The 2013 American Heart Association/American College of Cardiology (AHA/ACC) Guidelines utilize an evidence-based Clinical Question (CQ) approach. The AHA/ACC evidence-based format takes into account the estimated certainty of response, size of treatment effect, strength of evidence for the recommendation, and a quality rating of the evidence.

Is this NCEP-ATP IV? No. The 2013 American Heart Association/American College of Cardiology (AHA/ACC) Guidelines essentially replaces NCEP-ATP and there are currently no plans for NCEP-ATP to release an updated cholesterol guideline.

Who are the treatment populations?

![ATP III vs. Clinical ASCVD](chart.png)

<table>
<thead>
<tr>
<th>2013 AHA/ACC Guidelines</th>
<th>ATP III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical ASCVD (Atherosclerotic Cardiovascular Disease)</td>
<td>- Acute Coronary Syndrome</td>
</tr>
<tr>
<td></td>
<td>- Myocardial Infarction</td>
</tr>
<tr>
<td></td>
<td>- Stable or Unstable Angina</td>
</tr>
<tr>
<td></td>
<td>- Revascularization Procedures</td>
</tr>
<tr>
<td></td>
<td>- Stroke or Transient Ischemic Attack</td>
</tr>
<tr>
<td></td>
<td>- Peripheral Arterial Disease Atherosclerotic in Origin</td>
</tr>
<tr>
<td>LDL &gt; 190 mg/dL</td>
<td>Type 1 or 2 Diabetes AND Age 40-75 years</td>
</tr>
<tr>
<td>10-year ASCVD Risk &gt; 7.5% AND Age 40-75 years</td>
<td></td>
</tr>
</tbody>
</table>

CHD vs. ASCVD…why the change? The previous guidelines focused on the coronary heart disease (CHD) outcomes of nonfatal myocardial infarction and CHD death. The 2013 guidelines incorporate fatal and nonfatal stroke as an outcome. As a result, the baseline risk may increase for certain patient populations and the benefit of treating cholesterol with specific doses of statin therapy increases. Of note, atherosclerotic revascularization procedures are not included as an outcome in these risk calculators.

What happened to targeted cholesterol treatment levels? There was insufficient evidence to support treating LDL or non-HDL to a targeted level. The emphasis of treatment should be placed on using the appropriate intensity of statin therapy for those patients most likely to derive benefit.

Why is percent-LDL reduction mentioned in the guidelines? Isn’t this similar to setting a cholesterol level goal? The percent LDL reduction reported in the guidelines is based on the mean LDL reductions reported in clinical trials. The percent reduction is intended to be used as an indication of response and adherence to therapy, but is not being advocated as a treatment goal, per se.
2013 AHA/ACC Cholesterol Guidelines (Replaces NCEP ATP Guidelines)
Primer and Frequently Asked Questions for Providers
Part 1

Major Recommendations for Statin Therapy for ASCVD Prevention

ASCVD Statin Benefit Groups
Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

- Adults age >21 y and a candidate for statin therapy
- Clinical ASCVD
- LDL–C ≥190 mg/dL
- Diabetes Type 1 or 2
  - Age 40-75 y

Estimate 10-y ASCVD Risk with Pooled Cohort Equations*

- ≥7.5% estimated 10-y ASCVD risk and age 40-75 y
- Moderate-to-high intensity statin

If calculated risk 5-7.5%, could consider additional factors that may warrant treatment? such as:
- LDL ≥ 160 mg/dL
- ASCVD 1st degree family history (males < 55 or females < 65)
- hsCRP ≥ 2 mg/dL
- Coronary artery calcium score ≥ 300 Agalston units or ≥ 75 percentile for age, sex, and ethnicity
- Ankle brachial index < 0.9
- Lifetime ASCVD risk

Definitions of High- and Moderate-Intensity Statin Therapy
(See Table 5)

- High
  - Daily dose lowers LDL–C by approx. ≥50%
- Moderate
  - Daily dose lowers LDL–C by approx. 30% to <50%

Age ≤75 y
- High-intensity statin
- (Moderate-intensity statin if not candidate for high-intensity statin)

Age >75 y or if not candidate for high-intensity statin
- Moderate-intensity statin

Patients > 75 years were excluded from the high-intensity trials

Also evaluate for secondary causes of very high LDL

In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.
### AHA/ACC Table 5: High-, Moderate-, and Low-Intensity Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C by approximately ≥50%</td>
<td>Daily dose lowers LDL–C by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin (40†)–80 mg</td>
<td>Atorvastatin 10 (20) mg</td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20 (40) mg</td>
<td>Rosuvastatin (5) 10 mg</td>
<td>Pravastatin 10–20 mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20–40 mg‡</td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40 (80) mg</td>
<td>Fluvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
<td>Pitavastatin 1 mg</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin XL 80 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluvastatin 40 mg bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pitavastatin 2–4 mg</td>
<td></td>
</tr>
</tbody>
</table>

**Bold** = evaluated in RCTs and demonstrated a reduction in major cardiovascular events.

**Italics** = approved by the U.S. FDA but not tested in RCTs

Individual responses to statins might vary in clinical practice.

