



Cardiovascular

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For the full version of the 2018 Cholesterol Guideline, see

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published online November 10, 2018]. *Circulation*.



Introduction

The "2018 Guideline on the Management of Blood Cholesterol" presents new guidelines to give healthcare providers consistent, clear, and evidence-based guidance for treating patients at risk for atherosclerotic cardiovascular disease (ASCVD).

The 2018 guideline covers risk assessment, primary and secondary prevention of ASCVD, lifestyle interventions, statin therapy, and nonstatin alternatives and adjuncts. To help clinicians bring the guidelines into clinical practice, we've created several resources focused on risk assessment and cholesterol management recommendations for primary and secondary prevention for those with elevated risk or high cholesterol levels, including printable tools to help you

- Assess patients' risk for ASCVD and the use of tools such as the <u>ASCVD Risk Calculator</u>
- Understand when and how to prescribe and manage statins and nonstatin therapies
- Discuss a patient's ASCVD risks as well as options for treatment
- Overcome common barriers to treatment

Key Points

- Use evidence-based tools such as the ASCVD Risk Calculator to identify patients at elevated risk who
 might benefit from treatment.
- Consider a patient's blood cholesterol level, a main modifiable risk factor, along with other health and lifestyle factors when assessing and calculating ASCVD risk.
- Statins are the first-line agents used to decrease cholesterol and reduce the risk of ASCVD events.
- Statin therapy is safe when used properly and monitored.
- Engage patients in the discussion before initiating statin therapy and lifestyle changes.
- Start with the appropriate intensity of statin therapy to reduce ASCVD risk, and regularly monitor patients for adherence to lifestyle changes and appropriate intensity of statin therapy.
- Evidence does not support treating to a specific LDL-C or non-HDL-C target.
- If a patient has problems taking a statin, or if a statin alone does not sufficiently lower cholesterol, consider a nonstatin drug therapy in combination or as monotherapy in selected individuals.



The 2018 guideline emphasizes the lifetime risk of unmanaged high cholesterol and the importance of primary and secondary prevention strategies to reduce a patient's risk of future ASCVD.







Top 10

Take-Home Messages to Reduce Risk of ASCVD Through Lipid Management

- 1. In all individuals, emphasize a heart-healthy lifestyle across the life course. A healthy lifestyle reduces atherosclerotic cardiovascular disease (ASCVD) risk at all ages. In younger individuals, healthy lifestyle can reduce development of risk factors and is the foundation of ASCVD risk reduction. In young adults 20 to 39 years of age, an assessment of lifetime risk facilitates the clinician-patient risk discussion (see No. 6) and emphasizes intensive lifestyle efforts. In all age groups, lifestyle therapy is the primary intervention for metabolic syndrome.
- 2. In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statins or maximally tolerated statins to decrease ASCVD risk. Greater LDL-C reductions on statin therapy, leading to lower LDL-C levels, lower subsequent risk; use a maximally tolerated statin to reduce LDL-C levels by ≥50%.
- 3. In very high-risk ASCVD, use an LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of nonstatins to statins. In very high-risk ASCVD patients, it is reasonable to add ezetimibe to maximally tolerated statin therapy when the LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L). In patients at very high risk whose LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L) on maximally tolerated statin and ezetimibe therapy, adding a proprotein convertase subtilisin/kexin type (PCSK9) inhibitor is reasonable, although the long-term safety (>3 years) is uncertain and cost-effectiveness is low at mid-2018 list prices.
- 4. In patients with severe primary hypercholesterolemia (LDL-C level ≥190 mg/dL [≥4.9 mmol/L]), without calculating 10-year ASCVD risk, begin high-intensity statin therapy. If the LDL-C level remains ≥100 mg/dL (≥2.6 mmol/L), adding ezetimibe is reasonable. If the LDL-C level on statin plus ezetimibe remains ≥100 mg/dL (≥2.6 mmol/L) and the patient has multiple factors that increase subsequent risk of ASCVD events, a PCSK9 inhibitor may be considered, although the long-term safety (>3 years) is uncertain and economic value is low at mid-2018 list prices.
- 5. In patients 40 to 75 years of age with diabetes mellitus and an LDL-C level of ≥70 mg/dL (≥1.8 mmol/L), start moderate-intensity statins without calculating 10-year ASCVD risk. In patients with diabetes mellitus at higher risk, especially those with multiple risk factors or those 50 to 75 years of age, it is reasonable to use a high-intensity statin to reduce the LDL-C level by ≥50%.
- **6.** In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician-patient risk discussion before starting statin therapy. Risk discussion should include a review of major risk factors (eg, cigarette smoking, elevated blood pressure, LDL-C, hemoglobin A1C [if indicated], and calculated 10-year risk of ASCVD); the presence of risk-enhancing factors (see No. 8); the potential benefits of lifestyle and statin therapies; the potential for adverse effects and drug-drug interactions; consideration of costs of statin therapy; and patient preferences and values in shared decision-making.







- 7. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL (≥1.8 mmol/L) at a 10-year ASCVD risk of ≥7.5%, start a moderate-intensity statin if a discussion of treatment options favors statin therapy. Risk-enhancing factors favor statin therapy (see No. 8). If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see No. 9). If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.
- 8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 5% to 19.9%, risk-enhancing factors favor initiation of statin therapy (see No. 7). Risk-enhancing factors include family history of premature ASCVD; persistently elevated LDL-C levels ≥160 mg/dL (≥4.1 mmol/L); metabolic syndrome; chronic kidney disease; history of preeclampsia or premature menopause (age <40 years); chronic inflammatory disorders (eg, rheumatoid arthritis, psoriasis, or chronic HIV); high-risk ethnic groups (eg, South Asian); persistent elevations of triglycerides ≥175 mg/dL (≥1.97 mmol/L); and, if measured in selected individuals, apolipoprotein B ≥130 mg/dL (≥2500 nmol/L), high-sensitivity C-reactive protein 2.0 mg/L (190 nmol/L), ankle brachial index <0.9, and lipoprotein (a) ≥50 mg/dL (125 nmol/L), especially at higher values of lipoprotein (a).
- 9. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 to 189 mg/dL (≥1.8 to 4.9 mmol/L), at a 10-year ASCVD risk of ≥7.5% to 19.9%, if a decision about statin therapy is uncertain, consider measuring CAC. If CAC is zero, treatment with statin therapy may be withheld or delayed, except in cigarette smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD. A CAC score of 1 to 99 favors statin therapy, especially in those >55 years of age. For any patient, if the CAC score is ≥100 Agatston units or ≥75th percentile, statin therapy is indicated unless otherwise deferred by the outcome of clinician-patient risk discussion.
- 10. Assess adherence and percentage response to LDL-C-lowering medications and lifestyle changes with repeat lipid measurement 4 to 12 weeks after statin initiation or dose adjustment, repeated every 3 to 12 months as needed. Define responses to lifestyle and statin therapy by percentage reductions in LDL-C levels compared with baseline. In ASCVD patients at very high risk, triggers for adding nonstatin drugs are defined by threshold LDL-C levels ≥70 mg/dL (≥1.8 mmol/L) on maximal statin therapy (see No. 3).





