%.[27]

Weight loss significantly decreases LDL and TG levels as well. A meta-analysis of 73 randomized controlled trials with more than 32,000 participants discovered that for every kilogram (2.2 pounds) of weight lost, LDL decreases by up to 1.3 mg/dL and TG levels decrease by 4 mg/dL.[28] The AHA recommends 150 minutes or more of moderate- to high-intensity aerobic exercise with resistance training to reduce the likelihood of cardiovascular events.[3] A meta-analysis conducted by the AHA demonstrated that weekly moderate-intensity exercise decreased the risk of cardiovascular mortality by 23%.[29] The analysis followed 3.4 million patients over 12 years, and found that 150 minutes of moderate-intensity aerobic exercise per week yielded a mortality benefit and a 17% decrease in new cardiovascular disease. Combining interventions can drastically lower LDL levels and, rarely, eliminate the need to initiate LLT altogether.[29]

Lipid-Lowering Medications—Statins

Medications augment lifestyle modifications when lifestyle modifications fail to decrease cholesterol below accepted thresholds. Statins are the backbone of LLT due to their robust ability to decrease LDL.[6] Low-, moderate-, and high-intensity statins decrease patients' LDL values by 30%, 30-49%, and 50% or more, respectively. **Figure 2** depicts statin intensity categories, available drugs, and equipotent statin doses.[30]

Figure 2. Statin Intensity Classifications and Equipotent Daily Doses



Statins reduce LDL by competitively inhibiting the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase enzyme, the rate-limiting enzyme in hepatic cholesterol synthesis.[31] Statin-induced enzyme inhibition decreases hepatic cholesterol synthesis, meaning less LDL circulates throughout the body. After the initial LDL reduction achieved with the starting dose, each subsequent statin dose doubling lowers LDL by an additional 6% to 8%.[32] Statins also decrease inflammation through antioxidant properties and stimulate the immune system. The liver primarily metabolizes statins. The liver cytochrome P450 (CYP) 3A4 enzyme metabolizes atorvastatin, simvastatin, and lovastatin, whereas CYP2C9 metabolizes fluvastatin and rosuvastatin to a lesser extent. Statins are eliminated through both hepatic and renal pathways, although the extent of renal excretion varies by agent. Therefore, statin dose adjustments may be necessary in patients with liver or kidney impairment. Statins are contraindicated in patients with active liver disease. Simvastatin is strictly contraindicated with CYP3A4 strong inhibitors, and has a maximum daily dose of 10 mg with diltiazem, verapamil, and dronedarone.[33] The maximum simvastatin daily dose for patients taking amiodarone, amlodipine, and ranolazine is 20 mg. Technician recognition of new drug interactions is crucial to prevent adverse effects and decreased efficacy. Pharmacy technicians can identify new statin drug interactions by reviewing medication profiles, recognizing interaction alerts, and promptly notifying pharmacists of suspected interactions to prevent adverse effects. Clinicians should dose adjust statins in patients taking CYP enzyme inducers or inhibitors.

Common Strong CYP3A4 inhibitors include:

- Ritonavir
- Itraconazole
- Ketoconazole
- Cobicistat
- Grapefruit Juice

Common Strong CYP3A4 and CYP2C9 inducers include:

- Rifampin
- Carbamazepine
- Phenytoin
- Phenobarbital

Common Strong CYP2C9 inhibitors include:

- Sulfamethoxazole/Trimethoprim
- Amiodarone
- Fluconazole

Statin-associated muscle symptoms (SAMS) are the most commonly reported adverse effects associated with statin therapy.[31] SAMS manifests as muscle aches, pain, and soreness primarily in the larger muscle groups of the body—the thighs, hips, and shoulders. High statin doses, advanced age, decreased thyroid function, diabetes, fibromyalgia, and CKD contribute to a patient's risk of developing SAMS. The incidence of SAMS increases greatly with concurrent fibrates, which are medications that reduce high TGs. Gemfibrozil is contraindicated with some statins (e.g., simvastatin) and should generally be avoided because it increases the risk of SAMS. [34]

