2018
AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA

Guideline on the Management of Blood Cholesterol: Executive Summary
2018 Cholesterol Guideline Writing Committee

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Measurements of LDL-C and Non-HDL-C

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C.</td>
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<tr>
<td>I</td>
<td>B-NR</td>
<td>In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL (≥4.5 mmol/L) or higher, a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C.</td>
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## Measurements of LDL-C and Non-HDL-C

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<td>IIa</td>
<td>C-LD</td>
<td>For patients with an LDL-C level less than 70 mg/dL (&lt;1.8 mmol/L), measurement of direct LDL-C or modified LDL-C estimate is reasonable to improve accuracy over the Friedewald formula.</td>
</tr>
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<td>IIa</td>
<td>C-LD</td>
<td>In adults who are 20 years of age or older and without a personal history of ASCVD but with a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.</td>
</tr>
<tr>
<td></td>
<td>High Intensity</td>
<td>Moderate Intensity</td>
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<tr>
<td>---------------------</td>
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</tr>
<tr>
<td>LDL-C lowering†</td>
<td>≥50%</td>
<td>30%–49%</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin (40 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin 20 mg</td>
<td>Atorvastatin 10 mg (20 mg)</td>
<td></td>
</tr>
<tr>
<td>40 mg</td>
<td>Rosuvastatin (5 mg) 10 mg</td>
<td></td>
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<tr>
<td></td>
<td>Simvastatin 20–40 mg§</td>
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<tr>
<td>...</td>
<td>Pravastatin 40 mg (80 mg)</td>
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<td>Lovastatin 40 mg (80 mg)</td>
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<td>Fluvastatin 40 mg BID</td>
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<td>Pitavastatin 1–4 mg</td>
<td>Pravastatin 10–20 mg</td>
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Table 4. Very High-Risk* of Future ASCVD Events

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<tr>
<th>Major ASCVD Events</th>
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<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)</td>
</tr>
</tbody>
</table>
### High-Risk Conditions

<table>
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<tr>
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<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)</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>
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Primary Prevention: Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → statin

Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

Age 40-75 y and
LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion

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

<5% “Low Risk”
Risk discussion: Emphasize lifestyle to reduce risk factors (Class I)

5% - <7.5% “Borderline Risk”
Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

≥7.5% - <20% “Intermediate Risk”
Risk discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

≥20% “High Risk”
Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)

If risk decision is uncertain:
- Considering 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
AHA/ACC Special Report

Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease

A Special Report From the American Heart Association and American College of Cardiology

Donald M. Lloyd-Jones, MD, ScM, FACC, FAHA
Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

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<tr>
<td>• Long duration (≥10 years for type 2 diabetes mellitus (S.4.3-20) or ≥20 years for type 1 diabetes mellitus)</td>
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<td>• Albuminuria ≥30 mcg of albumin/mg creatinine</td>
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<td>• Retinopathy</td>
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<tr>
<td>• Neuropathy</td>
</tr>
<tr>
<td>• ABI &lt;0.9</td>
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Table 6. Risk-Enhancing Factors for Clinician–Patient Risk Discussion

<table>
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<tr>
<th>Risk-Enhancing Factors</th>
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<tr>
<td>• Family history of premature ASCVD (males, age &lt;55 y; females, age &lt;65 y)</td>
</tr>
<tr>
<td>• 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])*</td>
</tr>
<tr>
<td>• Metabolic syndrome (increased waist circumference, elevated triglycerides [&gt;175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [&lt;40 mg/dL in men; &lt;50 in women mg/dL] are factors; tally of 3 makes the diagnosis)</td>
</tr>
<tr>
<td>• Chronic kidney disease (eGFR 15–59 mL/min/1.73 m² with or without albuminuria; not treated with dialysis or kidney transplantation)</td>
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<tr>
<td>• Chronic inflammatory conditions such as psoriasis, RA, or HIV/AIDS</td>
</tr>
<tr>
<td>• History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia</td>
</tr>
<tr>
<td>• High-risk race/ethnicities (e.g., South Asian ancestry)</td>
</tr>
<tr>
<td>Risk-Enhancing Factors</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td><strong>Lipid/biomarkers</strong>: Associated with increased ASCVD risk</td>
</tr>
<tr>
<td>o Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL);</td>
</tr>
<tr>
<td>o If measured:</td>
</tr>
<tr>
<td>▪ Elevated high-sensitivity C-reactive protein (≥2.0 mg/L)</td>
</tr>
<tr>
<td>▪ 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).</td>
</tr>
<tr>
<td>▪ 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 &gt;160 mg/dL and constitutes a risk-enhancing factor</td>
</tr>
<tr>
<td>▪ ABI &lt;0.9</td>
</tr>
</tbody>
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Figure 2. Overall conceptual approach to risk assessment and decision-making regarding the intensity of prevention efforts and use of drug therapy in primary prevention of ASCVD.