Highlights of the 2018 Guideline on the Management of Blood Cholesterol

Importance of Cholesterol Management

The "2018 Guideline on the Management of Blood Cholesterol" is an update to the 2013 guideline on diagnosing, treating, and monitoring high cholesterol.

Fifty-six million (48.6%) US adults over 40 years of age are eligible for statin therapy on the basis of the 2013 guideline for managing blood cholesterol from the American College of Cardiology and the American Heart Association. This is significant when you consider that having a high level of low-density lipoprotein cholesterol (LDL-C) is a major risk factor for atherosclerotic cardiovascular disease (ASCVD). Because LDL-C contributes to fatty buildups and narrowing of the arteries (atherosclerosis), it's often called the "bad" cholesterol, and in fact, high LDL-C at any age can cumulatively increase the risk for heart disease and stroke.

While there is no *ideal* target blood level for LDL-C, the 2018 guideline recognizes, in principle, that "lower is better." Studies suggest that an optimal total cholesterol level is about 150 mg/dL, with LDL-C at or below 100 mg/dL, and adults with LDL-C in this level have lower rates of heart disease and stroke.

Risk Assessment

The 2018 guideline recommends that healthcare providers conduct a detailed risk assessment with their patients through an ASCVD risk calculator (static.heart.org/riskcalc/app/index.html#!/baseline-risk), which providers can use to discuss risks and treatment options with patients. A consumer-facing risk calculator is available as well at www.heart.org/ccccalculator. This calculator combines all major risk factors to estimate a patient's probability for developing ASCVD. Risk factors include smoking, high blood pressure, abnormal cholesterol, and diabetes. Because atherosclerosis progresses over a lifetime, age counts as a risk factor, too. When the ASCVD risk status is uncertain, a coronary artery calcium test may clarify risk for patients aged 40 to 75, and it may also help decide whether to start or restart statin therapy.

Along with traditional cardiovascular disease risk factors like smoking, high blood pressure, high cholesterol, and high blood sugar, the guideline now calls for further review in some people aged 40 to 75 of **risk-enhancing factors** such as family history and other health conditions. The presence or absence of risk-enhancing factors in this age group without diabetes and 10-year risk of 7.5% to 19.9% can help further determine whether patients should start or intensify statin therapy.

Patients with extremely high LDL-C (190 mg/dL or more) or other conditions that can increase their ASCVD risk, and those who have been diagnosed with cardiovascular disease, need immediate intervention with high-intensity statins to manage their cholesterol without further risk assessment.

The 2018 guideline also recognizes the importance of identifying and managing high LDL-C in children, adolescents, and young adults to reduce their lifetime exposure to the health effects of high cholesterol. Most children can reduce their lifetime ASCVD risk by practicing healthier lifestyles. In some cases, high cholesterol in children can point to a genetic issue like familial hypercholesteremia, prompting screening of family members to identify those who are at increased risk.

Primary Prevention

The 2018 guideline recommends that for adults 20 years or older who are free from ASCVD (and not on lipid-lowering therapy), measure LDL-C with either a fasting or nonfasting plasma lipid profile when estimating ASCVD risk, and document baseline LDL-C. For adults 20 years or older who have an initial nonfasting lipid profile with triglycerides 400 mg/dL or higher, repeat the lipid profile with the patient fasting to establish fasting triglyceride levels and baseline LDL-C.



As with children, most patients can reduce their lifetime ASCVD risk through healthier lifestyle practices. Encourage patients to reduce their caloric intake of saturated fat and dietary cholesterol and to eliminate trans fat completely. In addition to these dietary changes, patients should strive for an average of 30 minutes of moderate to vigorous physical activity 5 times per week. But even moderate amounts of activity can reduce risk for patients who achieve this goal, and patients with metabolic syndrome may also benefit from physical activity.

When lifestyle interventions alone are not enough to lower LDL-C, statins generally provide the most effective lipid-lowering treatment. There are 3 main treatment regimens for statins:

- High intensity, which typically lowers LDL-C by 50% or more
- Moderate intensity, which lowers LDL-C by 30% to 49%
- Low intensity, which lowers LDL-C by 30% or less

Use a stepwise approach to manage high cholesterol, adding therapies as tolerated until the cholesterol levels are lowered adequately. If a patient has problems taking a statin or if a statin alone doesn't sufficiently lower LDL-C, additional drug options are available. Adding a bile acid sequestrant or ezetimibe to a statin regimen further lowers LDL-C, by approximately 15% to 30% and 13% to 20%, respectively. And adding a PCSK9 inhibitor to a statin regimen has been shown to further reduce LDL-C by 43% to 64%.

Patients with extremely high LDL-C (190 mg/dL or higher) have a high lifetime risk for a cardiovascular event. For patients aged 20 to 75, providers should prescribe a maximally tolerated statin.

Adults **aged 40 to 75 who have diabetes** are usually considered at moderate to high risk for cardiovascular disease. The guideline recommends moderate-intensity statins, regardless of the patient's estimated 10-year risk for ASCVD (Figure 1).

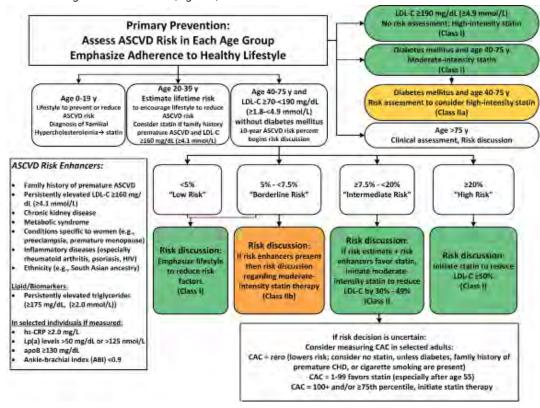


Figure 1. Primary prevention.

