

Guideline Update

2013 ACC/AHA

Cholesterol Guidelines

American College of Cardiology/American Heart Association Guidelines on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults by the National Cholesterol Education Program Adult Treatment Panel (ATP IV)¹



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Healthcare and
Family Services
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Statin Therapy

The ATP IV guidelines recommend treating blood cholesterol to reduce atherosclerotic cardiovascular (ASCVD) risk in adults.^{1,2} Treatment will no longer be adjusted or target specific lipid values, as fixed doses of statins were assessed in randomized clinical trials (RCTs). There is no data showing that titrating drug therapy to specific LDL-C or non-HDL-C goals improves ASCVD outcomes. Current evidence shows that a reduction in ASCVD events is accomplished by using the maximum-tolerated statin intensity in specific patient populations that have been shown to benefit.

Findings of the ATP IV Panel

- Lifestyle modifications should be emphasized for all patients, both prior to the initiation of and while on lipid-lowering pharmacotherapy.**^{1,2,3}
 - Adhering to a heart healthy diet (e.g., *increased vegetables, fruits, whole grains; limited sodium, sweets, sugar-sweetened beverages, red meats, saturated/trans fats*)
 - Regular aerobic physical activity (i.e., *moderate-to-vigorous intensity physical activity, 3-4 sessions per week, averaging 40 minutes per session*)
 - Avoidance of tobacco products
 - Maintenance of a healthy weight
 - Adequately controlling any comorbid hypertension and diabetes
- Statin therapy has shown clear benefits and is recommended in four major groups of patients (strong evidence):**^{1,2}

Patient Subgroups for Which the Benefits of Statins Outweigh the Risks

Patient Group	Recommended Intensity of Statin Treatment	
Clinical ASCVD* (secondary prevention)	Age ≤ 75 years with no statin-related safety concerns †	High
	Age > 75 years or with statin-related safety concerns	Moderate
LDL ≥ 190 mg/dL without clinical ASCVD	Ages ≥ 21 years	High
Diabetic patients without clinical ASCVD, ages 40-75 years, with LDL 70-189 mg/dL	10-year ASCVD risk < 7.5% ‡	Moderate
	10-year ASCVD risk ≥ 7.5%	High
Non-diabetic patients without clinical ASCVD, ages 40-75 years, with LDL 70-189 mg/dL	10-year ASCVD risk ≥ 7.5%	Moderate-to-high

* defined as: acute coronary syndromes, history of myocardial infarction, stable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease of atherosclerotic origin.

† characteristics that may predispose patients to statin adverse effects include (but are not limited to): multiple or serious comorbidities, including impaired renal or hepatic function; history of previous statin intolerance or muscle disorders; unexplained ALT elevations ≥3 times upper limit of normal; patient characteristics or concomitant use of drugs affecting statin metabolism; age > 75 years.

‡ 10-year ASCVD risk is calculated using the Pooled Cohort Equations, which may be found at <http://tools.acc.org/ASCVD-Risk-Estimator/>.

- Benefits of statin therapy are less certain in other populations.**
 - Consider the use of moderate-intensity statins in patients without clinical ASCVD (i.e., *primary prevention*) with a 10-year ASCVD risk of 5% to < 7.5%.
 - Only moderate evidence is available to support this practice; a net benefit, though likely marginal, exists. A clinician-patient discussion is necessary when considering the potential initiation of a statin.
 - Routine initiation of statin therapy is not recommended for patients with New York Heart Association (NYHA) heart failure class II – IV or those on maintenance hemodialysis; studies have shown no benefit or ASCVD risk-reduction.

High-Intensity Statins

(daily dose lowers LDL-C on average by approximately ≥ 50%)

Atorvastatin (40)-80 mg

Rosuvastatin 20 (40) mg (non-preferred)

Moderate-Intensity Statins

(daily dose lowers LDL-C on average by approximately 30% to < 50%)

Atorvastatin 10 (20) mg

Rosuvastatin (5) 10 mg (non-preferred)

Simvastatin 20-40 mg

Pravastatin 40 (80) mg

Lovastatin 40 mg

Fluvastatin XL 80 mg (non-preferred)

Fluvastatin 40 mg BID (non-preferred)

Pitavastatin 2-4 mg (non-preferred)

Low-Intensity Statins

(daily dose lowers LDL-C on average by approximately < 30%)