- Estimate Absolute 10-year ASCVD Risk
  - Low Risk: 0 – <5%
  - Borderline Risk: 5% – <7.5%
  - Intermediate Risk: 7.5% – <20%
  - High Risk: ≥20%

- Clinician-patient discussion considering risk-enhancing factors and net benefit of therapy

- If uncertainty remains, consider CAC score and revise decision based on results

- Lifestyle modification
- Lifestyle and drug therapy
Figure 3. Algorithm of clinical approach to incorporate CAC measurement in risk assessment for borderline- and intermediate-risk patients.

10-Year Risk:
- 5% - <7.5% or 7.5% - <20%

Consider Risk-Enhancing Factors

Engage Patient in Discussion Regarding Net Benefit of Statin Therapy

Decision

Decision for No Drug Therapy

Decision for Drug Therapy

Patient Undecided or Clinical Uncertainty Regarding Net Benefit of Statin Therapy

Consider CAC measurement if performed:

- CAC = 0 AU
- CAC 1-99 AU and <75th %ile for age/sex/race/ethnicity
- CAC ≥100 AU or ≥75th %ile for age/sex/race/ethnicity

See 2018 Cholesterol Clinical Practice Guidelines

Below Threshold for Statin Benefit Consider avoiding or postponing drug therapy.*

Subclinical atherosclerosis present; risk estimate similar. Repeat clinician-patient discussion with new information. Consider statin therapy now or postpone statin and consider repeat CAC in 5 years.

Above Threshold for Statin Benefit Recommend statin therapy.

*Clinicians and patients may not wish to postpone therapy in patients with a CAC score of 0 and diabetes mellitus, heavy current cigarette smoking, or strong family history of premature ASCVD.
Case Discussion
Case 1

• 50 y/o female, BMI 28, WC 30”
• No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking
• TC 224 mg/dL, LDL 140 mg/dL, HDL 51 mg/dL, TG’s 165 mg/dL, nonHDL 173 mg/dL
• Rx: Risk Scoring
  High intensity statin
  Moderate intensity statin
  Lifestyle intervention
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a) etc
  CAC
Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

- Age 0-19 y
  - Lifestyle to prevent or reduce ASCVD risk
  - Diagnosis of Familial Hypercholesterolemia → statin

- Age 20-39 y
  - Estimate lifetime risk
  - Encourage lifestyle to reduce ASCVD risk
  - Consider statin if family history of premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

- Age 40-75 y and
  - LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L)
  - Without diabetes mellitus
  - 10-year ASCVD risk percent begins risk discussion

- LDL-C ≥190 mg/dL (≥4.9 mmol/L)
  - No risk assessment; High-intensity statin (Class I)

- Diabetes mellitus and age 40-75 y
  - Moderate-intensity statin (Class I)

- Diabetes mellitus and age 40-75 y
  - Risk assessment to consider high-intensity statin (Class IIa)

- Age >75 y
  - Clinical assessment, Risk discussion
Case 1

- 50 y/o female, BMI 28, WC 30”
- No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking
- TC 224 mg/dL, LDL 140 mg/dL, HDL 51 mg/dL, TG’s 165 mg/dL, nonHDL 173 mg/dL. BP 130/78
- Rx: Risk Scoring ✔
  - High intensity statin ✗
  - Moderate intensity statin ✗
  - Lifestyle intervention ✔
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a) etc ✗
  - CAC ✗
Case 1

• 50 y/o female, BMI 28, WC 30”
• No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking
• TC 224 mg/dL, LDL 140 mg/dL, HDL 51 mg/dL, TG’s 165 mg/dL, nonHDL 173 mg/dL. BP 130/78
• Rx: Risk Scoring ✔ 1.6%
  High intensity statin ✗
  Moderate intensity statin ✗
  Lifestyle intervention ✔
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a) etc ✗
  CAC ✗
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:
- Low Risk:
  - Emphasize lifestyle to reduce risk factors (Class I)

Risk discussion:
- Borderline Risk:
  - If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

Risk discussion:
- Intermediate Risk:
  - If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30%-49% (Class I)

