This evidence-based guideline summary is based on the November 2013 AHA/ACC Cholesterol and Risk Assessment Guidelines, which were adopted with slight modifications by the National Guideline Directors to become the National Dyslipidemia guideline. This guideline was developed by the Kaiser Permanente ICVH Clinical Leads and the National CVD RR Guideline Development Team (GDT) to assist primary care physicians and other health care professionals in the management of dyslipidemia for primary and secondary prevention of atherosclerotic disease.


**Frequency of Risk Assessment**

It is reasonable to assess traditional ASCVD risk factors every 4 to 6 years in adults 20 to 79 years of age who are free from ASCVD and to estimate 10-year ASCVD risk every 4 to 6 years in adults 40 to 79 years of age without ASCVD.

(Moderate Recommendation-Grade B)

**Lifetime Risk Assessment**

Assessing 30-year or lifetime ASCVD risk based on traditional risk factors may be considered in adults 20 to 59 years of age without ASCVD and who are not at high short-term risk.

(Weak Recommendation-Grade C)

**Additional Risk Factors**

ABI, hsCRP, CAC, Family History, Lifetime Risk

Use of additional factors (baseline LDL-C ≥ 160 or other evidence of genetic hyperlipidemias, family history of premature ASCVD with onset < 55 years in a first degree male relative, or < 65 in a first degree female relative, or lifetime risk of ASCVD, testing for hsCRP, ABI, or CAC), is an option for individuals who are not otherwise identified in a statin benefit group, or those for whom a risk-based treatment decision is uncertain after quantitative risk assessment. Testing should only be ordered if the result will prompt a therapeutic decision and the clinician and patient have agreed to initiate statin therapy if the result is abnormal, and to forgo statin therapy if the result is normal. Testing should be discussed in shared decision-making, taking into consideration the significant differences in convenience, cost, invasiveness, and radiation exposure.

(KP Weak Recommendation)

**ApoB, CKD, Albuminuria, Cardiorespiratory Fitness**

The contribution to risk assessment for a first ASCVD event using ApoB, CKD, albuminuria, or cardiorespiratory fitness is uncertain at present.

(No Recommendation For or Against-Grade N)
The Carotid Intima-Media Test (CIMT)

The CIMT is not recommended for routine measurement in clinical practice for risk assessment for a first ASCVD event.

(Recommendation Against-Grade D)

Primary Prevention

Primary Prevention in Individuals ≥ 21 Years of Age with LDL–C ≥ 190 mg/dL

Individuals with LDL–C ≥ 190 mg/dL or triglycerides ≥ 500 mg/dL should be evaluated for secondary causes of hyperlipidemia

(Moderate Recommendation-Grade B)

Adults ≥ 21 years of age with primary LDL–C ≥ 190 mg/dL should be treated with statin therapy (10-year ASCVD risk estimation is not required):

• Use high-intensity statin therapy unless contraindicated.
• For individuals unable to tolerate high-intensity statin therapy, use the maximum tolerated statin intensity.

(Moderate Recommendation-Grade B)

For individuals ≥ 21 years of age with an untreated primary LDL–C ≥ 190 mg/dL, it is reasonable to intensify statin therapy to achieve at least a 50% LDL–C reduction.

(Expert Opinion-Grade E)

For individuals ≥ 21 years of age with an untreated primary LDL–C ≥ 190 mg/dL, after the maximum intensity of statin therapy has been achieved, addition of a nonstatin drug may be considered to further lower LDL–C. Evaluate the potential for ASCVD risk reduction benefits, adverse effects, drug-drug interactions, and consider patient preferences.

(Expert Opinion-Grade E)

Primary Prevention in Individuals with Diabetes Mellitus and LDL–C 70 to 189 mg/dL

Moderate-intensity statin therapy should be initiated or continued for adults 40 to 75 years of age with diabetes mellitus who have LDL 70-189 and who do not have ASCVD.

(Strong Recommendation-Grade A)

High-intensity statin therapy is reasonable for adults 40 to 75 years of age with diabetes mellitus, who have LDL 70-189 and who do not have ASCVD, with a ≥ 7.5% estimated 10-year ASCVD risk unless contraindicated.

(Expert Opinion-Grade E)

In adults with diabetes mellitus, who have LDL 70-189 and who do not have ASCVD, who are < 40 or > 75 years of age, it is reasonable to evaluate the potential for ASCVD benefits and for adverse effects, for drug-drug interactions, and to consider patient preferences when deciding to initiate, continue, or intensify statin therapy.