As noted above, strong evidence suggests that most muscle symptoms are not attributable to statins.[35] Authors of a meta-analysis of 19 trials and 35,000 patients concluded that up to 90% of muscle symptoms attributed to statin therapy were not due to the medication.[31] Instead, underlying conditions and advanced age played a large role in the misinterpretation. To classify a patient as statin intolerant, clinicians should rechallenge with at least two statins at the lowest approved dose.[35] Additionally, switching from statins that are highly lipid-soluble like atorvastatin and simvastatin to a highly water-soluble statin like rosuvastatin could decrease muscle symptoms, but data are inconsistent.[36] When initiating statins, clinicians should inform patients that the risk of statin-associated adverse effects is small and the cardiovascular benefits far outweigh the negative aspects of the medication. If patients experience severe muscle symptoms, creatine kinase measurements should be taken to rule out rare, life-threatening muscle breakdown like rhabdomyolysis.[31]

Other rare adverse effects include mild nausea, diarrhea, or constipation, and small increases in blood sugar.[31] Advising patients to take the medication with food and in the evening alleviates stomach discomfort. For statins with shorter half-lives (simvastatin and lovastatin), evening administration is traditionally recommended because hepatic cholesterol synthesis is greatest overnight. However, statins with longer half-lives, such as atorvastatin, and rosuvastatin maintain therapeutic activity throughout the day and may be taken at any time. Figure 3 summarizes statin administration instructions and counseling.

The prescriber discusses doubling Nick's rosuvastatin dose to 10 mg. George points out that rosuvastatin 5 mg and 10 mg are both moderate-intensity doses, and because Nick's LDL remains above his goal, his dose should be increased to a high-intensity dose. George recommends increasing to rosuvastatin 20 mg, granted Nick agrees with the plan and has no contraindications. George also recommends obtaining a repeat lipid panel in 4 to 12 weeks to monitor adherence and response.

Nonstatin Lipid-Lowering Medications

A staple of oral nonstatin therapy, ezetimibe (Zetia) does not decrease cholesterol synthesis—instead, it inhibits intestinal absorption of dietary cholesterol by blocking the Niemann-Pick C1-Like-1 (NPC1L1) transporter. [37] Ezetimibe decreases LDL levels by 13% to 20%, making it a useful adjunct to statin therapy, or as monotherapy for less intensive lipid lowering.[37] Prescribers should not use ezetimibe in people who have moderate and severe hepatic impairment, but the medication is generally well tolerated. Limited adverse effects include headache, congestion, and sore throat—a rarity for the majority of patients.

For patients who require drastic reductions in LDL with or without statin therapy, subcutaneous proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor injections decrease LDL-C by 45-65%.[3] The medication blocks PCSK9 enzymatic activity, raising levels of LDL-receptors in the body, allowing the liver to remove more LDL from the bloodstream. When the ACC/AHA published cholesterol guidelines in 2018, clinicians lacked sufficient evidence to determine the long-term effects of the monoclonal antibody PCSK9 inhibitors evolocumab (Repatha) and alirocumab (Praluent).[6] Today, more recent studies demonstrate that evolocumab and alirocumab significantly reduce heart attack, stroke, and cardiovascular death over a five-year period.[38],[39] Injected into the abdomen, thigh, or upper buttock once every few weeks, these medications offer less frequent dosing than any other lipid-lowering medication. Patients rarely experience significant adverse effects; injection-site reactions and hypersensitivity reactions occur most frequently.[40]

Additionally, the 2018 AHA/ACC cholesterol guidelines did not include inclisiran (Leqvio), a novel small-interfering RNA PCSK9 inhibitor that blocks production of the PCSK9 protein in the liver.[6] The Lancet Diabetes & Endocrinology published data demonstrating the twice-yearly injection provided sustained LDL reductions and medication tolerability in patients over a four-year period.[41] The updated 2026 AHA/ACC guidelines recommend inclisiran as an alternative to monoclonal antibody PCSK9 inhibitors, but high cost and absence of completed cardiovascular outcome evidence are barriers for initiation. [3] Another difference between inclisiran and the monoclonal antibody PCSK9 inhibitors evolocumab and alirocumab is that a healthcare professional must administer inclisiran. For patients who want less frequent administration or prefer not to inject their medication themselves, inclisiran is a useful alternative.