Risk discussion:
- High Risk:
  - 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
Case 2

- 45 y/o female, BMI 38, WC 36”
- No ASCVD, DM2 for 12 years, HTN on Rx, no FHx of early CAD, + smoking
- TC 174 mg/dL, LDL 100 mg/dL, HDL 42 mg/dL, TG’s 162 mg/dL, nonHDL 132 mg/dL, BP 140/85, ACR 38 mg/g creat
- Rx: Risk Scoring
  - High intensity statin
  - Moderate intensity statin
  - Lifestyle intervention
  - Risk Enh Fc: hsCRP, ABI, apoB, LP(a), etc
  - CAC
Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → statin

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Age 40-75 y and
LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion

Age ≥75 y
Clinical assessment, Risk discussion

LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

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Risk assessment to consider high-intensity statin (Class IIa)
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- 45 y/o female, BMI 38, WC 36”
- No ASCVD, DM2 for 12 years, HTN, no FHx of early CAD, + smoking
- TC 174 mg/dL, LDL 100 mg/dL, HDL 42 mg/dL, TG’s 162 mg/dL, nonHDL 132 mg/dL, BP 140/85, ACR 38 mg/g creat
- Rx: Risk Scoring ✓ **optional as DM already high risk
  - High intensity statin ✓ (option due to multiple RF’s)
  - Moderate intensity statin ✓
  - Lifestyle intervention ✓
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✗
  - CAC ✓ (in some cases)
Case 3

• 48 y/o male, BMI 27, WC 42”
• No ASCVD, DM2 for 8 years, no HTN, no FHx of early CAD, no smoking, ACR 45 mg/g creat
• TC 162 mg/dL, LDL 90 mg/dL, HDL 42 mg/dL, TG’s 150 mg/dL, nonHDL 120 mg/dL
• Rx: Risk Scoring
  High intensity statin
  Moderate intensity statin
  Lifestyle intervention
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a) etc
  CAC
Case 3

- 48 y/o male, BMI 27, WC 42”
- No ASCVD, DM2 for 8 years, no HTN, no FHx of early CAD, no smoking, ACR 45 mg/g creat
- TC 162 mg/dL, LDL 90 mg/dL, HDL 42 mg/dL, TG’s 150 mg/dL, nonHDL 120 mg/dL
- Rx: Risk Scoring ✗
  - High intensity statin ✗
  - Moderate intensity statin ✔
  - Lifestyle intervention ✔
- Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✗
- CAC ✔ (in some cases)
Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → statin

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Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

Age 40-75 y and
LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion

LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion
Case 4

• 62 y/o female, BMI 30, WC 45”, BP 148/85
• No ASCVD, no DM, HTN, no FHx of early CAD, no smoking, hx of RA. Do not want statin “because it cause dementia”
• TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
• Rx: Risk Scoring
  High intensity statin
  Moderate intensity statin
  Lifestyle intervention
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a) etc
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Case 4

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- TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
- Rx: Risk Scoring ✔
  - High intensity statin ✗
  - Moderate intensity statin ✗
  - Lifestyle intervention ✔
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✗
  - CAC ✗
Case 4

• 62 y/o female, BMI 30, WC 45”, BP 148/85
• No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking, hx of RA. Do not want statin “because it cause dementia”
• TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
• Rx: Risk Scoring 9.9%
  High intensity statin
  Moderate intensity statin
  Lifestyle intervention
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc
  CAC
Case 4

- 62 y/o female, BMI 30, WC 45”, BP 148/85
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- TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
- Rx: Risk Scoring 9.9%
  - High intensity statin ×
  - Moderate intensity statin ✔ after discussion
  - Lifestyle intervention ✔
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✔ No hsCRP - RA
  - CAC ✔
ASCVD Risk Enhancers:
- Family history of premature ASCVD
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- Chronic kidney disease
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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:
- <5% “Low Risk”
  - Emphasize lifestyle to reduce risk factors (Class I)
- 5% - <7.5% “Borderline Risk”
  - If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)
- ≥7.5% - <20% “Intermediate Risk”
  - If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)
- ≥20% “High Risk”
  - 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
Case 4

- 62 y/o female, BMI 30, WC 45”, BP 148/85
- No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking, hx of RA. Do not want statin “because it cause dementia”
- TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
- Rx: Risk Scoring 9.9%
  - High intensity statin
  - Moderate intensity statin
  - Lifestyle intervention ✔
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✔ No hsCRP - RA
  - CAC 74
Figure 3. Algorithm of clinical approach to incorporate CAC measurement in risk assessment for borderline- and intermediate-risk patients.

