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PHARMACIST'S LETTER / PRESCRIBER'S LETTER
January 2014

2013 ACC/AHA Cholesterol Guidelines

The 2013 American Heart Association (AHA)/American College of Cardiology (ACC) lipid guidelines represent a paradigm shift in the treatment of dyslipidemia. These guidelines focus on reducing cardiovascular risk using proven interventions. Per the new guidelines, patients receive high- or moderate-dose statin therapy, depending on which of four "statin benefit groups" they fit into. The guidelines introduce a new risk calculator for estimation of 10-year cardiovascular disease risk. This calculator can be used to determine if a high- or moderate-dose statin is appropriate for primary prevention. Unlike previous guidelines, the 2013 guidelines do not recommend titrating the statin dose to achieve a specific LDL target. This is because randomized controlled trials have demonstrated cardiovascular risk reduction using specific statin doses, not LDL targets. Treating to a given target may result in statin undertreatment if an evidence-based statin dose is not used, or overtreatment. The addition of a nonstatin has not been proven to further reduce cardiovascular risk; therefore, nonstatins are no longer routinely recommended. The table below provides a summary of these guidelines, with an emphasis on pharmacotherapy.

--Information in table is from reference 1 unless otherwise denoted.--

Who should be assessed for cardiovascular risk, and how?	For patients without atherosclerotic cardiovascular disease: • Assess traditional risk factors (e.g., lipids, blood pressure, diabetes) every four to six years in patients 20 to 79 years of age.[2,3] • In patients 40 to 75 years of age not receiving cholesterol-lowering therapy, and with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L), also estimate 10-year risk using the **Pooled Cohort Equations Cardiovascular Risk Calculator**, available at http://my.americanheart.org/cvriskcalculator. Get an app from iTunes (for iPhone, iPad, and iPod), or Google Play (for Android).
What lifestyle changes are recommended to reduce cardiovascular risk?	Adhere to a heart-healthy diet: • Eat vegetables, fruits, whole grain, low-fat dairy, poultry, fish, beans, nontropical vegetable oils, and nuts, but avoid red meat (i.e., Mediterranean-style diet, DASH [Dietary Approaches to Stop Hypertension] diet).[2] • Limit sugary drinks and sweets.[2] • Limit saturated and trans fat to 5% to 6% of calories.[2] • Limit sodium intake to 2400 mg daily (about one teaspoon table salt [kosher/sea salt have less sodium per teaspoon]).[2] • For adults who would benefit from blood pressure lowering, further reduction to1500 mg daily is ideal. Combine sodium restriction with the DASH diet.[2] Exercise regularly: • Engage in moderate-to-vigorous aerobic activity for at least 40 minutes (on average) three to four times each week.[2] Avoid tobacco. Maintain a healthy weight.

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<table>
<tr><td>Who should be treated with a statin?</td><td colspan="2">There are four major statin benefit groups:
Patients with clinical atherosclerotic cardiovascular disease.
Patients with LDL 190 mg/dL (5 mmol/L) or higher.
Patients age 40 to 75 years of age with diabetes (but without clinical atherosclerotic cardiovascular disease) and LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L).
Patients without clinical atherosclerotic cardiovascular disease or diabetes with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L), with an estimated 10-year risk of atherosclerotic cardiovascular disease of 7.5% or higher.
If a patient does not fit into one of the four statin benefit groups (e.g., LDL 70 to 189 mg/dL [1.8 to 4.9 mmol/L] with 10-year risk 5% to 7.5%) , but there is clinical suspicion that they may benefit from a statin, additional factors can be taken into consideration:
LDL 160 mg/dL or higher or other evidence of genetic hyperlipidemia.
Cardiovascular disease onset in a first degree male relative before age 55, or in a first degree female relative before age 65.
High-sensitivity C-reactive protein 2 mg/dL or higher.
Ankle-brachial index <0.9.
Elevated lifetime risk of atherosclerotic cardiovascular disease.
Coronary artery calcium (CAC) score 300 Agatston units or higher, or 75th percentile or higher for age, gender, and ethnicity.
Statin adverse effects.
Statin drug interactions.
Patient preferences.</td></tr>
<tr><td rowspan="2">What are the pharmacologic treatment options?

