Latest Guidelines for Lipid Management
GOALS

- Recognize the differences between different guidelines
- Understand the effective strategies to tailor lipid lowering therapies based on evidence and guideline recommendation.
Dyslipidemia and CV risk

- Treatment of dyslipidemia is a cornerstone of preventive cardiology, and reduction in low-density lipoprotein (LDL-C) in select populations reduces risk of atherosclerotic cardiovascular disease (ASCVD) events in both primary and secondary prevention.

- The wealth of evidence for LDL-lowering to prevent ASCVD has been synthesized in a variety of dyslipidemia guidelines.
# Major Atherosclerotic Cardiovascular Disease Risk Factors

<table>
<thead>
<tr>
<th>Major risk factors</th>
<th>Additional risk factors</th>
<th>Non-traditional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advancing age</td>
<td>Obesity, abdominal obesity</td>
<td>† Lipoprotein (a)</td>
</tr>
<tr>
<td>† Total serum cholesterol level</td>
<td>Family history of hyperlipidemia</td>
<td>† Clotting factors</td>
</tr>
<tr>
<td>† Non–HDL-C</td>
<td>† Small, dense LDL-C</td>
<td>† Inflammation markers</td>
</tr>
<tr>
<td>† LDL-C</td>
<td>† Apo B</td>
<td></td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>† LDL particle concentration</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Fasting/postprandial</td>
<td>Apo E4 isoform</td>
</tr>
<tr>
<td>Hypertension</td>
<td>hypertriglyceridemia</td>
<td>† Uric acid</td>
</tr>
<tr>
<td>Stage 3 or 4 chronic kidney disease</td>
<td>PCOS</td>
<td>† TG-rich remnants</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>Dyslipidemic triad</td>
<td></td>
</tr>
<tr>
<td>Family history of ASCVD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Atherosclerosis is a preventable disorder

- Of all the lipoproteins, LDL Cholesterol plays a central role not only in the initiation of atherosclerosis but also in the progression of atherosclerosis ending in clinical CV events.
- Most robust evidence for the role played by LDL –C comes from RCT’s which had used statins.
- The evidence clearly shows that by reducing LDL –e, we get substantial reduction in CV morbidity & mortality.
For every 30 mg/dl change in LDL-C, the relative risk for CHD changes by about 30%
LDL-C reduction of at least 50% was required to halt progression.

LDL-C reduces the risk.

Graph showing the relationship between change in LDL-C and change in atheroma volume.
History of US Dyslipidemia Guideline Development

1988
- ATP I
  - Exclusive focus on LDL-C

1993
- ATP II
  - Risk assessment guides therapy

2001
- ATP III
  - Lower LDL-C threshold for therapy initiation in high risk patients

2004
- ATP III Update
  - Lower LDL-C threshold for therapy initiation in very high risk patients

2013
- ACC/AHA Guidelines
  - Use of moderate- or high-intensity statin therapy for patients across 4 major groups at risk for ASCVD*

*ASCVD, Atherosclerotic Cardiovascular Disease

NCEP ATP III Updated Report: LDL-C Goals Based on Risk Category

Increasing Risk

Lower Risk
- LDL-C Goal <160 mg/dL

Moderate Risk
- LDL-C Goal <130 mg/dL

Moderately High-Risk
- LDL-C Goal <130 mg/dL

High-Risk
- LDL-C Goal <100 mg/dL

Very High-Risk
- LDL-C Goal <100 mg/dL

Optional Goal
- Optional Goal <100 mg/dL
- Optional Goal <70 mg/dL

Recent Dyslipidemia Guidelines: Quick Overview

2013 ACC/AHA Cholesterol Treatment Guidelines

2014 NICE Guideline for Lipid Modification

2016 ESC/EAS Guideline for Dyslipidemia Management

2016 LAI Expert Consensus Dyslipidemia Management in India

2017 AACE/ACE Guideline for Dyslipidemia Management

2018 ACC/AHA Cholesterol Treatment Guidelines
2013 ACC/AHA Cholesterol Treatment Guideline

- Identification of 4 major statin benefit groups
- Shift away from treat to target approach
- Definitions of statin intensity provided
- Global risk assessment tool for primary prevention
- Addition of non-statin drug therapy to statins to further decrease ASCVD risk addressed
Four high-risk groups were described in the 2013 ACC/AHA cholesterol guidelines:

- Patients with established cardiovascular disease;
- Patients with high LDL-C levels;
- Patients with diabetes; and
- Patients with an elevated 10-year risk.
# Major Statin Benefit Group

<table>
<thead>
<tr>
<th>Group</th>
<th>ASCVD</th>
<th>LDL (mg/dL)</th>
<th>DM (40 – 75 years)</th>
<th>10 year risk ASCVD ≥ 7.5 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patients with clinical ASCVD (ACS, history of MI, angina, stroke, TIA, PAD)</td>
<td>Yes</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2. Patients with primary elevations of LDL–C ≥190 mg/dL</td>
<td>--</td>
<td>&gt;190</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>3. Patients with DM, with LDL 70-189 mg/dL and no ASCVD</td>
<td>No</td>
<td>70 - 189</td>
<td>Yes</td>
<td>--</td>
</tr>
<tr>
<td>4. Patients without ASCVD or DM with LDL–C 70 to 189 mg/dL and estimated 10-year ASCVD risk ≥7.5%</td>
<td>No</td>
<td>70 - 189</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Major Statin Benefit Group: Guideline recommendations

<table>
<thead>
<tr>
<th>Group</th>
<th>ASCVD</th>
<th>LDL (mg/dL)</th>
<th>DM (40 – 75 years)</th>
<th>10 year risk ASCVD ≥ 7.5 %</th>
<th>Guideline direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Patients with clinical ASCVD</td>
<td>Yes</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>High-intensity statin therapy should be initiated or continued as first-line therapy in women and men ≤75 years of age, unless contraindicated</td>
</tr>
<tr>
<td>2 Patients with primary elevations of LDL-C ≥190 mg/dL</td>
<td>--</td>
<td>&gt;190</td>
<td>--</td>
<td>--</td>
<td>Adults ≥21 yrs should be treated with statin therapy (10-year ASCVD risk estimation is not required): Use high-intensity statin therapy unless contraindicated</td>
</tr>
<tr>
<td>3 Patients with DM, with LDL 70-189 mg/dL and no ASCVD</td>
<td>No</td>
<td>70 - 189</td>
<td>Yes</td>
<td>--</td>
<td>Moderate-intensity statin therapy should be initiated or continued. High-intensity statin therapy reasonable for ≥7.5% estimated 10-year ASCVD risk unless contraindicated</td>
</tr>
<tr>
<td>4 Patients without ASCVD or DM with LDL-C 70 to 189 mg/dL and estimated 10-year ASCVD risk ≥7.5%</td>
<td>No</td>
<td>70 - 189</td>
<td>No</td>
<td>Yes</td>
<td>Should be treated with moderate- to high-intensity statin therapy</td>
</tr>
</tbody>
</table>
ASCVD risk calculator: Pooled Cohort Equation

10-year risk (%) of ASCVD (non-fatal MI, CHD death, or fatal/non-fatal stroke) is calculated from simple parameters:

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>10 year risk and Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male or female)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Race (African-American or White/other)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Treatment for high BP (yes or no)</td>
<td></td>
</tr>
<tr>
<td>Diabetes (yes or no)</td>
<td></td>
</tr>
<tr>
<td>Smoker (yes or no)</td>
<td></td>
</tr>
</tbody>
</table>

BP, blood pressure
HDL-C, high density lipoprotein-cholesterol
SBP, Systolic blood pressure

### Guidelines specify statin doses

<table>
<thead>
<tr>
<th>Statin</th>
<th>High-intensity ↓ LDL-C by ≥50%</th>
<th>Moderate-intensity ↓ LDL-C by 30–50%</th>
<th>Low-intensity ↓ LDL-C by &lt;30%*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>(40)–80 mg</td>
<td>10–20 mg</td>
<td>–</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>20–40 mg</td>
<td>5–10 mg</td>
<td>–</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>–</td>
<td>20–40 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>–</td>
<td>40–80 mg</td>
<td>10–20 mg</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>–</td>
<td>40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Fluvastatin XL</td>
<td>–</td>
<td>80 mg</td>
<td>–</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>–</td>
<td>40 mg bid</td>
<td>20–40 mg</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>–</td>
<td>2–4 mg</td>
<td>1 mg</td>
</tr>
</tbody>
</table>