Abbreviations: apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; $LP(\alpha)$, lipoprotein (α).

Secondary Prevention

For patients who have had a serious cardiovascular incident or procedure, secondary prevention may reduce the risk of another event. Providers should use an ideal LDL-C threshold of less than 70 mg/dL when considering adding ezetimibe and PCSK9 inhibitors to an existing statin therapy (Figure 2).

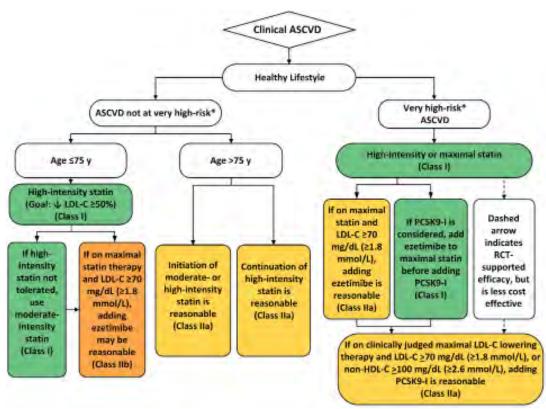


Figure 2. Secondary prevention.

Abbreviations: ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCSK9i, PCSK9 inhibitor. *Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.

Monitoring

Once patients begin a treatment plan, providers should reassess at 4 to 12 weeks with a fasting or non-fasting lipid test and check for statin intolerance, and retest every 3 to 12 months if needed. Using the percentage reduction in LDL-C (rather than total cholesterol) in follow-up monitoring of patients can help you estimate how well the statin medication is working.

Lowering LDL-C levels by 1% generally equals about 1% reduction in heart disease and stroke risk, but the effect can be even greater when starting with higher baseline levels of LDL-C. On the basis of several large studies, it's estimated that reducing LDL-C levels with statins by about 38.7 mg/dL can reduce heart disease and stroke risk by about 21%, based on the results of several large studies.



Implementing the 2018 Guideline Recommendations

When initiating treatment plans and before prescribing therapy, providers should

- Allow patients to ask questions and express concerns and preferences about their ability and likelihood to follow and stick to the lifestyle and medication plan
- Emphasize the potential for lowering the patient's cardiovascular disease risk
- Discuss any possible drug interactions and adverse effects
- Address issues that factor into, or may become a barrier to, a shared-decision plan, such as costs and the patient's overall health

The 2018 guideline recommends offering options such as phone and calendar reminders, educational activities, and simplified medication doses to help patients stick to their treatment plans. The 2018 guideline also includes considerations for special populations in the United States:

- Racial/ethnic groups (Section 4.5.1)
- Women (Section 4.5.3)
- People with diabetes mellitus (Section 4.3)
- People with chronic kidney disease (Section 4.5.4)
- People with chronic inflammatory conditions/HIV (Section 4.5.5)
- Older adults (Section 4.4.4.1)
- People with hypertriglyceridemia (Section 4.5.2)





Lipoproteins

Low-density lipoprotein cholesterol (LDL-C) is a primary cause of atherosclerosis, but cigarette smoking, hypertension, dysglycemia, other lipoprotein abnormalities, and advancing age can contribute as well. By combining major risk factors into a prediction equation, you can estimate a person's probability of developing atherosclerotic cardiovascular disease (ASCVD). Because fasting and nonfasting total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels have fairly similar prognostic value and associations with cardiovascular disease outcomes, the "2018 Guideline on the Management of Blood Cholesterol" recommends measuring either a fasting or a nonfasting plasma lipid profile to estimate ASCVD risk and document baseline LDL-C in adults who are 20 years or older and not on lipid-lowering therapy (Figure 3).

In adults 20 years or older with an initial nonfasting lipid profile triglycerides level of ≥400 mg/dL (≥4.5 mmol/L), repeat a lipid profile in the fasting state to assess fasting triglyceride levels and baseline LDL-C.

For patients with an LDL-C level <70 mg/dL (<1.8 mmol/L), measurement of direct LDL-C or modified LDL-C estimate is reasonable to improve accuracy over the Friedewald formula.

In adults 20 years or older with no personal history of ASCVD but a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable to help understand and identify familial lipid disorders.

Figure 3. Recommendations for measuring LDL-C and non-HDL-C.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Lipoproteins and ASCVD Risk

Serum cholesterol and its lipoprotein carriers (LDL, very low-density lipoprotein [VLDL], and HDL) are related to ASCVD. LDL-C is the dominant form of atherogenic cholesterol. VLDL is the chief carrier of triglycerides, and VLDL cholesterol is atherogenic while HDL-C is seemingly nonatherogenic. Chylomicrons transport dietary fat; chylomicron atherogenicity is uncertain.

US population studies suggest that optimal total cholesterol levels are about 150 mg/dL (3.8 mmol/L), corresponding to an LDL-C level of about 100 mg/dL (2.6 mmol/L). Confirming the general principle that "lower is better," randomized controlled trials of cholesterol-lowering drugs in high-risk patients show that reducing LDL-C reduces instances of ASCVD. Generally, lowering LDL-C levels by 1% gives an approximate 1% reduction in the risk of ASCVD.



For easy and useful tools to help identify patients at risk for heart attack and stroke who might benefit from preventive treatment, see the American Heart Association's <u>ASCVD Risk Calculator</u> and the patient-facing <u>Check. Change. Control. Calculator</u>[™].





Ten-Year ASCVD Risk

In adults without ASCVD, assess traditional ASCVD risk factors every 4 to 6 years, and assess lifetime ASCVD risk for adults younger than 40 years and consider adding a statin medication to lifestyle changes if the patient's LDL-C levels are higher than 160 mg/dL or if the patient has a family history of early cardiovascular disease. Note that adults aged 40 to 75 years may receive statin therapy, but selecting patients for this therapy is a multistep process. The first step is to categorize patients into 4 categories of risk. One of the categories includes adults 40 to 75 years of age whose 10-year ASCVD risk is estimated by using the pooled cohort equations. The 10-year risk for ASCVD is categorized as low risk (<5%), borderline risk (5% to <7.5%), intermediate risk (≥7.5% to <20%), and high risk (≥20%) (Figure 4). Once you determine your patient's risk level, talk with your patient about his or her risk level and specific risk factors, adherence to a healthy lifestyle, the potential for cardiovascular disease risk-reduction benefits, and the potential for adverse effects and drug-drug interactions, as well as the patient's personal preferences for a treatment decision.