10-Year Risk:
5% – <7.5% or 7.5% – <20%

Consider Risk-Enhancing Factors

Engage Patient in Discussion Regarding Net Benefit of Statin Therapy

Decision

Decision for No Drug Therapy

Decision for Drug Therapy

Patient Undecided or Clinical Uncertainty Regarding Net Benefit of Statin Therapy

Consider CAC measurement. (if performed):

CAC = 0 AU

Below Threshold for Statin Benefit
Consider avoiding or postponing drug therapy.*

CAC 1–99 AU and <75th %ile for age/sex/race/ethnicity

Subclinical atherosclerosis present; risk estimate similar. Repeat clinician-patient discussion with new information. Consider statin therapy now or postpone statin and consider repeat CAC in 5 years.

CAC ≥100 AU or ≥75th %ile for age/sex/race/ethnicity

Above Threshold for Statin Benefit
Recommend statin therapy.

See 2018 Cholesterol Clinical Practice Guidelines

*Clinicians and patients may not wish to postpone therapy in patients with a CAC score of 0 and diabetes mellitus, heavy current cigarette smoking, or strong family history of premature ASCVD.
Case 4

• 62 y/o female, BMI 30, WC 45”, BP 148/85
• No ASCVD, no DM, no HTN, no FHx of early CAD, no smoking, hx of RA. Do not want statin “because it cause dementia”
• TC 197 mg/dL, LDL 135 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 166 mg/dL
• Rx: Risk Scoring 9.9%
  - High intensity statin ✗
  - Moderate intensity statin ✔
  - Lifestyle intervention ✔
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc  ✔ No hsCRP - RA
  - CAC 74
Case 5

- 59 y/o male, BMI 30, WC 45”, BP 145/90 on Rx
- No ASCVD, no DM, HTN on Rx, + FHx of early CAD, no smoking
- TC 187 mg/dL, LDL 125 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 156 mg/dL, FBS 107
- Rx: Risk Scoring
  - High intensity statin
  - Moderate intensity statin
  - Lifestyle intervention
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc
  - CAC
Case 5

- 59 y/o male, BMI 30, WC 45”, BP 145/90 on Rx
- No ASCVD, no DM, HTN, + FHx of early CAD, no smoking
- TC 187 mg/dL, LDL 125 mg/dL, HDL 31 mg/dL, TG’s 155 mg/dL, nonHDL 156 mg/dL, FBS 107
- Rx: Risk Scoring ✔ May skip: already > 3 major RF
  - High intensity statin ✗
  - Moderate intensity statin ✔
  - Lifestyle intervention ✔
- Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✗
- CAC ✗ (Depends on risk scoring and other RF)
**ASCVD Risk Enhancers:**
- Family history of premature ASCVD
- Persistently elevated LDL-C \( \geq 160 \text{ mg/dL} \) \( \geq 4.1 \text{ mmol/L} \)
- 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 \( \geq 175 \text{ mg/dL} \), \( \geq 2.0 \text{ mmol/L} \)

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

---

**Risk discussion:**
- **<5% “Low Risk”**
- **5% - <7.5% “Borderline Risk”**
- **\( \geq 7.5\% - <20\% “Intermediate Risk”**
- **\( \geq 20\% “High Risk”**

---

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 \( \geq 75\% \) percentile, initiate statin therapy
Case 6

• 55 y/o male, BMI 35, WC 43”, BP 145/85 on Rx
• + ASCVD, s/p CABG, DM, HTN, + FHx of early CAD, no smoking, + DR, severe claudication sx. Grade 3 SEM
• TC 181 mg/dL, LDL 110 mg/dL, HDL 40 mg/dL, TG’s 155 mg/dL, nonHDL 141 mg/dL
• On high intensity statin: rosuvastatin 40 mg
Case 6

- 55 y/o male, BMI 35, WC 43”, BP 145/85 on Rx
- + ASCVD, s/p CABG, DM, HTN, + FHx of early CAD, no smoking, + DR, severe claudication sx. Grade 3 SEM
- TC 181 mg/dL, LDL 110 mg/dL, HDL 40 mg/dL, TG’s 155 mg/dL, nonHDL 141 mg/dL
- Rx: Risk Scoring
  - Lifestyle intervention
  - Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc
  - CAC
Case 6