**Bold:** Statins and doses evaluated in RCTs

**Italics:** Statins and doses approved by US FDA but not tested in RCTs reviewed

*Should be used in patients unable to tolerate moderate-to high-intensity therapy

Asian ancestry may modify the statin dose prescribed

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L lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease

Issued: July 2014

NICE clinical guideline 181
guidance.nice.org.uk/cg181
Key priorities for implementation – NICE 2014

Identifying and assessing CVD risk

• For the primary prevention of CVD in primary care, use a systematic strategy to **identify people who are likely to be at high risk**.

• Prioritize people for a full formal **risk assessment** if their estimated 10-year risk of CVD is **10%** or more.

• Use the **QRISK2 risk assessment tool** to assess CVD risk for the primary prevention of CVD in people up to and including age 84 years.

• Do not use a risk assessment tool to assess CVD risk in **people with an eGFR <60 ml/min/1.73 m² and/or albuminuria**. These people are at increased risk of CVD.
Key priorities for implementation – NICE 2014

Lipid modification therapy for the primary and secondary prevention of CVD

- Before starting lipid modification therapy for the primary prevention of CVD, take at least 1 lipid sample to measure a full lipid profile. A fasting sample is not needed.

- Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD. Estimate risk using the QRISK2 assessment.

- Start statin treatment in people with CVD with atorvastatin 80 mg. Use a lower dose of atorvastatin if any of the following apply:
  - potential drug interactions
  - high risk of adverse effects
  - patient preference
# Grouping of Statins as per NICE

<table>
<thead>
<tr>
<th>Dose (mg/day)</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>40</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluvastatin</td>
<td>-</td>
<td>-</td>
<td>21%¹</td>
<td>27%¹</td>
<td>33%²</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>-</td>
<td>20%¹</td>
<td>24%¹</td>
<td>29%¹</td>
<td>-</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>-</td>
<td>27%¹</td>
<td>32%²</td>
<td>37%³</td>
<td>42%³⁴</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>-</td>
<td>37%²</td>
<td>43%³</td>
<td>49%³</td>
<td>55%³</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>38%²</td>
<td>43%³</td>
<td>48%³</td>
<td>53%³</td>
<td>-</td>
</tr>
</tbody>
</table>

¹ 20%–30%: low intensity.
² 31%–40%: medium intensity.
³ Above 40%: high intensity.
⁴ Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.
2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)
2016 ESC Guideline suggested target for LDL treatment

Table 5 Risk categories

<table>
<thead>
<tr>
<th>Very high-risk</th>
<th>Subjects with any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.</td>
</tr>
<tr>
<td></td>
<td>DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.</td>
</tr>
<tr>
<td></td>
<td>Severe CKD (GFR &lt;30 mL/min/1.73 m²).</td>
</tr>
<tr>
<td></td>
<td>A calculated SCORE ≥10%.</td>
</tr>
</tbody>
</table>

High-risk

<table>
<thead>
<tr>
<th>Subjects with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markedly elevated single risk factors, in particular cholesterol &gt;8 mmol/L (&gt;310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg.</td>
</tr>
<tr>
<td>Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk).</td>
</tr>
<tr>
<td>Moderate CKD (GFR 30–59 mL/min/1.73 m²).</td>
</tr>
<tr>
<td>A calculated SCORE ≥5% and &lt;10%.</td>
</tr>
</tbody>
</table>

Moderate risk

| SCORE ≥1% and <5% at 10 years. Many middle-aged subjects belong to this category. |

Low-risk

| SCORE <1%. |

2016 European Guidelines on cardiovascular disease prevention in clinical practice

The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)