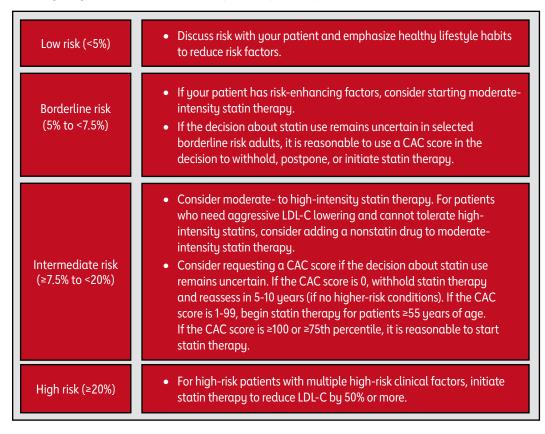


Figure 4. Ten-year ASCVD risk categories and interventions to include in a risk discussion with patients.

Abbreviations: CAC, coronary artery calcium; LDL-C, low-density lipoprotein cholesterol.

In addition to the 10-year risk assessment, other risk-enhancing factors can increase risk of atherosclerotic disease and should be discussed with patients to help guide treatment decision-making.



Risk-Enhancing Factors

- Family history of early ASCVD (men, aged <55 years; women, aged <65 years)
- Current high cholesterol (LDL-C, 160-189 mg/dL [4.1-4.8 mmol/L]; non-HDL-C, 190-219 mg/dL [4.9-5.6 mmol/L])
- Metabolic syndrome
- Chronic kidney disease
- Chronic inflammatory conditions (eg, rheumatoid arthritis, psoriasis, or HIV/AIDS)
- History of preeclampsia or early menopause (before 40 years of age)
- High-risk ethnicity (eg, South Asian ancestry)
- High lipid biomarkers
 - Triglycerides 175 mg/dL or greater
 - High-sensitivity C-reactive protein 2.0 mg/dL or greater
 - Elevated lipoprotein (a) 50 mg/dL or greater or 125 nmol/L or greater
 - Elevated apolipoprotein B 130 mg/dL or greater
 - Ankle-brachial index less than 0.9

Other Considerations

The 2018 guideline includes considerations for special populations in the United States:

- Racial/ethnic groups (Section 4.5.1)
- Women (Section 4.5.3)
- People with diabetes (Section 4.3)
- People with chronic kidney disease (Section 4.5.4)
- People with chronic inflammatory conditions/HIV (Section 4.5.5)
- Older adults (Section 4.4.4.1)
- People with hypertriglyceridemia (Section 4.5.2)



The AHA's <u>Go Red For Women® movement</u> encourages awareness of heart disease in women and actions to save more lives.







Primary Prevention

Across Your Patients' Life Course

Atherosclerosis begins in young adulthood and progresses to atherosclerotic cardiovascular disease (ASCVD) in middle age or later, so you can help your patients reduce the risk of ASCVD by preventing or managing risk factors early in life. For instance, young adults who rapidly develop atherosclerosis usually have multiple risk factors, such as hypercholesterolemia, hypertension, cigarette smoking, diabetes mellitus, and obesity. The "2018 Guideline on the Management of Blood Cholesterol" recommends that most of these patients can reduce their lifetime ASCVD risk through healthier lifestyle practices, and only select patients with moderately high low-density lipoprotein cholesterol (LDL-C) (≥160 mg/dL) or those with very high LDL-C levels (≥190 mg/dL [≥4.9 mmol/L]) need drug therapy.

Risk-Enhancing Factors

For primary prevention, choose appropriate treatment interventions that are based on your patient's age and health status (Figure 5).

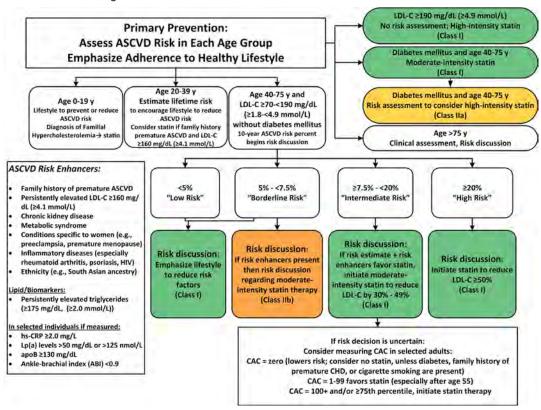


Figure 5. Primary prevention.

Abbreviations: apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a).

Children and Adolescents (10-19 Years of Age)

For children and adolescents, promote healthy lifestyle practices to prevent or reduce ASCVD risk.

- In patients without cardiovascular risk factors or family history of early cardiovascular disease, you may measure a fasting lipid profile or nonfasting non-HDL-C once between the ages of 9 and 11 years, and again between the ages of 17 and 21 years, to detect lipid abnormalities (Table 1).
- In obese patients or those with other metabolic risk factors, measure a fasting lipid profile to detect lipid disorders. Encourage your patients with obesity-related lipid disorders to reduce their caloric intake and increase their aerobic activity.
- In patients with a family history of early cardiovascular disease or significant hypercholesterolemia, you may measure a lipoprotein profile when the patient is as young as 2 years old to detect familial hypercholesterolemia (FH) or rare forms of hypercholesterolemia. In those with moderate or severe hypercholesterolemia, screen relatives to identify those with hypercholesterolemia. If patients 10 years or older have an LDL-C level persistently 190 mg/dL (4.9 mmol/L) or higher, or 160 mg/dL (4.1 mmol/L) or higher with FH, and they don't respond adequately to lifestyle therapy within 6 months, start statin therapy.

Table 1. Normal and Abnormal Lipid Values in Childhood*†

	Acceptable, mg/dL (mmol/L)	Borderline, mg/dL (mmol/L)	Abnormal, mg/dL (mmol/L)
TC	<170 (<4.3)	170-199 (4.3-5.1)	≥200 (≥5.1)
Triglycerides, 0-9 y	<75 (<0.8)	75-99 (0.8-1.1)	≥100 (≥1.1)
Triglycerides, 10-19 y	<90 (<1.0)	90-129 (1.0-1.5)	≥130 (≥1.4)
HDL-C	>45 (>1.2)	40-45 (1.0-1.2)	<40 (<1.0)
LDL-C	<110 (<2.8)	110-129 (2.8-3.3)	≥130 (≥3.4)
Non-HDL-C	<120 (<3.1)	120-144 (3.1-3.7)	≥145 (≥3.7)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NCEP, National Cholesterol Education Program: TC, total cholesterol.

*Values for plasma lipid and lipoprotein levels are from the NCEP Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cutpoints for LDL-C.