†Evidence from one RCT only (down-titration if unable to tolerate atorvastatin 80 mg)

‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

---

### What labs should be drawn prior to starting statin therapy?

The AHA/ACC recommends a baseline fasting lipid panel and ALT prior to starting statin therapy. A creatinine kinase level (CK) may be drawn if clinically indicated (see below).

### Which LDL measurement should I use (calculated or direct LDL)?

Calculation of LDL using the Friedewald equation is highly robust and reproducible with respect to accuracy in laboratories that participate in standardization programs. It is useful only when TG levels are <400 mg/dL and when the calculated LDL is >70 mg/dL. The majority of lipid clinical trials used the Friedewald calculated LDL value.

### Are there any dietary recommendations?

The AHA/ACC is promoting a Heart Healthy Diet based on their evidence review of different diet-/lifestyle-focused studies. The Heart Healthy Diet is defined as a diet rich in vegetables, fruits, low-fat dairy products, whole grains, poultry, fish, legumes, nuts, and vegetable oil. It limits intake of red meat, sweets, sugar-containing beverages, trans fat, sodium, and it restricts intake of saturated fat to 5-6% of total daily calories. The Heart Healthy Diet emphasizes caloric intake levels consistent with achieving and maintaining a healthy weight and has shown a benefit with respect to lipid profiles and blood pressure.

### Should other lipid-lowering medications be added to statin therapy?

Recommendations that support the addition of adjunctive antihyperlipidemic medication to statin therapy are limited to expert opinion (for patients who have not achieved “sufficient” LDL-lowering on statin monotherapy), but is not supported by clinical evidence that combination therapy lowers risk for cardiovascular events.
What about using non-statin therapy in place of statins? There are a few individual placebo-controlled trials that demonstrate some benefit in specific patient populations (e.g. niacin and gemfibrozil have shown some benefit in men with CHD and hyperlipidemia compared to placebo). However, there are currently no head-to-head randomized controlled trials that compare non-statin therapy to statins. Therefore the guidelines emphasize statins as first-line therapy due to the strong body of supporting evidence."

Special Populations:

Should I be starting a statin for primary prevention in women? The 10-year ASCVD calculator should be used to determine the 10-year ASCVD risk for women without diabetes who are between 40-75 years of age. A moderate-intensity statin should be considered for those women with a calculated 10-year ASCVD risk of 7.5% or greater.

If the female patient is considering pregnancy, or is premenopausal and not protected against pregnancy, a discussion about the ASCVD benefits and risks of statin therapy (pregnancy category X) should be held prior to, and during statin treatment. Statins should not be used in women of childbearing potential unless they are using effective contraception. Statins must be avoided during pregnancy and lactation.

Should statins be used in patients with heart failure, NYHA Class II-IV? The AHA/ACC found insufficient evidence for or against the use of statin therapy for the purpose of ASCVD risk reduction in this population. Patient ASCVD risk factors and risk/benefit of statins should be considered on an individual basis.

What about patients on hemodialysis? Similar to those with NYHA Class II-IV heart failure, there was insufficient evidence for or against the use of statin therapy for the purpose of ASCVD risk reduction in those on hemodialysis. Patient ASCVD risk factors and risk/benefit of statins should be considered on an individual basis.

Does there need to be renal dose adjustments for statins? Although not specifically mentioned in the AHA/ACC guidelines, there are some renal dosing recommendations for specific statins. Atorvastatin is the only statin currently on the market that does not have a recommendation for renal dose adjustments.
**Hypertriglyceridemia:** The guidelines advocate use of medications to lower triglycerides only when the TG level is above 1000 mg/dL. NCEP-ATP III recommended treating TG ≥ 500 mg/dL. **Why the change?**

The AHA/ACC could not find evidence that starting triglyceride-lowering medication therapy for TG levels of 500-1000 mg/dL lowered the risk of hyperlipidemic pancreatitis. They recommend evaluating and addressing secondary causes of elevated TG levels, and implementing diet and lifestyle modifications first for these patients.