Recommendations for lipid control

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients at VERY HIGH CV risk, an LDL-C goal &lt;1.8 mmol/L (&lt;70 mg/dL), or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.</td>
<td>I</td>
<td>B</td>
<td>350–353</td>
</tr>
<tr>
<td>In patients at HIGH CV risk, an LDL-C goal &lt;2.6 mmol/L (&lt;100 mg/dL), or a reduction of at least 50% if the baseline is between 2.6 and 5.1 mmol/L (100 and 200 mg/dL) is recommended.</td>
<td>I</td>
<td>B</td>
<td>350–353</td>
</tr>
<tr>
<td>In the remaining patients on LDL-C lowering treatment, an LDL-C goal &lt;3.0 mmol/L (&lt;115 mg/dL) should be considered.</td>
<td>IIa</td>
<td>C</td>
<td>350–353</td>
</tr>
</tbody>
</table>

AACE 2017 Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF ATHEROSCLEROSIS

EXECUTIVE SUMMARY

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Non-HDL is important lipid parameter in T2DM patients

Statin and fibrates are preferred drugs for non-HDL reduction
• Indians have high prevalence of DM, obesity and metabolic syndrome, all of which are characterized by high TG levels, low HDLc and higher prevalence of small dense LDL particles, which is also known as **atherogenic dyslipidemia**.

• Accordingly, the **Lipid Association of India** recommends **non-HDLc as a co-primary target**, as important as LDLc for lipid lowering therapy in Indians.
The world of cholesterol management and coronary disease prevention has come a long way since 2013, when a major practice guideline document called for radical shifts in strategies for lowering LDL-C, drawing praise, reproach, and puzzlement.
From 2013 to 2018 ACC/AHA Cholesterol Guideline: Filling gaps & Expanding Opportunities

✓ Cholesterol guidelines in **2013 takes a much narrower approach** to evidence assessment than prior guidelines

✓ **Focused predominantly on evidence from high quality RCTs**, resulting in the elimination of LDL-C treatment goals, a mainstay in prior guidelines and clinical practice.

✓ **Simplified algorithm of 4 groups**, expanded the number of individuals eligible for statins in the population.

✓ In addition to eliminating LDL-C treatment goals, the old guideline recommended **minimal use of non-statin therapies**.

✓ There were **sparse data supporting the addition of non-statin** therapies to statins to further lower ASCVD events.
From 2013 to 2018 ACC/AHA Cholesterol Guideline: Filling gaps & Expanding Opportunities

- High cholesterol treatment is **not one size fits all**.
- Over the past five years, we've learned even more about **new treatment options** and which patients may benefit from them.
- New guideline provide a **treatment roadmap for clinicians** and tools to help their patients understand and manage their risk and live longer, healthier lives.
- **2018 ACC/AHA Cholesterol Guideline** strongly establishes the importance of **personalized care**.
The New 2018 ACC/AHA Cholesterol Guidelines: What is New

- **LDL-C Targets are back.** LDL-C <70 mg/dl is required for very high risk ASCVD patients.

- For patients with severe primary hypercholesterolemia, achieve LDL-C <100 mg/dl with statins. Add **Ezetimibe** and/or **PCSK9 inhibitors** if required.

- Start **moderate dose statin in DM patients without** measuring 10 years ASCVD risk.

- For 40-75 years, non-DM patients (with LDL-C 70-189 mg/dl) clinician patient discussion is required to start statin if 10 years ASCVD risk is ≥7.5%

- **CAC** (Coronary Artery Calcium Score) can help to take decision on starting statin in primary prevention.

- Being **South Asian** is a risk enhancer for ASCVD, favors initiation of statin therapy in non-DM patients for primary prevention.
Primary Prevention: Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

**ASCVD Risk Enhancers:**
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:
- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

**Risk Discussion:**
- If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class Iib)
- If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)
- Initiate statin to reduce LDL-C ≥50% (Class I)

**If risk decision is uncertain:**
- Consider measuring CAC in selected adults:
  - CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
  - CAC = 1-99 favors statin (especially after age 55)
  - CAC = 100+ and/or ≥75th percentile, initiate statin therapy
## Risk-Enhancing Factors