(Expert Opinion-Grade E)

Primary Prevention in Individuals without Diabetes Mellitus and With LDL–C 70 to 189 mg/dL

Use of the The Pooled Cohort Equations [AHA/ACC CV Risk Calculator] or other risk calculator to estimate 10-year ASCVD risk for individuals with LDL–C 70 to 189 mg/dL without clinical ASCVD is an option.

(KP Weak Recommendation)

If using The Pooled Cohort Equations for populations other than Non-Hispanic Whites or African Americans, use the equations for Non-Hispanic Whites.

(Expert Opinion-Grade E)

Because no cardiovascular risk calculator has been studied prospectively and compared to another risk calculator, some clinicians may choose a different risk calculator to estimate cardiovascular risk. Clinicians selecting a different risk calculator may decide to apply different treatment thresholds than those proposed in the Pooled Cohort Equations [AHA/ACC CV Risk Calculator].

For adults 40 to 75 years of age with LDL–C 70 to 189 mg/dL, without clinical ASCVD or diabetes at elevated risk (e.g. 7.5-14.9% risk by the AHA/ACC Pooled Cohort Equations) treatment with moderate- to high-intensity statin therapy is an option, after a discussion which considers the potential for ASCVD risk reduction benefits and for adverse effects, for drug-drug interactions, and patient preferences for treatment.

(KP Weak Recommendation)

For Adults 40 to 75 years of age with LDL–C 70 to 189 mg/dL, without clinical ASCVD or diabetes and a very elevated estimated 10-year ASCVD risk (e.g. ≥ 15% risk by the AHA/ACC Pooled Cohort Equations), treatment with moderate- to high-intensity statin therapy is recommended.

(KP Strong Recommendation)

It is reasonable to offer treatment with a moderate intensity statin to adults 40 to 75 years of age, with LDL–C 70 to 189 mg/dL, without clinical ASCVD or diabetes and a slightly elevated estimated 10-year ASCVD risk (e.g. ≥ 5% to 7.4% risk by the AHA/ACC...
Secondary Prevention

Clinical ASCVD

High-intensity statin therapy should be initiated or continued as first-line therapy in women and men ≤ 75 years of age who have clinical ASCVD, unless contraindicated.

In individuals with clinical ASCVD in whom high-intensity statin therapy would otherwise be used, when high-intensity statin therapy is contraindicated or when characteristics predisposing to statin-associated adverse effects are present, moderate-intensity statin should be used as the second option if tolerated.

Asymptomatic Non-Coronary Atherosclerosis

For patients with asymptomatic non-coronary atherosclerosis, including asymptomatic peripheral arterial disease (PAD), carotid stenosis and aortic atherosclerosis, a statin is an option to reduce the risk of developing symptomatic cardiovascular disease.

Unrepaired AAA

Statin Therapy: For patients with unrepaired abdominal aortic aneurysm (AAA), the use of statins is an option to reduce the risk of cardiovascular disease progression.

Heart Failure and Hemodialysis

The Expert Panel makes no recommendations regarding the initiation or discontinuation of statins in patients with NYHA class II–IV ischemic systolic heart failure or in patients on maintenance hemodialysis.

Triglyceride Treatment

There is evidence that elevated TG is independently associated with increased risk of atherosclerosis.

However, not all people with high TGs are at increased risk, and neither the threshold for initiation of therapy, nor the goal of therapy, is known. Although there is direct evidence that lowering LDL–C reduces the risk of CAD events, there are no clinical trials to demonstrate that reducing TG levels will reduce CAD events. There is expert opinion that a desirable TG level is < 150 mg/dL, but there are no studies to support the benefit of obtaining this level. Treatment decisions should be influenced by a person’s other lipid levels and nonlipid CAD risk factors. Although there is no direct evidence, there is consensus that TG > 500 mg/dL warrants treatment to prevent pancreatitis. Specific recommendations for treating high TG level are presented in the Triglyceride Algorithm.

Treatment Targets

No recommendation for or against specific LDL–C or non-HDL–C targets for the primary or secondary prevention of ASCVD.

Monitoring Statin Therapy

Adherence to medication and lifestyle, and safety should be regularly assessed. Safety measurements should be measured as clinically indicated.

Optimizing Statin Therapy

The maximum tolerated intensity of statin should be used in individuals for whom a high- or moderate-intensity statin is recommended, but not tolerated.

Insufficient Response to Statin Therapy

In individuals who have a less-than anticipated therapeutic response or are intolerant of the recommended intensity of statin therapy, the following should be performed:

- Reinforce medication adherence.
- Reinforce adherence to intensive lifestyle changes.
- Exclude secondary causes of hyperlipidemia.