- 55 y/o male, BMI 35, WC 43”, BP 145/85 on Rx
- + ASCVD, s/p CABG, DM, HTN, + FHx of early CAD, no smoking, + DR, severe claudication sx. Grade 3 SEM
- TC 181 mg/dL, LDL 110 mg/dL, HDL 40 mg/dL, TG’s 155 mg/dL, nonHDL 141 mg/dL
- Rx: Risk Scoring ✗
  
  Lifestyle intervention ✔
  
  Risk Enh Fc: hsCRP, ABI, apoB, Lp(a), etc ✔
  
  CAC ✗
Cholesterol Calculator App

Includes:
• Current LDL-C
• Current statin Rx
• Current non statin Rx (if available)
Case 6

• 55 y/o male, BMI 35, WC 43”, BP 145/85 on Rx
• + ASCVD, s/p CABG, DM, HTN, + FHx of early CAD, no smoking, + DR, severe claudication sx. Grade 3 SEM
• TC 181 mg/dL, LDL 110 mg/dL, HDL 40 mg/dL, TG’s 155 mg/dL, nonHDL 141 mg/dL, Lp(a): 86
• Baseline untreated estimated LDL 231 mg/dL (not a 50% decrease from baseline with current therapy)
• Next STEP??
Case Study 9

DEFINITE FAMILIAL HYPERCHOLESTEROLEMIA
Table 4. 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 1 major ASCVD event and multiple high-risk conditions.
Figure 1. 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)
  - If on maximal statin therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe may be reasonable (Class IIa)

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)
Summary of Effects of PCSK9i Evolocumab

- 27,564 pts w/ stable ASCVD & LDL-C ≥70mg/dL on a statin
- ↓ LDL-C by 59% down to a median of 30 mg/dL
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated

**Placebo**

- 59% reduction
- P < 0.00001

**Evolocumab**

- Absolute ↓ 56 mg/dL
- (median 30 mg/dL, IQR 19-46 mg/dL)

**HR 0.85 (0.79-0.92)**
**P < 0.0001**

**KIM Rate (%) at 3 Years**

- **CVD, MI, stroke**
  - UA, cor revasc: 14.6 vs 12.6
  - CVD, MI, stroke: 9.9 vs 7.9
  - **HR 0.80 (0.73-0.88)**
  - **P < 0.0001**

Sabatine MS et al. NEJM 2017;376:1713-22
Landmark Analysis

16% RRR

HR 0.84 (95% CI 0.74-0.96)
P = 0.008

25% RRR

HR 0.75 (95% CI 0.66-0.85)
P < 0.00001

CV Death, MI, Stroke

Placebo

Evolocumab

Months from Randomization

Sabatine MS et al. NEJM 2017;376:1713-22
Impact of PCSK9 Inhibition Among Patients with Recent ACS

ODYSSEY Outcomes Trial

18,924 high-risk patients with an ACS within the preceding 1-12 months and an LDL-C ≥70 mg/dL on background high-intensity statin therapy randomized to alirocumab or placebo for a median of 2.8 years

ARR 1.6%
(tased on cumulative incidence)

MACE: CHD death, non-fatal MI, ischemic stroke, or unstable angina requiring hospitalization

HR 0.85
(95% CI 0.78, 0.93)
P=0.0003

Beg PG, et al. Presented at: ACC.18 Scientific Sessions; March 10, 2018; Orlando, FL.
Primary Efficacy Endpoint (MACE) in Prespecified Baseline LDL-C Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Patients</th>
<th>Incidence (%)</th>
<th>HR (95% CI)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;80</td>
<td>7164</td>
<td>8.3</td>
<td>9.5</td>
<td>0.86 (0.74, 1.01)</td>
</tr>
<tr>
<td>80 - &lt;100</td>
<td>6128</td>
<td>9.2</td>
<td>9.5</td>
<td>0.96 (0.82, 1.14)</td>
</tr>
<tr>
<td>≥100</td>
<td>5629</td>
<td>11.5</td>
<td>14.9</td>
<td>0.76 (0.65, 0.87)</td>
</tr>
</tbody>
</table>

*P-values for interaction

Steg PG, et al. Presented at: ACC.18 Scientific Sessions; March 10, 2018; Orlando, FL.
Case Study 6: Treatment

• Started on SC injection of PCSK9i Q2W on top of high intensity statin. TLC’s encouraged.
• After 3 months:
  
  * LDL-C 52 mg/dL (>50% reduction)
  * nonHDL-C 64 mg/dL (>50% reduction)
“Good news.
Your cholesterol has stayed the same,
but the research findings have changed.”