Trying to Make Sense of the Latest Blood Cholesterol Guidelines

_Carmine D’Amico, D.O._


A Report of the American College of Cardiology / American Heart Association Task Force on Clinical Practice Guidelines
2018 Blood Cholesterol Clinical Practice Guideline

Overview

• Learning Objectives
• Abbreviations
• Historical Perspective
• New Blood Cholesterol Guideline
• Clinical Application
• Summary
Learning Objectives


2. Estimate individual patients’ 10-year and lifetime atherosclerotic cardiovascular disease (ASCVD) risk using the “Pooled Cohort Equations” risk assessment tool (ASCVD risk estimator) that has been incorporated into the current ACC/AHA Blood Cholesterol (and Hypertension) Guidelines.

   (cont.)

Learning Objectives (cont.)

3. “Appreciate” (or more likely, loathe) the convoluted complexity of the new ACC/AHA Blood Cholesterol Guidelines.

Abbreviations

• ACC: American College of Cardiology
• AHA: American Heart Association
• AACVPR: American Association of Cardiovascular and Pulmonary Rehabilitation
• AAPA: American Academy of Physician Assistants

Abbreviations (cont.)

• ABC: Association of Black Cardiologists
• ACPM: American College of Preventive Medicine
• ADA: American Diabetes Association
• AGS: American Geriatrics Society
• APhA: American Pharmacists Association
Abbreviations (cont.)

- ASPC: American Society of Preventive Cardiology
- NLA: National Lipid Association
- PCNA: Preventive Cardiovascular Nurses Association
- NCEP ATP III: Third Report of the National Cholesterol Education Program Adult Treatment Panel

Historical Perspective

- NCEP ATP III Guidelines
  - Original report: 2001
  - Guideline update: 2004
- 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Risk in Adults 2013
- 2018 ACC/AHA Guideline on the Management of Blood Cholesterol 2018
Identifies four statin benefit groups:

- Secondary ASCVD prevention
- Severe hypercholesterolemia (LDL > 190 mg/dL)
- Diabetes mellitus in adults
- Primary prevention over the lifespan
2018 Blood Cholesterol Clinical Practice Guideline

Clinical ASCVD:

- Acute coronary syndrome
- Angina pectoris (stable or unstable)
- Arterial revascularization (coronary or other)
- History of MI
- History of stroke or TIA
- Peripheral arterial disease presumed to be of atherosclerotic origin, including aortic aneurysm
Secondary Prevention

Clinical ASCVD

Healthy Lifestyle

ASCVD not at very high-risk*

Age ≤ 75 y

High-intensity statin
(Goal: LDL-C ≤ 70 mg/dL)
(Class I)

If on maximal statin therapy and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), adding ezetimibe may be reasonable (Class IIb)

If high-intensity statin not tolerated, use moderate-intensity statin (Class II)

Continuation of high-intensity statin is reasonable (Class IIa)

Age > 75 y

High-intensity or maximal statin
(Class III)

If on maximal statin and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), adding ezetimibe may be reasonable (Class IIa)

If on clinically judged maximal LDL-C-lowering therapy and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), or non-HDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L), adding PCSK9-I is reasonable (Class IIa)

Very high-risk* ASCVD

If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class IIa)

Dashed arrow indicates RCT-supported efficacy, but is less cost effective

Very High-Risk for Future ASCVD Events*

Table 4

<table>
<thead>
<tr>
<th>Major ASCVD Events</th>
<th>High-Risk Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent acute coronary syndrome (within the past 12 months)</td>
<td>Age ≥ 65 years</td>
</tr>
<tr>
<td>History of myocardial infarction (other than recent acute coronary syndrome event listed above)</td>
<td>Heterozygous familial hypercholesterolemia</td>
</tr>
<tr>
<td>History of ischemic stroke</td>
<td>History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)</td>
</tr>
<tr>
<td>Symptomatic peripheral arterial disease (history of claudication with ankle brachial index &lt; 0.85, or previous revascularization or amputation)</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Chronic kidney disease (eGFR 15-59 ml/min/1.73 m²)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
</tr>
<tr>
<td></td>
<td>Persistently elevated LDL-C (LDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L)) despite maximally tolerated statin therapy and ezetimibe</td>
</tr>
<tr>
<td></td>
<td>History of congestive heart failure</td>
</tr>
</tbody>
</table>

*Very high-risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.
According to current guidelines, there are only two groups of patients for whom PCSK9 inhibitors should be considered:

- Those with very high risk ASCVD
  - If their LDL remains ≥ 70 mg/dL or non-HDL-C remains ≥ 100 mg/dL despite maximally tolerated statin therapy and ezetimibe

(cont.)
PCSK9 inhibitors (cont.)