It is reasonable to use the following as indicators of anticipated therapeutic response to the recommended intensity of statin therapy. Focus is on the intensity of the statin therapy. As an aid to monitoring:
• High-intensity statin therapy† generally results in an average LDL–C reduction of ≥ 50% from the untreated baseline;
• Moderate-intensity statin therapy generally results in an average LDL–C reduction of 30 to < 50% from the untreated baseline;
• LDL–C levels and percent reduction are to be used only to assess response to therapy and adherence. They are not to be used as performance standards.

(Expert Opinion-Grade E)

In individuals at higher ASCVD risk receiving the maximum tolerated intensity of statin therapy who continue to have a less-than-anticipated therapeutic response, addition of a nonstatin cholesterol-lowering drug(s) may be considered if the ASCVD risk-reduction benefits outweigh the potential for adverse effects. Higher-risk individuals include:

• Individuals with clinical ASCVD a < 75 years of age.
• Individuals with baseline LDL–C ≥ 190 mg/dL.
• Individuals 40 to 75 years of age with diabetes mellitus.

Preference should be given to nonstatin cholesterol-lowering drugs shown to reduce ASCVD events in RCTs. (Expert Opinion-Grade E)

In individuals who are candidates for statin treatment but are completely statin intolerant, it is reasonable to use nonstatin cholesterol lowering drugs that have been shown to reduce ASCVD events in RCTs if the ASCVD risk-reduction benefits outweigh the potential for adverse effects. (Expert Opinion-Grade E)

Safety

To maximize the safety of statins, selection of the appropriate statin and dose in men and nonpregnant/nonnursing women should be based on patient characteristics, level of ASCVD**, risk, and potential for adverse effects.

Moderate-intensity statin therapy should be used in individuals in whom high-intensity statin therapy would otherwise be recommended when characteristics predisposing them to statin-associated adverse effects are present.

Characteristics predisposing individuals 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 ULN.
• Patient characteristics or concomitant use of drugs affecting statin metabolism.
• > 75 years of age.

Additional characteristics that may modify the decision to use higher statin intensities may include, but are not limited to:

• History of hemorrhagic stroke.
• Asian ancestry.

(Strong Recommendation-Grade A)

**Based on the presence of clinical ASCVD, a, diabetes mellitus, LDL–C > 190 mg/dL, or level of estimated 10-year ASCVD risk.

CK should not be routinely measured in individuals receiving statin therapy (Strong Recommendation-Grade A)

Baseline measurement of CK is reasonable for individuals believed to be at increased risk for adverse muscle events based on a personal or family history of statin intolerance or muscle disease, clinical presentation, or concomitant drug therapy that might increase the risk for myopathy (Expert Opinion-Grade E)

During statin therapy, it is reasonable to measure CK in individuals with muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue (Expert Opinion-Grade E)

Baseline measurement of hepatic transaminase levels (ALT) should be performed before initiating statin therapy (Moderate Recommendation-Grade B)

During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark colored urine or yellowing of the skin or sclera) (Expert Opinion-Grade E)

Decreasing the statin dose may be considered when 2 consecutive values of LDL–C levels are < 40 mg/dL (Weak Recommendation-Grade C)
It may be harmful to initiate simvastatin at 80 mg daily or increase the dose of simvastatin to 80 mg daily. (Moderate Recommendation-Grade B)

Individuals receiving statin therapy should be evaluated for new-onset diabetes mellitus according to the current diabetes screening guidelines (93). Those who develop diabetes mellitus during statin therapy should be encouraged to adhere to a heart healthy dietary pattern, engage in physical activity, achieve and maintain a healthy body weight, cease tobacco use, and continue statin therapy to reduce their risk of ASCVD events (Moderate Recommendation-Grade B)

For individuals taking any dose of statins, it is reasonable to use caution in individuals > 75 years of age, as well as in individuals that are taking concomitant medications that alter drug metabolism, taking multiple drugs, or taking drugs for conditions that require complex medication regimens (e.g., those who have undergone solid organ transplantation or are receiving treatment for HIV). A review of the manufacturer’s prescribing information may be useful before initiating any cholesterol-lowering drug. (Expert Opinion-Grade E)

It is reasonable to evaluate and treat muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or fatigue, in statin-treated patients according to the following management algorithm:

- 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 symptoms 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. (Expert Opinion-Grade E)

For individuals presenting with a confusional state or memory impairment while on statin therapy, it may be reasonable to evaluate the patient for nonstatin 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. (Expert Opinion-Grade E)

Safety of Niacin

Baseline hepatic transaminases, fasting blood glucose or hemoglobin A1c, and uric acid should be obtained before initiating niacin, and again during up-titration to a maintenance dose and periodically thereafter. (Moderate Recommendation-Grade B)

Niacin should not be used if:

- Hepatic transaminase elevations are higher than 2 to 3 times ULN. (Strong Recommendation-Grade A)
- Persistent severe cutaneous symptoms, persistent hyperglycemia, acute gout or unexplained abdominal pain or gastrointestinal symptoms occur. (Moderate Recommendation-Grade B)
- New-onset atrial fibrillation or weight loss occurs. (Weak Recommendation-Grade C)

In individuals with adverse effects from niacin, the potential for ASCVD benefits and the potential for adverse effects should be reconsidered before reinitiating niacin therapy. (Expert Opinion-Grade E)

To reduce the frequency and severity of adverse cutaneous symptoms, it is reasonable to:
• Start niacin at a low dose and titrate to a higher dose over a period of weeks as tolerated.