†The cutpoints for high and borderline high represent approximately the 95th and 75th percentiles, respectively. Low cutpoints for HDL-C represent approximately the 10th percentile.



Patient Discussion Tip

See Figure 8 in Your Patient Is Your Partner section of this guide for specific topics to discuss with your patients about ASCVD risk assessment, lifestyle modifications, and more.





Young Adults (20-39 Years of Age)

Even moderate hypercholesterolemia can lead to atherosclerosis, so encourage young adults to make lifestyle changes that reduce their risk for hyperlipidemia and associated ASCVD. Along with lifestyle changes, young adults with primary elevations of LDL-C 190 mg/dL or greater may take statins. Stress to young adults that prolonged hyperlipidemia before age 55 increases their risk of coronary heart disease significantly. In addition, an elevated LDL-C that persists after you've excluded secondary causes suggests FH, so perform cascade screening to identify other affected family members.

Adults (40-75 Years of Age)

Three major high-risk categories for adults are severe hypercholesterolemia, diabetes, and ages 40 to 75 years.

- For patients with severe hypercholesterolemia (LDL-C levels ≥190 mg/dL [4.9 mmol/L]), begin immediate statin therapy.
- Start adults with diabetes on a moderate-intensity statin, and as they develop multiple risk factors, move up to a high-intensity statin.
- Use the 10-year ASCVD risk to guide your therapeutic considerations for other adults because those
 with higher estimated ASCVD risk are more likely to benefit from statin treatment. In addition,
 consider several "risk enhancers" that you can use to initiate or intensify statin therapy. If you can't
 determine risk or you find problems with statin therapy, measure coronary artery calcium (CAC) to
 refine risk assessment.

Older Adults (Older Than 75 Years)

In older adults with an LDL-C level of 70 to 189 mg/dL (1.7-4.8 mmol/L), you may initiate a moderate-intensity statin. However, statin therapy may be stopped when the patient's physical or cognitive functional decline, multimorbidity, frailty, or reduced life expectancy limit the potential benefits. In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7-4.8 mmol/L), measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.



You should also address secondary causes of hypercholesterolemia, including hypothyroidism, obstructive liver disease, renal disease, and nephrosis, as well as dietary and medication history.





Secondary Prevention

For patients who have had a serious cardiovascular incident or procedure, secondary prevention may reduce the risk of another event. You have several considerations to make based on your patient's condition (Figure 6).

The clinical diagnosis of atherosclerotic cardiovascular disease (ASCVD) includes

- Acute coronary syndrome (ACS)
- Myocardial infarction, also known as a heart attack
- Stable or unstable angina or other arterial revascularization
- Stroke and transient ischemic attack
- Peripheral artery disease, including aortic aneurysm, all of atherosclerotic origin

For patients with clinical ASCVD, the "2018 Guideline on the Management of Blood Cholesterol" recommends beginning high-intensity statin therapy. But if your patient cannot tolerate the initial prescription, consider a different dose or statin instead. Note that patients with ASCVD who are older than 75 years may experience adverse effects with statins, so weigh potential benefits against adverse effects before initiating statin therapy. Your first goal is to reduce low-density lipoprotein cholesterol (LDL-C) by 50% or more in all patients with ASCVD, but if LDL-C levels remain 70 mg/dL or greater (≥1.8 mmol/L) despite maximally tolerated statin therapy, consider adding ezetimibe therapy to the regimen. In patients with heart failure due to ischemic heart diseases, consider moderate-intensity statins.

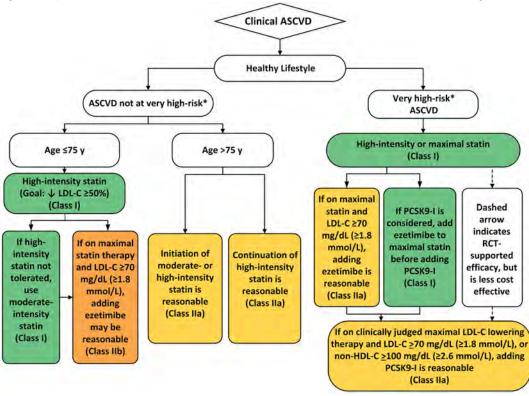


Figure 6. Secondary prevention.

Abbreviations: ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCSK9-I, PCSK9 inhibitor. *Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.



Very High Risk of ASCVD Events

In very high-risk patients with multiple high-risk clinical factors, ezetimibe can be added to maximally tolerated statin therapy. Furthermore, if LDL-C levels remain 70 mg/dL or greater (≥1.8 mmol/L), adding a PCSK9 inhibitor is reasonable if the cost/benefit ratio is favorable. Very high-risk conditions include a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions. Major ASCVD events include

- ACS within the past 12 months
- History of myocardial infarction (other than the recent ACS event previously listed) or ischemic stroke
- Symptomatic peripheral artery disease (history of claudication with ankle-brachial index less than 0.85, or previous revascularization or amputation)

High-risk conditions include

- Aged 65 years or older
- Heterozygous familial hypercholesterolemia
- History of previous coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD events
- Diabetes mellitus
- Hypertension
- Chronic kidney disease (estimated glomerular filtration rate 15-59 mL/min per 1.73 m²)
- Current smoking
- Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
- History of congestive heart failure

Severe Hypercholesterolemia (LDL-C ≥190 mg/dL)

Because patients with severe hypercholesterolemia have a high lifetime risk, they don't require ASCVD risk scoring before you initiate high-intensity statins. Statin randomized controlled trials have demonstrated greater risk reduction with statins than with placebo and greater reduction from higher-intensity statin therapy than with moderate-intensity statin therapy.

Additional Medications and Treatment Options

However, if statins alone are insufficient, you may try additional treatment options. Adding ezetimibe to a moderate-intensity statin reduces LDL-C more than statin monotherapy. The addition of PCSK9 inhibitors can further reduce LDL-C levels. Bile acid sequestrants have also been shown to lower LDL-C; however, there are limitations with these medications, including twice-daily dosing, high pill burden, the absence of well-tolerated generic formulations, drug interactions, and the potential for triglyceride elevation. Finally, LDL apheresis is an option in select patients with severe hypercholesterolemia whose LDL-C is inadequately controlled with drug therapy. Refer to a lipid specialist if necessary. In addition, in children and adolescents with severe hypercholesterolemia, you may conduct reverse-cascade screening of family members to detect familial hypercholesterolemia.