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*  
- **Metabolic syndrome** (increased waist circumference, elevated triglycerides [≥175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m² with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS
- **History of premature menopause** (before age 40 y) and **history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia**
- **High-risk race/ethnicities** (e.g., South Asian ancestry)
- **Lipid/biomarkers**: Associated with increased ASCVD risk  
  - Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL);  
  - If measured:  
    - **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)  
    - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).  
    - **Elevated apoB** ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor  
    - **ABI** <0.9
Secondary Prevention in Patients With Clinical ASCVD

Clinical ASCVD

Healthy Lifestyle

ASCVD not at very high-risk*

Age ≤75 y
- High-intensity statin (Goal: ↓ LDL-C ≥50%) (Class I)
  - If high-intensity statin not tolerated, use moderate-intensity statin (Class I)

Age >75 y
- Initiation of moderate- or high-intensity statin is reasonable (Class IIa)
- Continuation of high-intensity statin is reasonable (Class IIa)

Very high-risk* ASCVD

High-intensity or maximal statin (Class I)

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

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

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

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* of Future ASCVD Events**

<table>
<thead>
<tr>
<th>Major ASCVD Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent ACS (within the past 12 mo)</td>
</tr>
<tr>
<td>History of MI (other than recent ACS event listed above)</td>
</tr>
<tr>
<td>History of ischemic stroke</td>
</tr>
<tr>
<td>Symptomatic peripheral arterial disease (history of claudication with ABI &lt;0.85, or previous revascularization or amputation (S4.1-39))</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High-Risk Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 y</td>
</tr>
<tr>
<td>Heterozygous familial hypercholesterolemia</td>
</tr>
<tr>
<td>History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>CKD (eGFR 15-59 mL/min/1.73 m²) (S4.1-15, S4.1-17)</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<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>History of congestive HF</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.*
## 2013 and 2018 ACC/AHA Cholesterol Guidelines: Key Comparisons

<table>
<thead>
<tr>
<th></th>
<th>2013 Cholesterol Guidelines</th>
<th>2018 Cholesterol Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statin treatment groups</strong></td>
<td>1. Clinical ASCVD, 2. DM with LDL-C ≥70 mg/dL, 3. 40–75 y of age with LDL-C 70–189 mg/dL and 10-y ASCVD risk ≥7.5%, and 4. severe hypercholesterolemia (LDL-C ≥190 mg/dL)</td>
<td>Unchanged</td>
</tr>
<tr>
<td><strong>Secondary prevention LDL-C threshold</strong></td>
<td>No thresholds</td>
<td>LDL-C ≥70 mg/dL as threshold for non-statin drug consideration</td>
</tr>
<tr>
<td><strong>Risk assessment</strong></td>
<td>Pooled Cohort Equations</td>
<td>Pooled Cohort Equations and <strong>categorization</strong> as low risk (&lt;5%), borderline risk (5%–&lt;7.5%), intermediate risk (7.5%–&lt;20%), and high risk (≥20%)</td>
</tr>
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## 2013 and 2018 ACC/AHA Cholesterol Guidelines: Key Comparisons

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<td><strong>Additional risk factors</strong></td>
<td>Can be considered if treatment decision uncertain: primary LDL-C $\geq 160$ mg/dL, family history of premature ASCVD, hs-CRP $\geq 2$ mg/L, CAC score $\geq 300$ Agatston units or $\geq 75$th percentile for age/sex/ethnicity, ABI $&lt; 0.9$, or high lifetime risk of ASCVD</td>
<td>In intermediate-risk adults, risk-enhancing factors favor statin initiation/intensification: same as 2013 guidelines (except CAC) and include metabolic syndrome, CKD, chronic inflammatory conditions, premature menopause and preeclampsia, high-risk race/ethnicity, persistent triglycerides $\geq 175$ mg/dL, elevated Lp(a) or apo B</td>
</tr>
<tr>
<td><strong>CAC testing</strong></td>
<td>In select individuals when statin decision uncertain, upgrade risk if CAC $\geq 300$ or $&gt; 75$th percentile for age/sex/ethnicity</td>
<td>Reasonable in intermediate-risk or selected borderline-risk adults with uncertainty about statins</td>
</tr>
<tr>
<td><strong>Fasting lipid measurements</strong></td>
<td>Fasting preferred</td>
<td>Fasting or non-fasting appropriate unless known triglycerides $\geq 400$ mg/dL</td>
</tr>
<tr>
<td><strong>Children and young adults</strong></td>
<td>No specific statements</td>
<td>Age $\geq 10$ y with persistent LDL-C $\geq 190$ mg/dL or $\geq 160$ with likely FH, statins reasonable</td>
</tr>
</tbody>
</table>
### 2013 and 2018 ACC/AHA Cholesterol Guidelines: Key Comparisons