• Take niacin with food or premedicating with aspirin 325 mg 30 minutes before niacin dosing to alleviate flushing symptoms.

• If an extended-release preparation is used, increase the dose of extended-release niacin from 500 mg to a maximum of 2,000 mg/day over 4 to 8 weeks, with the dose of extended release niacin increasing not more than weekly.

• If immediate-release niacin is chosen, start at a dose of 100 mg 3 times daily and up-titrated to 3 g/day, divided into 2 or 3 doses. (Expert Opinion-Grade E)

Safety of Bile Acid Sequestrants (BAS)

Safety BAS should not be used in individuals with baseline fasting triglyceride levels ≥ 300 mg/dL or type III hyperlipoproteinemia, because severe triglyceride elevations might occur. (A fasting lipid panel should be obtained before BAS is initiated, 3 months after initiation, and every 6 to 12 months thereafter.) (Weak Recommendation-Grade C)

It is reasonable to use BAS with caution if baseline triglyceride levels are 250 to 299 mg/dL, and evaluate a fasting lipid panel in 4 to 6 weeks after initiation. Discontinue the BAS if triglycerides exceed 400 mg/dL. (Expert Opinion-Grade E)

Safety of Cholesterol-Absorption Inhibitors

It is reasonable to obtain baseline hepatic transaminases before initiating ezetimibe. When ezetimibe is coadministered with a statin, monitor transaminase levels as clinically indicated, and discontinue ezetimibe if persistent ALT elevations > 3 times ULN occur. (Weak Recommendation-Grade C)

Safety of Fibrates

Gemfibrozil should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis. (Moderate Recommendation-Grade B)

Fenofibrate may be considered concomitantly with a low- or moderate-intensity statin only if the benefits from ASCVD risk reduction or triglyceride lowering when triglycerides are > 500 mg/dL, are judged to outweigh the potential risk for adverse effects. (Expert Opinion-Grade E)

Renal status should be evaluated before fenofibrate initiation, within 3 months after initiation, and periodically thereafter. Assess renal safety with both a serum creatinine level and an eGFR based on creatinine.

• If eGFR is between 30 and 59 mL/min per 1.73 m2, the dose of fenofibrate should not exceed 54 mg/day.

• Fenofibrate should not be used if moderate or severe renal impairment, defined as eGFR < 30 mL/min per 1.73 m2, is present.

• If, during follow-up, the eGFR decreases persistently to ≤ 30 mL/min per 1.73 m2, fenofibrate should be discontinued. (Moderate Recommendation-Grade B)

Safety of Omega-3 Fatty Acids

If EPA and/or DHA are used for the management of severe hypertriglyceridemia, defined as triglycerides ≥ 500 mg/dL, it is reasonable to evaluate the patient for gastrointestinal disturbances, skin changes, and bleeding. (Weak Recommendation-Grade C)
# NHLBI Grading the Strength of Recommendation

<table>
<thead>
<tr>
<th>Category</th>
<th>Recommendation Strength</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strong</td>
<td>High certainty based on evidence that net benefit&lt;sup&gt;†&lt;/sup&gt; is substantial.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate</td>
<td>Moderate certainty based on evidence that net benefit is moderate to substantial, or high certainty that net benefit is moderate.</td>
</tr>
<tr>
<td>C</td>
<td>Weak</td>
<td>At least moderate certainty based on evidence of small net benefit.</td>
</tr>
<tr>
<td>E</td>
<td>Expert Opinion</td>
<td>Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the Panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended.</td>
</tr>
<tr>
<td>N</td>
<td>No Recommendation For or Against</td>
<td>Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence or conflicting evidence, and the Panel thought no recommendation should be made. Further research is recommended.</td>
</tr>
<tr>
<td>D</td>
<td>Against</td>
<td>At least moderate certainty based on evidence of no net benefit or that risks/harms outweigh benefits.</td>
</tr>
</tbody>
</table>

<sup>†</sup>For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparators should involve direct comparisons of the treatments or strategies being evaluated.