Patient Discussion Tip

Before adding a PCSK9 inhibitor to a statin and ezetimibe regimen, discuss the net benefit, safety, and cost with your patient.





Cholesterol and Comorbidities

Metabolic Syndrome

Metabolic syndrome is a cluster of risk factors that increase the risk of atherosclerotic cardiovascular disease (ASCVD), diabetes mellitus, and all-cause death. You can diagnose metabolic syndrome in a patient if any 3 of the risk factors shown in Figure 7 are present.

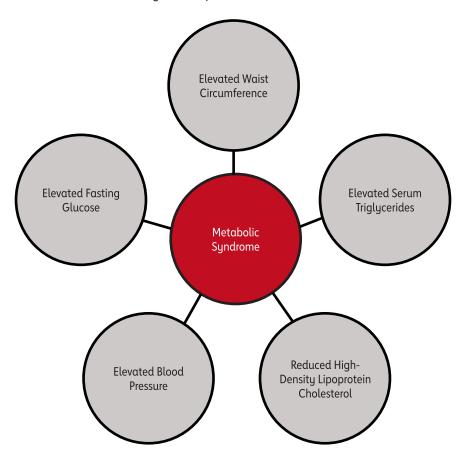


Figure 7. Risk factors for metabolic syndrome.

Diabetes Mellitus

Although most adults 40 to 75 years of age with diabetes mellitus are at intermediate or high risk of their first ASCVD event, evaluating ASCVD risk will help refine risk estimates and therapeutic decision-making. In adults with diabetes mellitus and a 10-year ASCVD risk of 20% or higher, adding ezetimibe to maximally tolerated statin therapy may be considered to reduce low-density lipoprotein cholesterol (LDL-C) levels by 50% or more.







Adults 20 to 39 Years of Age With Diabetes Mellitus

Consider initiating moderate-intensity statin therapy in adults 20 to 39 years of age who have had type 2 diabetes mellitus for at least 10 years or type 1 diabetes mellitus for at least 20 years and with patients with 1 or more major cardiovascular disease risk factors or complications, such as

- Albuminuria (≥30 mcg of albumin/mg creatinine)
- Estimated glomerular filtration rate less than 60 mL/min per 1.73 m²
- Retinopathy
- Neuropathy
- Ankle brachial index less than 0.9

Adults 40 to 75 Years of Age With Diabetes Mellitus

Regardless of estimated 10-year ASCVD risk, start moderate-intensity statin therapy for adults with diabetes mellitus who are 40 to 75 years of age. In these patients with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7-4.8 mmol/L), assess the 10-year risk of a first ASCVD event by using the race- and sex-specific pooled cohort equations to help stratify ASCVD risk. In adults with diabetes mellitus who have multiple ASCVD risk factors, high-intensity statin therapy is preferred to reduce LDL-C levels by 50% or more.

Adults Older Than 75 Years

In adults with diabetes mellitus who are older than 75 years, statin therapy may be considered after discussing the potential benefits and risks with your patient. But if the patient is already on statins, it is reasonable to continue on statin therapy.

Hypertriglyceridemia

Elevated triglyceride categories consist of moderate hypertriglyceridemia (fasting or nonfasting triglycerides 175 to 499 mg/dL [1.9-5.6 mmol/L]) and severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.6 mmol/L]). The "2018 Guideline on the Management of Blood Cholesterol" recommends the following for patients with hypertriglyceridemia:

- In adults 20 years or older with moderate hypertriglyceridemia, address and treat lifestyle factors, secondary factors, and medications that increase triglycerides.
- In adults 40 to 75 years of age with moderate or severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, address lifestyle and secondary factors, reevaluate ASCVD risk, and consider initiating or intensifying statin therapy.
- In adults 40 to 75 years of age with severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, it is reasonable to address reversible causes of high triglycerides and begin statin therapy.
- In adults with severe hypertriglyceridemia, and especially those with fasting triglycerides 1000 mg/dL or higher (≥11.3 mmol/L), identifying and addressing other causes of hypertriglyceridemia is beneficial. If triglycerides remain elevated or increase, encourage patients to implement a verylow-fat diet, eliminate refined carbohydrates and alcohol, and add omega-3 fatty acids. In addition, if necessary to prevent acute pancreatitis, start patients on fibrate therapy.





Heart Failure

In patients with heart failure due to ischemic heart disease, moderate-intensity statins may be considered.

Chronic Kidney Disease

In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7-4.8 mmol/L) who have a 10-year ASCVD risk of 7.5% or higher, chronic kidney disease that is not treated with dialysis or kidney transplantation is a risk-enhancing factor. Moderate-intensity statin therapy or a combination with ezetimibe can be useful. In adults who need dialysis for advanced kidney disease and are currently receiving statin therapy, continue the statin. However, if an adult needs dialysis for kidney disease and is not already on a statin, do not initiate statin therapy.

Adults With Chronic Inflammatory Disorders and HIV

Because chronic inflammatory disorders and HIV infection are also risk-enhancing factors, first focus on helping patients with chronic inflammatory disorders or HIV to optimize their lifestyle habits. In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7-4.8 mmol/L) who have a 10-year ASCVD risk of 7.5% or higher and who have these conditions, begin moderate-intensity statin therapy or high-intensity statin therapy. In patients with chronic inflammatory disorders or HIV, measuring a fasting lipid profile and assessing ASCVD risk factors can be useful as a guide to statin therapy benefit and for monitoring or adjusting lipid-lowering drug therapy before and 4 to 12 weeks after starting inflammatory disease-modifying therapy or antiretroviral therapy. In adults with rheumatoid arthritis who undergo ASCVD risk assessment with measurement of a lipid profile, it can be useful to recheck lipid values and other major ASCVD risk factors 2 to 4 months after the patient's inflammatory disease has been controlled. If you or your patient are uncertain about the need for statin therapy, or if the patient has previously had adverse effects with a statin, consider a coronary artery calcium scan to determine risk. Patients with no coronary artery calcium are at a very low risk of an ASCVD event over the next decade, so they can delay statin therapy and instead focus on healthy lifestyle habits.





Your Patient Is Your Partner

Building a Successful Treatment Plan

A successful cholesterol treatment plan is one that your patients will follow. The "2018 Guideline on the Management of Blood Cholesterol" emphasizes discussing any plan with your patients first to improve their chances of successfully starting and continuing guideline-directed management and therapy. During your discussion, include the patient's atherosclerotic cardiovascular disease (ASCVD) risk, lifestyle habits and modifications, the potential benefits of pharmacotherapy, and cost, and ask patients for ways they can successfully contribute to their own treatment (Figure 8). Remember that your patients are key players in their therapy, so encourage them to ask questions, express their own values and preferences, discuss adverse effects and drug-drug interactions, and honestly assess their ability to pay for treatment and adhere to new lifestyle changes before you prescribe a specific therapy.