Simvastatin 10 mg

Pravastatin 10-20 mg

Lovastatin 20 mg

Fluvastatin 20-40 mg (non-preferred)

Pitavastatin 1 mg (non-preferred)

***bolded** = statin/dose studied in randomized controlled trials (RCTs)

**italicized* = FDA-approved statin/dose, but not evaluated in RCTs

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4. **Statin therapy is safe when used in properly selected individuals who are appropriately monitored.**
 - a. Routine monitoring of creatine kinase and hepatic transaminase levels is not necessary (unless the patient's symptoms indicate a possibility of myopathy or hepatotoxicity).
 - b. Statins may increase risk for type 2 diabetes, but benefits of statin therapy far outweigh the risks in the aforementioned patient populations.
 - c. For those unable to tolerate the recommended-intensity statin, use the maximum intensity statin the patient can tolerate.
 - i. For unexplained severe muscle symptoms or fatigue: discontinue statin and evaluate for possible rhabdomyolysis.
 - ii. For mild-to-moderate muscle symptoms:
 1. Discontinue statin. Should symptoms resolve, restart the same statin at the original or lower dose.
 2. If a causal relationship is confirmed, discontinue the statin, wait for symptoms to resolve, and initiate low dose of a different statin; increase as tolerated.
 - iii. If patient remains symptomatic for >2 months after statin discontinuation, reassess for other causes of muscle symptoms.
 - d. For those who may require non-statin therapy: please see section 7b below or section 6.3.2 of the guideline.¹
5. **For patients who do not fall into the above statin-benefit groups, clinicians and patients should engage in a discussion regarding the risks and benefits of therapy, addressing the following:**
 - a. ASCVD risk reduction benefits
 - b. Adverse effects and drug-drug interactions
 - c. Heart healthy lifestyle
 - d. Management of other risk factors
 - e. Patient preferences
 - f. If decision to treat with statin therapy remains unclear, consider factors that may inform ASCVD risk, including primary LDL-C ≥ 160 mg/dL, family history of premature ASCVD, abnormal coronary artery calcium (CAC) score or ankle-brachial index (ABI), or high-sensitivity C-reactive protein (hs-CRP) ≥ 2 mg/L .
6. **There is insufficient evidence to support treating patients to specific LDL-C or non-HDL-C goals.**
 - a. An approach of "treating to goal" has not been found to result in improved ASCVD outcomes; it may lead to the patient receiving inappropriate therapy. This current guideline does not recommend such goals as performance measures.
 - i. The addition of non-statin therapies to existing statin treatment may necessitate a reduction in statin intensity for safety issues, resulting in suboptimal statin treatment for a patient's specific level of ASCVD risk.
 - ii. Conversely, the use of a higher-than-recommended intensity statin has not shown a greater reduction in ASCVD risk, nor is the use of such a statin known to be acceptably safe in a particular lower-risk patient population.
7. **There is insufficient evidence to support routine use of non-statin drugs for reducing ASCVD events, either in addition to statin therapy or as monotherapy in statin-intolerant patients.**
 - a. Non-statin therapy: niacin, bile acid sequestrants, cholesterol-absorption inhibitors (i.e., ezetimibe), fibrates, omega-3 fatty acids
 - b. For high risk patients (includes those with clinical ASCVD < 75 years of age; baseline LDL-C ≥ 190 mg/dL; diabetic patients 40-75 years of age), non-statin therapy may be considered if:
 - i. Patient has a less-than-anticipated response to statins
 - ii. Patient is unable to tolerate a less-than-recommended intensity statin
 - iii. Patient is completely statin intolerant
 - c. If non-statin therapy is warranted, the guideline advocates the use of non-statin medications studied in RCTs that have shown the benefits of ASCVD reduction to far outweigh the risks for adverse effects and drug-drug interactions; patient preferences should also be considered.
 - d. Fibrates:
 - i. Avoid initiation of gemfibrozil in patients currently on a statin due to the risks for rhabdomyolysis.
 - ii. Consider use of fenofibrate in conjunction with a low- or moderate-intensity statin when triglycerides are ≥ 500 mg/dL and the benefits of reductions in ASCVD risk or triglycerides are deemed to outweigh risks for adverse effects.

REFERENCES

1. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S1-S45.
2. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA Cholesterol Guideline Panel. Treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: synopsis of the 2013 American College of Cardiology/American Heart Association cholesterol guideline. *Ann Intern Med*. 2014;160:339-343.
3. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S76-S99.