2019 ESC/EAS Guidelines for the management of dyslipidaemias: 
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lipid modification to reduce cardiovascular risk
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Conflict of Interest:

Research support, speaking and consulting honoraria from several diagnostic and pharmaceutical companies
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (1)

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¹Representing the European Atherosclerosis Society (EAS)
Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

Low-density lipoprotein cholesterol (LDL-C) values and treatment goals:
- **3.0 mmol/L (116 mg/dL)**: Treatment goal for Low CV Risk
- **2.6 mmol/L (100 mg/dL)**: Treatment goal for Moderate CV Risk
- **1.8 mmol/L (70 mg/dL)**: Treatment goal for High CV Risk
- **1.4 mmol/L (55 mg/dL)**: Treatment goal for Very-High CV Risk

**Treatment goals for LDL-C**
- **Low CV Risk (SCORE ≤1%)**: LDL-C target ≤3.0 mmol/L (116 mg/dL)
- **Moderate CV Risk (SCORE 1% to 5%)**: LDL-C target ≤2.6 mmol/L (100 mg/dL)
- **High CV Risk (SCORE 5% to 10%)**: LDL-C target ≤1.8 mmol/L (70 mg/dL)
- **Very-High CV Risk (≥10%)**: LDL-C target ≤1.4 mmol/L (55 mg/dL)

**Low CV Risk**
- Low risk without other risk factors
- SCORE <1%

**Moderate CV Risk**
- Moderate risk without other risk factors
- SCORE 1% to 5%
- Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors

**High CV Risk**
- High risk without other risk factors
- SCORE 5% to 10%
- Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
- FH without other major risk factors
- Moderate CKD (eGFR 30–59 mL/min)
- DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor

**Very-High CV Risk**
- Very high risk without other risk factors
- SCORE ≥10%
- FH with ASCVD or with another major risk factor
- Severe CKD (eGFR <30 mL/min)
- DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)

New recommendations (1)

Cardiovascular imaging for assessment of ASCVD risk
Assessment of arterial (carotid and/or femoral) plaque burden on arterial ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.

Cardiovascular imaging for assessment of ASCVD risk
CAC score assessment with CT should be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.

Lipid analyses for CVD risk estimation
Lp(a) measurement should be considered at least once in each adult person’s lifetime to identify those with very high inherited Lp(a) levels >180 mg/dL (>430 nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolaemia.
New recommendations (2)

Drug treatments of patients with hypertriglyceridaemia
In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135 - 499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2g/day) should be considered in combination with statins.

Treatment of patients with heterozygous FH
In primary prevention, for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.

Treatment of dyslipidaemias in older people
Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75.

Treatment of dyslipidaemias in older people
Initiation of statin treatment for primary prevention in older people aged >75 may be considered, if at high risk or above.
New recommendations (3)

**Treatment of dyslipidaemias in DM**

In patients with T2DM at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55mg/dL) is recommended.

In patients with T2DM at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) is recommended.

Statins are recommended in patients with T1DM who are at high or very-high risk.

**Intensification of statin therapy should be considered before the introduction of combination therapy.**

If the goal is not reached, statin combination with ezetimibe should be considered.

**Treatment of dyslipidaemias in DM**

Statin therapy is not recommended in pre-menopausal patients with DM who are considering pregnancy or not using adequate contraception.
<table>
<thead>
<tr>
<th>2016</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacological LDL-C lowering</td>
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</tr>
<tr>
<td>If the LDL goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.</td>
<td>If the goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.</td>
</tr>
</tbody>
</table>
### Changes in recommendations (3)

<table>
<thead>
<tr>
<th>2016</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacological LDL-C lowering</strong>&lt;br&gt;In patients at very-high risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.</td>
<td><strong>Pharmacological LDL-C lowering</strong>&lt;br&gt;For secondary prevention, patients at very-high risk not achieving their goal on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.</td>
</tr>
<tr>
<td>Changes in recommendations (4)</td>
<td></td>
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<tr>
<td>------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>2016</strong></td>
<td><strong>2019</strong></td>
</tr>
<tr>
<td>Drug treatments of hypertriglyceridaemia</td>
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</tr>
<tr>
<td>Statin treatment may be considered as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia.</td>
<td>Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [TG &gt;2.3 mmol/L (200 mg/dL)].</td>
</tr>
</tbody>
</table>
## Changes in recommendations (5)

<table>
<thead>
<tr>
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<tr>
<td><strong>Treatment of patients with heterozygous FH</strong></td>
<td><strong>Treatment of patients with heterozygous FH</strong></td>
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<tr>
<td>Treatment should be considered to aim at reaching an LDL-C &lt;2.6 mmol/L (&lt;100 mg/dL) or in the presence of CVD &lt;1.8 mmol/L (&lt;70 mg/dL). If targets cannot be reached, maximal reduction of LDL-C should be considered using appropriate drug combinations.</td>
<td>For FH patients with ASCVD who are at very-high risk, treatment to achieve at least a 50% reduction from baseline and an LDL-C &lt;1.4 mmol/L (&lt;55 mg/dL) is recommended. If goals cannot be achieved, a drug combination is recommended.</td>
</tr>
<tr>
<td>2016</td>
<td>2019</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
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<tr>
<td><strong>Treatment of patients with heterozygous FH</strong></td>
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</tr>
<tr>
<td>Treatment with a PCSK9 antibody should be considered in FH patients</td>
<td>Treatment with a PCSK9 inhibitor is recommended in very-high-risk</td>
</tr>
<tr>
<td>with CVD or with other factors putting them at very-high risk for</td>
<td>FH patients if the treatment goal is not achieved on maximal</td>
</tr>
<tr>
<td>CHD, such as other CV risk factors, family history, high Lp(a), or</td>
<td>tolerated statin plus ezetimibe.</td>
</tr>
<tr>
<td>statin intolerance.</td>
<td></td>
</tr>
</tbody>
</table>
### Changes in recommendations (7)