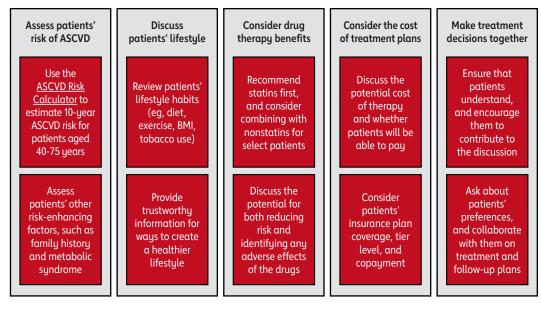


Figure 8. Work with your patients to develop a successful treatment plan.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index.

Here are a few tips to help patients follow their treatment plans:

- Ask specific questions about how well they're adhering to their prescribed therapy.
- Aim for once-daily dosing.
- Use automated reminders.
- Participate in multidisciplinary educational activities.
- Use pharmacist-led interventions.



Implementing the Guideline

We face many challenges in delivering quality healthcare to our patients, and these challenges can result in guidelines that, while crucial to patient health, are not always effectively implemented. By adopting multifaceted strategies that include patients, clinicians, the patients' health plans, and the health system, generally, you can overcome the barriers to fully implementing guidelines for care. You can help by identifying patients who are not receiving guideline-directed therapy and initiating the appropriate treatment plan—health plans and health systems should do the same. Additionally, using multiple interventions can help ensure that patients can better follow guideline-directed treatment plans.

Addressing Challenges

Barriers to implementing the guideline can happen at the patient, clinician, health system, and health plan level, which can lead to gaps in care. Open discussions are critical to successfully starting and continuing guideline-directed management and therapy, and patients should feel free to ask questions and to express their concerns and preferences about whether they can follow the treatment plan, including any cost factors.

If patients have problems taking statins, or if a statin alone isn't lowering their low-density lipoprotein cholesterol enough, you have some additional drug options. Drugs called *ezetimibe* and *PCSK9 inhibitors* can be used in addition to statins for some patients with very high low-density lipoprotein cholesterol. The 2018 guideline recommends a stepped approach: generally, you should give patients statins first, and then give them ezetimibe if you need to further lower their cholesterol. Prescribe PCSK9 inhibitors only for those who are not responding as desired to the combination of statins and ezetimibe.





Medications

Statins

Before initiating statin therapy, talk about the benefits and risks with your patients. Help them weigh the potential for reducing the risk of atherosclerotic cardiovascular disease (ASCVD) against the potential for statin-associated side effects, statin-drug interactions, and safety while reassuring them that side effects can occur but can be addressed successfully.

Statin therapy can be high, moderate, or low intensity. High-intensity statins typically reduce low-density lipoprotein cholesterol (LDL-C) levels by 50% or more while moderate-intensity statins reduce LDL-C by 30% to 49% and low-intensity statins reduce LDL-C by less than 30%, as shown in Table 2 in this guide (for more information on the specific statins, doses, and randomized controlled trials reviewed, see Table 3 in the "2018 Guideline on the Management of Blood Cholesterol").

Table 2. High-, Moderate-, and Low-Intensity Statin Therapy

High Intensity	Moderate Intensity	Low Intensity
Lowers LDL-C by ≥50%	Lowers LDL-C by 30%-49%	Lowers LDL-C by <30%
Atorvastatin (40 mg) 80 mg	Atorvastatin 10 mg (20 mg)	Simvastatin 10 mg
Rosuvastatin 20 mg (40 mg)	Rosuvastatin (5 mg) 10 mg	Pravastatin 10-20 mg
	Simvastatin 20-40 mg	Lovastatin 20 mg
	Pravastatin 40 mg (80 mg)	Fluvastatin 20-40 mg
	Lovastatin 40 mg (80 mg)	
	Fluvastatin XL 80 mg	
	Fluvastatin 40 mg BID	
	Pitavastatin 1-4 mg	

Abbreviation: LDL-C, low-density lipoprotein cholesterol.

Boldface type indicates specific statins and doses that were evaluated in randomized controlled trials and the Cholesterol Treatment Trialists' 2010 meta-analysis. All these randomized controlled trials demonstrated a reduction in major cardiovascular events. Nonbold type indicates statins and doses that have been approved by the FDA but were not tested in the RCTs reviewed.

Lowering LDL-C levels by 1% generally equals about 1% reduction in heart disease and stroke risk, but it can be higher when starting out with higher baseline levels of LDL-C. When beginning or changing medications, test levels at 4 to 12 weeks and retest every 3 to 12 months if needed. In follow-up monitoring of patients, use the percentage reduction in LDL-C rather than total cholesterol to estimate how well the statin medication is working.





Statin-Associated Side Effects

Statin therapy is usually well tolerated and safe, but as with other classes of medications, statins can have associated side effects. The 2018 guideline prefers the term *statin-associated side effects* to *statin intolerance*. Most patients can tolerate an alternative statin or regimen, such as reducing the dose or combining with nonstatins.

During follow-up and monitoring, assess the patient's response to statins, emphasize the need for adherence, and reaffirm the benefit. Assess statin-associated side effects comprehensively and optimize patient-centered strategies for ASCVD prevention. Some patients may experience myalgia, which, in the absence of other symptoms, is more likely to be statin associated if the following is true (see Table 11 in the 2018 guideline for more details):

- It is bilateral
- It involves proximal muscles
- It starts within weeks to months after the patient begins taking statins
- It resolves after discontinuation of statins

Statins are reasonable when indicated for patients at increased ASCVD risk with chronic, stable liver disease (including nonalcoholic fatty liver disease). Obtain baseline measurements first and determine a schedule of monitoring and safety checks. Routine measurements of creatine kinase and transaminase levels are not useful tests for patients taking statins.