PCSK9 inhibitors excel in older adults. Researchers at the Erasmus MC Cardiovascular Institute concluded that patients older than

Figure 3. Lipid-Lowering Therapy Quick Guide[3]

LIPID-LOWERING THERAPIES: *QUICK* STORAGE & ADMINISTRATION GUIDE

THERAPY	STORAGE	SHELF LIFE (Unopened / Once Opened)	WHERE TO ADMINISTER	COUNSELING POINTS
PCSK9 INHIBITORS (evolocumab, alirocumab) 	Refrigerate (36°F to 46°F / 2°C to 8°C). Do not freeze.	**Unopened:** 18–24 months (varies by product; see labeling) **Once opened:** 28 days Store in the refrigerator or at room temperature (up to 77°F / 25°C). Discard after 28 days.	Subcutaneous (SC) injection in:  Abdomen, thigh, or upper arm	• Allow to come to room temperature for 30–60 minutes before injection for more comfortable administration. • Inject subcutaneously as directed. • Rotate injection sites (abdomen, thigh, or upper arm). • Dispose of used pens/syringes in a sharps container.
INCLISIRAN (Leqvio®) 	Refrigerate (36°F to 46°F / 2°C to 8°C). Do not freeze.	**Unopened:** 24 months **Once opened:** Do not store once opened. Use immediately and discard any unused portion.	Subcutaneous (SC) injection in:  Abdomen	• Administered by a healthcare professional. • Dosage: at baseline, at 3 months, then every 6 months. • Report any injection site reactions.
STATINS (e.g., atorvastatin, rosuvastatin, simvastatin) 	Room temperature (68°F to 77°F / 20°C to 25°C). Keep away from excess heat and moisture.	**Unopened:** See labeling (oral tablets) **Once opened:** See labeling (oral tablets)	Oral  By mouth with or without food	• Take exactly as prescribed (time of day may vary). • Report unexplained muscle pain, tenderness, or weakness. • Do not take if pregnant; use effective contraception.
EZETIMIBE (Zetia®) 	Room temperature (68°F to 77°F / 20°C to 25°C). Keep away from excess heat and moisture.	**Unopened:** 2–3 years (varies by product; see labeling) **Once opened:** See labeling (oral tablets)	Oral  By mouth with or without food	• Take once daily with or without food. • Report any unusual muscle pain or dark urine. • Do not take if pregnant; use effective contraception.
BEMPEDOIC ACID (Nexletol®) 	Room temperature (68°F to 77°F / 20°C to 25°C). Keep away from excess heat and moisture.	**Unopened:** See labeling (oral tablets) **Once opened:** See labeling (oral tablets)	Oral  By mouth with or without food	• Take once daily with or without food. • Report unexplained muscle pain or weakness. • Do not take if pregnant; use effective contraception.
BILE ACID SEQUESTRANTS (cholestyramine, colestipol, colesevelam)  TABLET FORMS AVAILABLE: COLESEVELAM & COLESTIPOL	Room temperature (68°F to 77°F / 20°C to 25°C). Keep away from excess heat and moisture.	**Unopened:** 2–3 years (varies by product; see labeling) **Once opened:** See labeling (powder – use as directed; other forms – see labeling)	Oral  Powder mixed with water/juice	• Mix powder with water/juice as directed; take other forms with a full glass of water. • Take other medications 1 hour before or 4–6 hours after to avoid interference with absorption. • Common side effects: constipation, bloating, gas.

Always follow the specific product labeling and your healthcare provider's instructions.

Note: Shelf life may vary by manufacturer. Check packaging for exact dates.

70 taking evolocumab and alirocumab had medication safety and efficacy profiles similar to those under 70.[42]

In July 2026, the FDA approved the first oral PCSK9 inhibitor, enlicitide (Lipfendra), but the guidelines do not address the medication because it received approval after they were published.[43] Decreasing LDL by 56% over 24 weeks, the medication has similar efficacy to injectable PCSK9 inhibitors, but is roughly half the out-of-pocket cost of injectables at $315 per month.[44] PCSK9-targeting therapies have demonstrated efficacy in lowering LDL-C regardless of formulation, including injectable monoclonal antibodies, injectable small interfering RNA (siRNA), and oral agents.