**AHA/ACC Table 6: Secondary Hyperlipidemia Causes Commonly Encountered in Clinical Practice**

<table>
<thead>
<tr>
<th>Secondary Cause</th>
<th>Elevated LDL−C</th>
<th>Elevated TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Saturated or trans fats, weight gain, anorexia</td>
<td>Weight gain, very low-fat diets, high intake of refined carbohydrates, excessive alcohol intake</td>
</tr>
<tr>
<td>Drugs</td>
<td>Diuretics, cyclosporine, glucocorticoids, amiodarone</td>
<td>Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sirolimus, raloxifene, tamoxifen, beta blockers (not carvedilol), thiazides</td>
</tr>
<tr>
<td>Diseases</td>
<td>Biliary obstruction, nephrotic syndrome</td>
<td>Nephrotic syndrome, chronic renal failure, lipidostrophies</td>
</tr>
<tr>
<td>Disorders and altered states of metabolism</td>
<td>Hypothyroidism, obesity, pregnancy*</td>
<td>Diabetes (poorly controlled), hypothyroidism, obesity; pregnancy*</td>
</tr>
</tbody>
</table>

*Cholesterol and triglycerides rise progressively throughout pregnancy; treatment with statins, niacin, and ezetimibe are contraindicated during pregnancy and lactation.

**Statin Safety:**

**Should I monitor ALT levels?** No, data from both primary- and secondary-prevention RCTs indicates that no clinically significant liver problems are associated with statin therapy. Elevated hepatic transaminase levels (AST and/or ALT) associated with high-intensity statin therapy occurred in fewer than 1.5% of individuals over 5 years, and elevations associated with low- or moderate-intensity statin therapy occurred at rates similar to those seen with placebo or no statin treatment controls.

**Should I be monitoring CK levels?** No, CK levels should not be routinely monitored. The AHA/ACC expert-opinion based algorithm is as follows:
- To avoid unnecessary discontinuation of statins, obtain a history of prior or current muscle symptoms to establish a baseline before initiating statin therapy.
If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK, creatinine, and a urinalysis for myoglobinuria.

If mild to moderate muscle symptoms develop during statin therapy:

- Discontinue the statin until the problem can be evaluated.
- Evaluate the patient for other conditions that might increase the risk for muscle symptoms (e.g., hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases.)
- If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship between the muscle symptoms and statin therapy.
- If a causal relationship exists, discontinue the original statin. Once muscle symptoms resolve, use a low dose of a different statin.
- Once a low dose of a statin is tolerated, gradually increase the dose as tolerated.
- If, after 2 months without statin treatment, muscle symptoms or elevated CK levels do not resolve completely, consider other causes of muscle symptoms listed above.
- If persistent muscle symptoms are determined to arise from a condition unrelated to statin therapy, or if the predisposing condition has been treated, resume statin therapy at the original dose.

**Do statins cause memory loss?** Data from RCTs could not find evidence to support the association that statins cause or contribute to memory loss. Expert opinion from the AHA/ACC suggests that individuals who present with a confusional state or memory impairment while on statin therapy be evaluated for non-statin causes, such as exposure to other drugs, as well as for systemic and neuropsychiatric causes, in addition to the possibility of adverse effects associated with statin drug therapy.

**Do statins cause diabetes?** There is moderate evidence that statin therapy is associated with an excess risk for incident diabetes (NNH = 100 in primary prevention, and 500-1000 in secondary prevention).

**How low is too low (for LDL levels)?** A systematic review did not identify evidence of harms when LDL remains <40 mg/dL on statin therapy. The AHA/ACC provides a weak recommendation that the statin dose may be decreased if there are two consecutive LDL levels below 40 mg/dL.
Figure 5. Statin Therapy: Monitoring therapeutic response and adherence

Assess medication and lifestyle adherence
Fasting lipid panel*

Anticipated therapeutic response?

Yes

Indicators of anticipated therapeutic response and adherence to selected statin intensity:
• High-intensity statin therapy† reduces LDL-C approx. 35-50% from the untreated baseline.
• Moderate-intensity statin therapy reduces LDL-C approx. 30% to <50% from the untreated baseline.

No

Reinforce continued adherence
Follow-up 3-12 mo

Yes

Reinforce improved adherence
Increase statin intensity‡
OR
Consider addition of non-statin drug therapy
Follow-up 4-12 wk. & thereafter as indicated

No

Intolerance to recommended dose of statin therapy

Yes

Management of statin intolerance (Table 6, Rec 8)

No

Intolerant therapeutic response

Reinforce medication adherence
Reinforce adherence to intensive lifestyle changes
Exclude secondary causes of hypercholesterolemia (Table 4)

Follow-up 4-12 wk.

Colors correspond to the class of recommendations in the ACC/AHA Table 1.
*Fasting lipid panel preferred. In a nonfasting individual, a nonfasting non-HDL-C >220 mg/dL may indicate genetic hypercholesterolemia that requires further evaluation or a secondary etiology. If nonfasting triglycerides are >500 mg/dL, a fasting lipid panel is required.
†In those already on a statin, in whom baseline LDL-C is unknown, an LDL-C <100 mg/dL was observed in most individuals receiving high-intensity statin therapy in RCTs.
‡See Section 6.3.1.