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<td><strong>Treatment of dyslipidaemias in older adults</strong></td>
<td><strong>Treatment of dyslipidaemias in older adults</strong></td>
</tr>
<tr>
<td>Since older people often have comorbidities and have altered pharmacokinetics, lipid-lowering medication should be started at a lower dose and then titrated with caution to achieve target lipid levels that are the same as in younger people.</td>
<td>It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.</td>
</tr>
</tbody>
</table>
## Changes in recommendations (8)

<table>
<thead>
<tr>
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<tr>
<td><strong>Lipid-lowering therapy in patients with ACS</strong></td>
<td><strong>Lipid-lowering therapy in patients with ACS</strong></td>
</tr>
<tr>
<td>If the LDL-C target is not reached with the highest tolerated statin</td>
<td>If the LDL-C goal is not achieved after 4 - 6 weeks despite maximal</td>
</tr>
<tr>
<td>dose and/or ezetimibe, PCSK9 inhibitors may be considered on top of</td>
<td>tolerated statin therapy and ezetimibe, addition of a PCSK9</td>
</tr>
<tr>
<td>lipid-lowering therapy; or alone or in combination with ezetimibe</td>
<td>inhibitor is recommended.</td>
</tr>
<tr>
<td>in statin-intolerant patients or in whom a statin is contraindicated.</td>
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</tr>
</tbody>
</table>

**Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies**

LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9.

### Intensity of lipid lowering treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average LDL-C reduction</th>
</tr>
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<tbody>
<tr>
<td>Moderate intensity statin</td>
<td>≈ 30%</td>
</tr>
<tr>
<td>High intensity statin</td>
<td>≈ 50%</td>
</tr>
<tr>
<td>High intensity statin plus ezetimibe</td>
<td>≈ 65%</td>
</tr>
<tr>
<td>PCSK9 inhibitor</td>
<td>≈ 60%</td>
</tr>
<tr>
<td>PCSK9 inhibitor plus high intensity statin</td>
<td>≈ 75%</td>
</tr>
<tr>
<td>PCSK9 inhibitor plus high intensity statin plus ezetimibe</td>
<td>≈ 85%</td>
</tr>
</tbody>
</table>

### Treatment outcomes

- **% reduction LDL-C**
- **Baseline LDL-C**
- **Absolute reduction LDL-C**
- **Relative risk reduction**
- **Baseline risk**
- **Absolute risk reduction**

**Intensity of lipid lowering treatment**

- Treatment: Moderate intensity statin, High intensity statin, High intensity statin plus ezetimibe, PCSK9 inhibitor, PCSK9 inhibitor plus high intensity statin plus ezetimibe
- Average LDL-C reduction: ≈ 30%, ≈ 50%, ≈ 65%, ≈ 60%, ≈ 75%, ≈ 85%
Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering
Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (1)

In selected low- and moderate-risk patients

Risk modifiers
Imaging (subclinical atherosclerosis)
Risk reclassification?

Total CV risk assessment
Baseline LDL-C levels
Indication for drug therapy?

Y
N

Central Illustration: Lower panel: Treatment algorithm for pharmacological LDL-C lowering (2)

1. Define treatment goal

2. High potency statin at highest recommended / tolerable dose to reach the goal

3. LDL-C goal reached?
   - Y
   - N

   - Y
   - N

   - N: Lifestyle advice / Lifestyle intervention

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Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (3)

- Follow-up annually, or more frequently if indicated
- Add ezetimibe
- Follow-up annually, or more frequently if indicated
- Add PCSK9 inhibitor

- LDL-C goal reached?
- Y
- N

- Secondary prevention (very-high-risk)
  - Primary prevention: patients with FH and another major risk factor (very-high-risk)
- Consider adding PCSK9 inhibitor

- Primary prevention: patients at very-high risk but without FH

Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

- **Low**
  - SCORE <1%
  - Treatment goal for LDL-C: 3.0 mmol/L (116 mg/dL)
  - ≥50% reduction from baseline: 2.6 mmol/L (100 mg/dL)
  - 1.8 mmol/L (70 mg/dL)
  - 1.4 mmol/L (55 mg/dL)

- **Moderate**
  - SCORE ≥1% and <5%
  - Treatment goal for LDL-C: 2.6 mmol/L (100 mg/dL)
  - Moderate CV Risk

- **High**
  - SCORE ≥5% and <10%
  - Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
  - FH without other major risk factors
  - Moderate CKD (eGFR 30–59 mL/min)
  - DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor

- **Very-High**
  - ASCVD (clinical/imaging)
  - SCORE ≥10%
  - FH with ASCVD or with another major risk factor
  - Severe CKD (eGFR <30 mL/min)
  - DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)

- **CV Risk**
  - Low
  - Moderate
  - High
  - Very-High