Clinicians can confidently prescribe PCSK9 inhibitors or ezetimibe as an adjunct or alternative to traditional statin therapy due to their robust reductions in LDL and low adverse effect profile.

The 2026 AHA/ACC guidelines added bempedoic acid (Nexletol), an adenosine triphosphate citrate lyase (ACL) inhibitor, as an alternative for statin-intolerant patients, or an alternative medication.[45] Bempedoic acid acts two enzymatic steps upstream from statins and reduces LDL by around 20%.[46] However, bempedoic acid is metabolized via glucuronidation and not a CYP enzyme, but data regarding dose adjustments is limited. Adverse effects include cold or flu-like symptoms, muscle spasms, back and stomach pain. In CLEAR Outcomes, which enrolled 13,970 statin-intolerant patients, bempedoic acid reduced the relative risk of major adverse cardiovascular events by 13% over a median follow-up of 40.6 months. The trial included patients at high risk for ASCVD or with established ASCVD who reported being unable or unwilling to receive statins due to adverse effects. After treatment with bempedoic acid, LDL values dropped from an average of 139 mg/dL to 107 mg/dL, a 30 mg/dL decrease compared to placebo.[45] Bempedoic acid is also available with ezetimibe as a once-daily fixed-dose combination tablet (Nexlizet; bempedoic acid 180 mg/ezetimibe 10 mg).[47]

Finally, bile acid sequestrants—colesevelam, colestipol, and cholestyramine—are members of a lipid-lowering medication class that decreases LDL without being systemically absorbed, making them a viable option for pregnant patients.[3] At full doses, they lower LDL by 15% to 30%.[48] Gastrointestinal adverse effects like nausea, vomiting, constipation, and bloating prevent some patients from reaching higher doses. Bile acid sequestrants should generally be avoided with TG levels above 300 mg/dL, but contraindications vary by agent. Dosage formulations may also contribute to intolerance. All three available agents come as oral powders for suspension which some patients describe as having a chalky texture or bitter aftertaste. However, colesevelam and colestipol have tablet formulations. Patients with partial biliary obstruction and those who are pregnant or planning to become pregnant may benefit from this medication class. However, more effective therapies are preferred for most other patients.

Administration instructions, storage, and patient counseling points can be found in **Figure 3** (on the previous page).

Triglyceride Lowering Medications

Statins remain the foundation for TG-lowering therapy.[3] While fibrates, niacin, and prescription-strength omega-3 fatty acids have been shown to reduce TG levels, they fail to reduce the risk of cardiovascular events and ASCVD.[49] The Reduction of Cardiovascular Events With Icosapent Ethyl–Intervention Trial (REDUCE-IT) trial demonstrates that icosapent ethyl (Vascepa) is beneficial in certain patient populations with high TG but normal LDL.[50] In patients with TG levels surpassing 1,000 mg/dL, the apolipoprotein C-III (apoC-III) inhibitor reduces TG levels and the risk for pancreatitis by 63%.[51]

Eight weeks later, Nick reports no adverse effects from rosuvastatin 20 mg daily. His repeat LDL has decreased to 78 mg/dL—closer to his goal but still above 70 mg/dL. The prescriber calls George again to ask what the next steps should be. George tells the prescriber that because Nick only needs modest additional LDL lowering, ezetimibe 10 mg is warranted. Ezetimibe is a once-daily pill that can be taken at the same time as Nick's statin, is generally well-tolerated, and can lower LDL-C by an additional 13% to 20%.

PAUSE and PONDER: If a patient who has an LDL of 53 mg/dL on a moderate-intensity statin has had a heart attack, is a high-intensity statin warranted?

Lipid-Lowering Therapy Treatment Algorithm

With defined lipid targets, initiating or optimizing LLT is crucial to reduce patients' risk for ASCVD.