- ... and the other of two groups of patients for whom PCSK9 inhibitors should be considered (according to current guidelines):
  - Those with severe primary hypercholesterolemia
    - If their LDL remains $\geq 100$ mg/dL despite maximally tolerated statin therapy and ezetimibe
• All diabetics (age 40–75 years) should be on statin therapy:

• High-intensity statin therapy for those 50–75 years of age, or those with multiple ASCVD risk factors

• Moderate-intensity statin therapy for others
Diabetes-specific Risk Enhancers
That Are Independent of Other Risk Factors in Diabetes

Table 5

- Long duration (≥10 years for type 2 diabetes or ≥ 20 years for type 1 diabetes)
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 ml/min/1.73 m²
- Retinopathy
- Neuropathy
- ABI <0.9

2018 Blood Cholesterol Clinical Practice Guideline

2018 Blood Cholesterol Guideline

ASCVD Risk Estimator

- The only time it is necessary to use the ASCVD risk estimator to help guide decision-making regarding statin therapy is in non-diabetics, without clinical ASCVD, with an LDL level between 70 and 189 mg/dL.

(cont.)
2018 Blood Cholesterol Guideline

ASCVD Risk Estimator (cont.)

• Available at:
  • http://tools.acc.org/ASCVD-Risk-Estimator-Plus/

• 10-year ASCVD risk categories:
  • Low risk: < 5%
  • Borderline risk: 5% to 7.4%
  • Intermediate risk: 7.5% to 19.9%
  • High risk: ≥ 20%

Clinical Application

• A random case…

62-year-old Caucasian male without clinical ASCVD presents for routine medical evaluation. He has an estimated 20 pack-year history of cigarette smoking, and he still smokes. He is not diabetic. He does, however, have a history of hypertension, for which he takes lisinopril/hydrochlorothiazide 10/12.5 mg PO daily. His total cholesterol is 234 mg/dL, his HDL-cholesterol is 38 mg/dL, triglycerides are 180 mg/dL, and his LDL-cholesterol is 126 mg/dL. His blood pressure is currently 128/78 mmHg.

According to the ACC/AHA 2018 Blood Cholesterol Guidelines, should statin therapy be recommended to him?
Top 10 Take-Home Messages

2018 Cholesterol Guidelines

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.
Top 10 Take Home Messages

2. In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin therapy or maximally tolerated statin therapy.

The more LDL-C is reduced on statin therapy, the greater will be subsequent risk reduction.

Use a maximally tolerated statin to lower LDL-C levels by ≥50%.
Top 10 Take Home Messages

3. In very high-risk ASCVD, use a LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of nonstatins to statin therapy.
   • Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.
   • 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 PCSK9 inhibitor is reasonable, although the long-term safety (>3 years) is uncertain and cost-effectiveness is low at mid-2018 list prices.

Top 10 Take Home Messages

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 without calculating 10-year ASCVD risk.
   • 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) & 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 LDL-C ≥70 mg/dL (≥1.8 mmol/L), start moderate-intensity statin therapy 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 (e.g., 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;
- the consideration of costs of statin therapy; and
- the patient preferences & values in shared decision-making.
Top 10 Take Home Messages

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%.

Top 10 Take Home Messages

8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), 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 yrs)
   - chronic inflammatory disorders (e.g., rheumatoid arthritis, psoriasis, or chronic HIV);
   - high-risk ethnic groups (e.g., South Asian);
   - persistent elevations of triglycerides ≥ 175 mg/dL (≥1.97 mmol/L);

9. (cont.)
Top 10 Take Home Messages

8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), risk-enhancing factors favor initiation of statin therapy (see No. 7).

Risk-enhancing factors include (cont.)

and, if measured in selected individuals
• apolipoprotein B ≥130 mg/dL
• high-sensitivity C-reactive protein ≥2.0 mg/L
• ankle-brachial index <0.9 and
• lipoprotein (a) ≥50 mg/dL or 125 nmol/L, especially at higher values of lipoprotein (a).

Risk-enhancing factors may favor statin therapy in patients at 10-year risk of 5-7.5% (borderline risk)

Top 10 Take Home Messages

9. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL- 189 mg/dL (≥1.8-4.9 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.
Top 10 Take Home Messages

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 drug therapy are defined by threshold LDL-C levels ≥70 mg/dL (≥1.8 mmol/L) on maximal statin therapy (see No. 3).

2018 Blood Cholesterol Clinical Practice Guideline

Dr. D’Amico’s Take Home Messages (Summary)

- Statin therapy is definitely indicated in:
  - All diabetics (age 40-75 years)
  - Adults with clinical ASCVD
  - Adults with LDL-C ≥ 190 mg/dL

- Statin therapy should also be recommended to:
  - Non-diabetics (age 40-75 years), without clinical ASCVD, with LDL level between 70 and 189 mg/dL and a 10-year ASCVD risk of ≥ 20%
2018 Blood Cholesterol Guideline

Current ACC/AHA Guidelines (Blood Cholesterol and many others):

• A free app is available...
  • Enter: “ACC Guideline Clinical Apps”
2018 Blood Cholesterol Clinical Practice Guideline

References


(cont.)


(continues)