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<th>Non-statin agents</th>
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</table>
| **Individuals at higher ASCVD risk with less-than anticipated response to statin or statin candidates who are completely statin intolerant; recommend non-statins with proven ASCVD benefit in RCTs** | ASCVD on maximal statin therapy:  
• **Ezetimibe** for clinical ASCVD and LDL-C ≥70  
• **Ezetimibe** and **PCSK9 inhibitor** as add-on therapy for very high-risk ASCVD and LDL-C ≥70 mg/dL | **Ezetimibe** should be initiated first, then PCSK9 inhibitor |
| | LDL-C ≥190 mg/dL on maximal statin therapy:  
• **Ezetimibe** if LDL-C <50% reduced on statin or remains ≥100 mg/dL  
• **Bile acid sequestrant** if LDL-C <50% reduced on statin and ezetimibe | **PCSK9 inhibitor after statin and ezetimibe** if LDL-C still ≥100 mg/dL or if LDL-C still ≥130 mg/dL and baseline LDL-C ≥220 mg/dL |
Major Dyslipidemia Guidelines and Their Discrepancies: A Need for Consensus

Estimating Risk

• Perhaps one of the most widely reported differences among the discussed guidelines is their use of different risk estimators.

• ACC/AHA and USPSTF recommend the ACC/AHA Pooled Cohort Risk Equations (PCRE), NICE recommends QRISK2 and ESC/EAS recommends the Systemic Coronary Risk Evaluation (SCORE) estimator.

• Risk estimators all include age, sex, total cholesterol, HDL cholesterol and systolic blood pressure, but vary on whether they include ethnicity, treatment for hypertension or diabetes, CKD.
Major Dyslipidemia Guidelines and Their Discrepancies: A Need for Consensus

Treatment Recommendations for Primary and Secondary Prevention

• Another contentious issue among different guideline committees that goes beyond risk estimation is the approach to treatment of moderate- to high-risk patients.

• Although all guidelines unanimously emphasize lifestyle changes as a first line intervention and agree that statin therapy is a mainstay for patients deemed to require lipid-lowering medications, dosing and titration of statin medications differ significantly.
Major Dyslipidemia Guidelines and Their Discrepancies: A Need for Consensus

Treatment in Special Groups and Safety Profile

- Guidelines differ in their recommendations for starting and continuing statin therapy for patients older than age 75 or those with life expectancy less than 5 years.
- ESC/EAS is most aggressive in these populations, recommending initiation of low-dose statin therapy for primary prevention if ASCVD is particularly high.
- ACC/AHA recommends statin usage in elderly primary prevention patients only if the patient is already tolerating statins and a moderate-intensity statin for secondary prevention.
- Most guidelines do not comment specifically on ESRD.
In 2013 ACC/AHA Guideline suggested treatment based on 30% and 50% reduction of LDL.

2014 NICE guideline suggested non-HDL-C is a target.


Lipid Association of India in 2017 suggested non-conventional risk factors and in very high risk group LDL<50 mg/dl.

AACE in 2017 suggested LDL-C <55 mg/dl in very high risk group.

In 2018 ACC/AHA suggested personalized treatment goal in Dyslipidemia management.
Key Message

- Guidelines are not static documents but rather iterative pieces that morph, grow, and build on one another.
- The new 2018 ACC/AHA cholesterol guidelines expand on the sturdy framework of the old guidelines to provide a more complete picture, one that takes into account the rapidly evolving landscape of the cholesterol field.
- Ultimately, the value of a guideline is determined by how effectively it is implemented into practice and by how much morbidity and mortality are avoided through its application.