For patients without established ASCVD and an LDL of 70 to 189, the 2026 AHA/ACC guidelines recommend using the PREVENT scoring system to estimate ASCVD risk.[3] The guidelines

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recommend initiating a statin in patients with an intermediate risk (5%) or above, while those with borderline risk (3% to less than 5%) should engage in shared decision-making with their clinician regarding treatment initiation. The guidelines support moderate-intensity statin initiation in intermediate risk patients, with high-intensity statins indicated in higher risk patients. Unlike previous guidelines, which emphasized percent LDL reduction from baseline, the 2026 recommendations incorporate individualized LDL targets.[6] If maximally tolerated statin therapy fails to reduce a patient's LDL target, additional therapy—ezetimibe or a PCSK9 inhibitor—is necessary to reduce all-cause mortality and CV events.[52],[53],[54] Bempedoic acid is a possible alternative, but ezetimibe and PCSK9 inhibitors alongside statins provide greater LDL reductions and are better tolerated.[3]

The 2026 AHA/ACC cholesterol guidelines recommend initiation or titration to a high-intensity statin for all patients with established ASCVD, regardless of comorbidities, risk factors, or baseline LDL.[3] As previously discussed, if patients remain above the LDL goal of 55 mg/dL, clinicians should add ezetimibe, a PCSK9 inhibitor, or bempedoic acid.[3]

Age and PREVENT score guide statin therapy for patients with diabetes who do not have established ASCVD.[3] The 2026 AHA/ACC guidelines recommend initiating at least a moderate-intensity statin, regardless of PREVENT score or LDL. For patients aged 30 to 39 years with PREVENT scores greater than 3%, clinicians should discuss cardiovascular risk reduction before considering moderate-intensity statin therapy. Beyond 75 years old, clinicians should engage in benefit-risk discussions with patients regarding statin therapy.[3]

Several lipid-lowering medications should be avoided in pregnant patients or patients who wish to become pregnant. Technician and pharmacist recognition of potentially harmful medications to the fetus, known as teratogens, is vital to prevent birth defects, premature births, and fetal harm. Because lipid management goals change with each trimester, lifestyle management is the safest option and can effectively manage high LDL and TG levels throughout pregnancy.[3] Women should stop statins one to two months before attempting to become pregnant or as soon as pregnancy is discovered. Some studies suggest statins decrease birth weights, and increase the risk of preterm birth, eclampsia, and preeclampsia.[55],[56] Newer data suggests that statin exposure during pregnancy is not associated with major fetal defects, and that spontaneous abortion rates could reflect other confounding factors like maternal comorbidities.[56]


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More data is needed to make definitive conclusions, but in 2021 the FDA revised statin warnings, indicating high-risk pregnant patients with established ASCVD could continue statin therapy when appropriate.[57] Statins should still be avoided when breastfeeding. Clinicians should continue statin therapy only after conducting an individualized risk assessment and engaging in shared decision-making with the patient. Limited evidence for alternative lipid-lowering therapies leaves bile acid sequestrants (BAS) as the only evidence-based medication class for cholesterol reduction during pregnancy because they are not systemically absorbed.[3] Unfortunately, BAS can impair fat-soluble vitamins (vitamin A, D, E, K) and folic acid, which can impact the fetus, maternal health and milk production.[58] To address TG levels above 500 mg/dL, fibrates and prescription-strength omega-three ethyl esters (DHA and EPA) can be initiated after the first trimester.[59]

Dialysis status determines the optimal lipid-lowering therapy for patients with chronic kidney disease (CKD).[3] Guidelines support primary prevention with a moderate-intensity statin with or without ezetimibe for patients 40 to 75 years old with an LDL of 70 to 189 mg/dL for patients not on dialysis. In contrast, statins have not demonstrated cardiovascular outcome benefits in patients receiving dialysis.[60]

Finally, patients with human immunodeficiency virus (HIV) are at heightened risk for ASCVD, particularly heart attack.[61] Moderate-intensity statins reduce ASCVD risk in this population. However, many antiretroviral medications strongly inhibit CYP3A4, requiring clinicians to monitor for drug interactions and statin-related adverse effects.