Nonstatins

Along with healthy lifestyle interventions, statins are the cornerstone of therapy for lowering LDL-C, but other nonstatin medications (ezetimibe, bile acid sequestrants, and PCSK9 inhibitors) can also be effective in combination with statin therapy:

- **Ezetimibe** is the most commonly used nonstatin agent. It lowers LDL-C levels by 13% to 20% and has a low incidence of side effects.
- Bile acid sequestrants reduce LDL-C levels by 15% to 30% depending on the dose. Bile acid sequestrants are not absorbed and do not cause systemic side effects, but they are associated with gastrointestinal complaints such as constipation and can cause severe hypertriglyceridemia when fasting triglycerides are ≥300 mg/dL (≥3.4 mmol/L).
- PCSK9 inhibitors are powerful LDL-lowering drugs. They generally are well tolerated, but long-term
 safety remains to be proven. Studies showed that the addition of a PCSK9 inhibitor to a statin regimen
 further reduced LDL-C levels by 43% to 64%. PCSK9 inhibitors are currently more expensive than other
 cholesterol-lowering drugs, and the cost value may be beneficial only for a very specific group of
 people for whom other treatments haven't worked.
- Niacin and fibrates may also mildly lower LDL-C levels in patients with normal triglycerides. They
 may be useful in some patients with severe hypertriglyceridemia, but research doesn't support their
 use as add-on drugs to statin therapy.







Lifestyle Therapies

Healthy Diet

The American Heart Association and the American College of Cardiology have long recommended a healthy diet for not only patients who are at risk for atherosclerotic cardiovascular disease (ASCVD) but also the general public. In keeping with this evidence-based recommendation, the "2018 Guideline on the Management of Blood Cholesterol" stresses that a healthy diet should include adequate intake of these essentials:

- Vegetables, fruits, and whole grains
- Legumes and nuts
- Low-fat dairy products
- Low-fat poultry (without the skin)
- Fish and seafood
- Nontropical vegetable oils

The 2018 guideline does provide room for cultural food preferences in a healthy diet, but in general, all patients should limit their intake of saturated and trans fats, sweets, sugar-sweetened beverages, and red meats.

Physical Activity

In addition to a healthy diet, all patients should include regular physical activity in their weekly routines, at moderate to vigorous intensity. Any activity is better than nothing, so if your patients can't meet the recommendation of vigorous activity, moderate-intensity activity can still help them reduce their risk of ASCVD.

Below are the American Heart Association's recommendations for physical activity *per week* (preferably spread throughout the week):

For Overall Cardiovascular Health and Lowering Cholesterol

- At least 150 minutes of moderate-intensity physical activity (for example, 30 minutes, 5 days a week),
 or
- At least 75 minutes of vigorous-intensity physical activity (for example, 25 minutes, 3 days a week); or
- A combination of moderate- and vigorous-intensity aerobic activity, and
- At least 2 days of moderate- to high-intensity muscle-strengthening activities (such as resistance weight training) for additional health benefits





Weight Control

It's important to work with patients to help them reach and maintain a healthy weight (Table 3). You may need to suggest that they adjust their caloric intake to avoid weight gain or, in overweight and obese patients, to promote weight loss.

Table 3. Body Mass Index

Height	Normal, BMI Under 25	Overweight, BMI 25-29.9	Obese, BMI 30 and Above
4′10″	≤118 lb	119-142 lb	≥143 lb
4'11"	≤123 lb	124-147 lb	≥148 lb
5′0″	≤127 lb	128-152 lb	≥153 lb
5′1″	≤131 lb	132-157 lb	≥158 lb
5′2″	≤135 lb	136-163 lb	≥164 lb
5′3″	≤140 lb	141-168 lb	≥169 lb
5'4"	≤144 lb	145-173 lb	≥174 lb
5′5″	≤149 lb	150-179 lb	≥180 lb
5'6"	≤154 lb	155-185 lb	≥186 lb
5′7″	≤158 lb	159-190 lb	≥191 lb
5′8″	≤163 lb	164-196 lb	≥197 lb
5′9″	≤168 lb	169-202 lb	≥203 lb
5′10″	≤173 lb	174-208 lb	≥209 lb
5′11″	≤178 lb	179-214 lb	≥215 lb
6′0″	≤183 lb	184-220 lb	≥221 lb
6′1″	≤188 lb	189-226 lb	≥227 lb
6'2"	≤193 lb	194-232 lb	≥233 lb
6'3"	≤199 lb	200-239 lb	≥240 lb
6'4"	≤204 lb	205-245 lb	≥246 lb

Abbreviation: BMI, body mass index.



Patient Discussion Tip

Use Table 3 in this guide to help identify your patient's body mass index, or use this <u>calculator</u> from the National Heart, Lung, and Blood Institute. Then, discuss any weight-control strategies with your patient as needed.





Additional Resources

Below are links to some additional publications about many of the topics covered in the "2018 Guideline on the Management of Blood Cholesterol."

Lifestyle Management

2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk

2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

Medical Training to Achieve Competency in Lifestyle Counseling: An Essential Foundation for Prevention and Treatment of Cardiovascular Diseases and Other Chronic Medical Conditions:

A Scientific Statement From the American Heart Association

Sleep Duration and Quality: Impact on Lifestyle Behaviors and Cardiometabolic Health:

A Scientific Statement From the American Heart Association

Healthy Diet

<u>Dietary Diversity: Implications for Obesity Prevention in Adult Populations:</u>

A Science Advisory From the American Heart Association

<u>Seafood Long-Chain n-3 Polyunsaturated Fatty Acids and Cardiovascular Disease:</u>

A Science Advisory From the American Heart Association

Medical Nutrition Education, Training, and Competencies to Advance Guideline-Based Diet Counseling by Physicians: A Science Advisory From the American Heart Association

Recommended Dietary Pattern to Achieve Adherence to the American Heart Association/

American College of Cardiology (AHA/ACC) Guidelines:

A Scientific Statement From the American Heart Association

Physical Activity

Sedentary Behavior and Cardiovascular Morbidity and Mortality:

A Science Advisory From the American Heart Association

Routine Assessment and Promotion of Physical Activity in Healthcare Settings:

A Scientific Statement From the American Heart Association

Sedentary Behaviors in Today's Youth: Approaches to the Prevention and Management of Childhood

Obesity: A Scientific Statement From the American Heart Association

General and Cardiovascular Health

The Role of Worksite Health Screening

<u>Current Science on Consumer Use of Mobile Health for Cardiovascular Disease Prevention</u>

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary

<u>Cardiovascular Health Promotion in Children: Challenges and Opportunities for 2020 and Beyond:</u>

A Scientific Statement From the American Heart Association

Nutrigenomics, the Microbiome, and Gene-Environment Interactions:

New Directions in Cardiovascular Disease Research, Prevention, and Treatment

Government Resources

Health.gov's Dietary Guidelines

Health.gov's Physical Activity Guidelines