Continued…</td><td>Pharmacotherapy</td><td>Use for…</td></tr>
<tr><td>High-dose Statin (average LDL reduction about 50% or higher):[a]
Atorvastatin 80 mg once daily (40 mg if 80 mg not tolerated).
Rosuvastatin 20 mg to 40 mg once daily.[b]</td><td>Secondary prevention in adults 75 years of age and younger. (Level A)
Primary prevention in adults with LDL 190 mg/dL (5 mmol/L) or higher. (Level A)
Primary prevention in adults 40 to 75 years of age with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L) and an estimated 10-year risk of atherosclerotic cardiovascular disease of 7.5% or higher (moderate-dose also an option). (Level A)
Primary prevention in diabetes patients 40 to 75 years of age with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L) and an estimated 10-year risk of atherosclerotic cardiovascular disease of 7.5% or higher. (Level C)</td></tr>
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Pharmacologic treatment options, continued	**Pharmacotherapy**	**Use for…**
	Moderate-dose Statin (average LDL reduction about 30 to <50%):[a] • Atorvastatin 10 to 20 mg once daily.[b] • Fluvastatin 40 mg twice daily or 80 mg (XL) once daily.[b] • Lovastatin 40 mg once daily. • Pitavastatin 2 to 4 mg once daily.[b] • Pravastatin 40 to 80 mg once daily.[b] • Rosuvastatin 5 to 10 mg once daily.[b] • Simvastatin 20 to 40 mg once daily.	• Secondary prevention in adults older than 75 years. (Level A) • Patients who cannot tolerate a high-dose statin. • Primary prevention in adults 40 to 75 years of age with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L) and an estimated 10-year risk of atherosclerotic cardiovascular disease of 7.5% or higher (high-dose also an option). (Level A) • Primary prevention in diabetes patients 40 to 75 years of age, with LDL 70 to 189 mg/dL (1.8 to 4.9 mmol/L) and an estimated 10-year risk of atherosclerotic cardiovascular disease of less than 7.5%. (Level A)
	Low-dose Statin (average LDL reduction <30%):[a] • Fluvastatin 20 to 40 mg once daily.[b] • Lovastatin 20 mg once daily. • Pitavastatin 1 mg once daily.[b] • Pravastatin 10 to 20 mg once daily. • Simvastatin 10 mg once daily.[b]	• For patients who cannot tolerate a high- or moderate-dose statin.
	Nonstatin • Reinforce statin adherence and lifestyle changes, and check for secondary causes before adding a nonstatin. • Do not add gemfibrozil to statin therapy. • No proof adding a nonstatin to a statin further reduces cardiovascular risk.	• Triglycerides 500 mg/dL or higher (use omega-3 fatty acids [e.g., fish oil], niacin, or fenofibrate). • Patients who cannot tolerate the recommended statin dose or do not achieve the expected statin response and are high-risk (i.e., patient with LDL 190 mg/dL [5 mmol/L] or higher at baseline, diabetes, or clinical atherosclerotic cardiovascular disease).
How is statin therapy monitored? *Continued…*	• Check ALT (alanine aminotransferase) at baseline. Repeat only if symptoms of hepatotoxicity occur. • Document any pre-existing muscle symptoms before starting a statin to establish a baseline. • Consider checking creatine kinase at baseline in patients at increased risk for myopathy (e.g., drug interactions, etc). Repeat only if symptomatic. • If severe muscle symptoms or fatigue of unknown cause develop, hold the statin and check creatinine and urinalysis to rule-out rhabdomyolysis.	

Statin monitoring, continued	• Check fasting lipid panel four to 12 weeks after statin initiation, then every three to 12 months. • Check adherence to statin and lifestyle interventions if LDL drop less than expected. • Consider statin dose reduction if two consecutive LDL measurements are less than 40 mg/dL (1.03 mmol/L). • Monitor for new-onset diabetes per diabetes screening guidelines.

a. Doses listed are for patients with normal renal function not taking an interacting medication. See our *PL Chart*, *Characteristics of the Various Statins*, for renal dosing and select drug interactions. High-dose, moderate-dose, and low-dose statin designations are categorical only. Actual statin percent LDL-lowering may vary in practice.

b. Atorvastatin 20 mg, fluvastatin extended-release (XL) 80 mg, fluvastatin 20 to 40 mg, pitavastatin, pravastatin 80 mg, rosuvastatin 5 mg and 40 mg, and simvastatin 10 mg are FDA-approved but lack evidence from randomized-controlled trials for reduction in major cardiovascular events.

Users of this PL Detail-Document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Levels of Evidence

In accordance with the trend towards Evidence-Based Medicine, we are citing the **LEVEL OF EVIDENCE** for the statements we publish.

Level	Definition
A	High-quality randomized controlled trial (RCT) High-quality meta-analysis (quantitative systematic review)
B	Nonrandomized clinical trial Nonquantitative systematic review Lower quality RCT Clinical cohort study Case-control study Historical control Epidemiologic study
C	Consensus Expert opinion
D	Anecdotal evidence In vitro or animal study

Adapted from Siwek J, et al. How to write an evidence-based clinical review article. *Am Fam Physician* 2002;65:251-8.

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References

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2. 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* 2013 Nov 12 [Epub ahead of print];doi:10.1161/01.cir.0000437740.48606.d1.
3. American Heart Association. 2013 Prevention Guidelines Tools. CV Risk Calculator. http://my.americanheart.org/cvriskcalculator. (Accessed November 23, 2013).

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