The 2026 AHA/ACC triglyceride recommendations remain mostly unchanged from the 2018 guidelines.[3],[6] LDL management through LLT decreases TG levels concurrently. In most cases, adequate LDL control and lifestyle management maintain healthy TG levels below 150 mg/dL. One major difference is the inclusion of icosapent ethyl (Vascepa) in the 2026 guidelines. The REDUCE-IT trial observed the effect icosapent ethyl had on patients with established ASCVD or diabetes with risk factors for ASCVD. Patients' TG levels were between 135 and 499 mg/dL and LDL-C values between 41 and 100 mg/dL.[50] When added to prior statin therapy, twice-daily icosapent ethyl reduced the relative risk of major cardiovascular events by over 20%. The medication also decreased TG levels by 40 mg/dL. So, clinicians can add icosapent ethyl in patients with diabetes and ASCVD risk factors or with established ASCVD already on statin therapy with high

SIDEBAR: Do patients with heart failure require lipid-lowering therapy? [3,63,64,65]

Heart failure alone is not an indication to initiate statin therapy. Irrespective of ejection fraction, the 2026 AHA/ACC guidelines quantify heart failure as a high-risk cardiovascular condition. Several conditions add to the progression of heart failure, with coronary artery disease being a major contributor. Coronary atherosclerosis restricts blood flow to the heart, increasing the risk of myocardial infarction. The resulting loss of viable cardiac cells triggers compensatory overactivation of the remaining healthy tissue, progressively impairing cardiac function and contributing to the development of heart failure. Lipid-lowering therapy may reduce heart failure-related hospitalizations in some patients with heart failure. However, without another indication for LLT, statins do not reduce sudden cardiac death and major cardiovascular events.

triglycerides. In patients with TG levels exceeding 500 mg/dL or familial chylomicronemia syndrome, olezarsen is indicated to reduce the risk of pancreatitis.[62] Other TG-lowering therapies remain last line and are not recommended in the 2026 guidelines.[3]

Whether preventing or managing ASCVD, clinicians must individualize lipid goals and consider special populations to reduce cardiovascular events and mortality.[3]

Ten weeks after adding ezetimibe, Nick's LDL is 65 mg/dL. He reports remaining adherent to his medications and has no new adverse effects. George recommends continuing the regimen and reinforces smoking cessation and lifestyle modifications. The prescriber thanks George for the assessment, as Nick has reached his LDL goals without unnecessary testing or premature initiation of costly injectable medications.

Optimizing Access to New Lipid-Lowering Therapy

The cost of new lipid-lowering medications can prevent patients from receiving guideline-directed treatment. Out-of-pocket costs for bempedoic acid and PCSK9 inhibitors can exceed $700 and $500 per month, respectively.[66],[67],[68] Inclisiran presents additional coverage challenges because healthcare professionals must administer it in a clinical setting. Patients in low socioeconomic groups can struggle to achieve recommended lipid goals due to cost. Even insured patients frequently encounter stringent prior authorization requirements.[69] Insurers frequently require medical records, specialist evaluation, and step-therapy requirements with statins before approving PCSK9 inhibitors or bempedoic acid.

Pharmacists and pharmacy technicians can increase medication access by helping patients reduce financial barriers. Many manufacturers offer copay cards that reduce out-of-pocket costs for privately insured patients.[70] Some manufacturers also provide patient assistance programs that offer free or reduced-price medications.[71],[72] These programs often require income documentation and provider approval. Evolocumab's manufacturer, Amgen, even offers patients a one-time, one-month free trial of evolocumab.[73] Coverage for these medications can reduce monthly costs to as little as $50 per month.

Additionally, Medicare Part D has an annual out-of-pocket spending cap of $2,100, meaning covered lipid-lowering therapies cost patients little or nothing after the cap is reached.[74] Pharmacists and technicians should familiarize themselves with available assistance programs and insurance requirements to identify eligibility and serve patients better. These resources improve medication access, boost adherence, and help patients achieve guideline-directed cholesterol goals to reduce ASCVD risk.

CONCLUSION

The update to the 2026 AHA/ACC Cholesterol Management Guidelines offers new guidance to clinicians on how to optimize lipid-lowering interventions to achieve individualized cholesterol targets. The guidelines equip pharmacists to calculate 10-year ASCVD risk, personalize patients' estimated risk using the PREVENT-ASCVD equation, reclassify risk with coronary artery calcium, and reassess treatment success. As newer lipid-lowering therapies are incorporated into standard practice, pharmacists should understand the updated treatment algorithm to improve medication selection and reduce ASCVD events. Pharmacy technicians can enhance patient care through recognition of potential drug interactions, identification of adverse effects, and improvement of medication access.

Figure 4 can help pharmacy teams excel at lipid management.

Figure 4. Putting Lipid Management into Practice: Good, Better, Best

Best

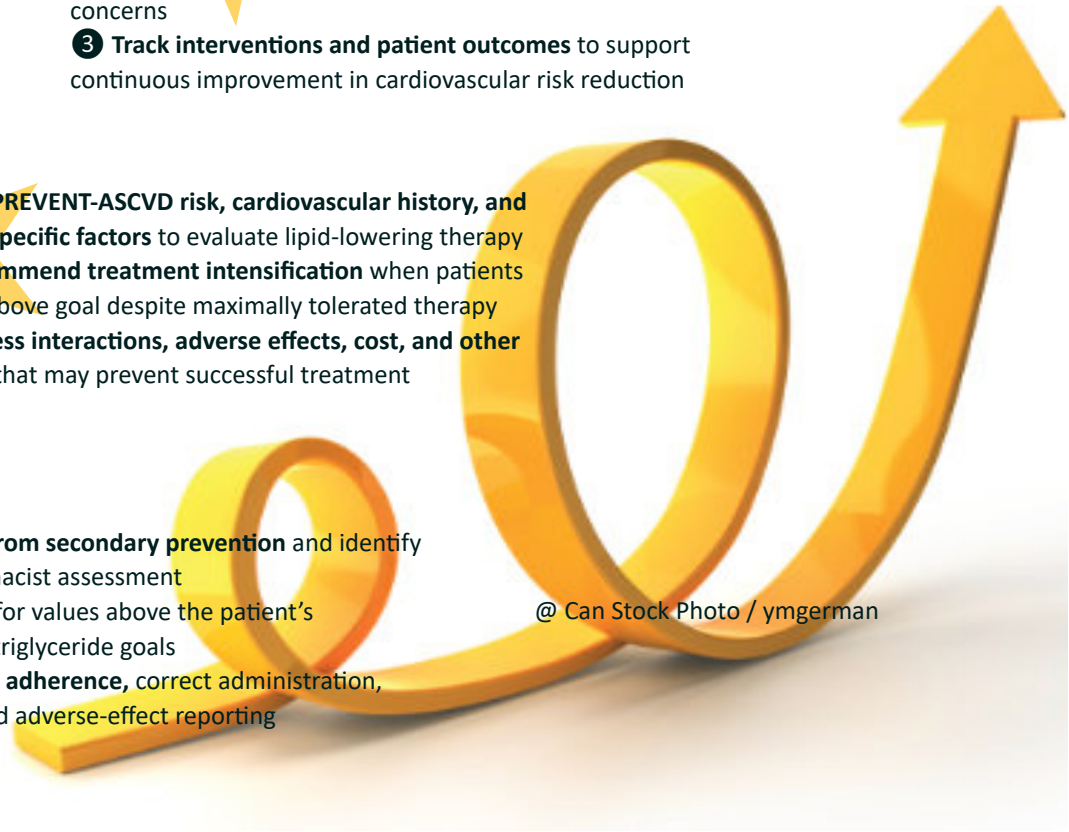
1. **Be COMMUNITY CHAMPIONS** and Collaborate with prescribers to optimize therapy, monitoring, adherence, and access to lipid-lowering medications
2. **Establish pharmacy workflows** to identify patients with uncontrolled lipids, overdue monitoring, or treatment-related concerns
3. **Track interventions and patient outcomes** to support continuous improvement in cardiovascular risk reduction

Better

1. **Use PREVENT-ASCVD risk, cardiovascular history, and patient-specific factors** to evaluate lipid-lowering therapy
2. **Recommend treatment intensification** when patients remain above goal despite maximally tolerated therapy
3. **Address interactions, adverse effects, cost, and other barriers** that may prevent successful treatment

Good

1. **Distinguish primary from secondary prevention** and identify patients who need pharmacist assessment
2. **Review lipid profiles** for values above the patient's individualized LDL-C and triglyceride goals
3. **Reinforce medication adherence,** correct administration, storage requirements, and adverse-effect reporting



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