**Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD**

**INITIAL CONSIDERATIONS:**
- Measure non-fasting **full lipid profile** (total cholesterol, HDL-C, non-HDL-C, triglycerides) and HbA1c as part of an initial baseline assessment.
- Consider secondary causes of hyperlipidaemia and manage as needed.
- Ensure appropriate baseline and follow up tests as detailed on page 2. Measure BMI. Identify and exclude people with contraindications/drug interactions. If non-fasting triglyceride above 4.5mmol/L see page 2.
- **High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline.** If not achieved after 3 months, measure full lipid profile again after 3 months (non-fasting).
- Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

### PRIMARY PREVENTION

<table>
<thead>
<tr>
<th>Age ≤ 64</th>
<th>QRSK &amp; QRSK ≥ 10% over next 10 years</th>
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<tbody>
<tr>
<td>Type 2 diabetes &amp; QRSK ≥ 10% over next 10 years</td>
<td>Refer to Lipid Clinic for further assessment if clinical diagnosis of FH or if TC &gt; 9.0mmol/L and/or LDL-C &gt; 6.5mmol/L and/or non-HDL-C &gt; 5.5mmol/L or Fasting triglycerides &gt; 10mmol/L (regardless of family history) (page 2)</td>
</tr>
<tr>
<td>CKD eGFR &lt; 60 mL/min/1.73m² and/or albuminuria</td>
<td>Do not use QRISK risk assessment tool</td>
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<tr>
<td>Age ≥ 65 if appropriate consider comorbidities, frailty &amp; life expectancy</td>
<td>Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)</td>
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**Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)**

<table>
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<tr>
<th><strong>PRIMARY PREVENTION</strong></th>
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<tr>
<td><strong>If lifestyle modification is ineffective or inappropriate offer statin treatment.</strong></td>
</tr>
<tr>
<td><strong>Atorvastatin 20mg daily</strong></td>
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<tr>
<td><strong>• Measure full lipid profile again after 3 months (non-fasting).</strong></td>
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<td><strong>• High intensity statin treatment should achieve reduction of non-HDL-C &gt; 40% from baseline. If not achieved after 3 months</strong></td>
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<td>- discuss treatment adherence, timing of dose, diet and lifestyle</td>
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<td>- If at higher risk (based on comorbidities, risk score or clinical judgement - see page 2 ‘Additional Risk Factors’), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see ‘Special Patient Populations’ (page 2)</td>
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<td><strong>• If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin</strong> (see page 2 ‘Extent of lipid lowering with available therapies’).</td>
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**If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient**

* If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects (see overleaf for recommendation). |

**SECONDARY PREVENTION**

**Offer statin therapy to adults with CVD, this includes CHD, angina, Acute Coronary Syndrome (MI or unstable angina), revascularisation, stroke or TIA, or asymptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours).**

**SECONDARY PREVENTION**

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<tr>
<td><strong>Do not delay statin treatment in secondary prevention while managing modifiable risk factors.</strong></td>
</tr>
<tr>
<td><strong>Prescribe a high intensity statin:</strong> Atorvastatin 80mg daily</td>
</tr>
<tr>
<td><strong>• Measure full lipid profile again after 3 months (non-fasting).</strong></td>
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<td><strong>• High intensity statin treatment should achieve reduction of non-HDL-C &gt; 40% from baseline. If not achieved after 3 months</strong></td>
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<tr>
<td>- discuss treatment adherence, timing of dose, diet and lifestyle measures</td>
</tr>
<tr>
<td>- If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement - see page 2 ‘Additional Risk Factors’), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see ‘Special Patient Populations’ (page 2)</td>
</tr>
<tr>
<td>- If non-HDL-C baseline value is not available*, consider target non-HDL-C &lt; 2.5mmol/L (approximately equivalent to LDL-C &lt; 1.8mmol/L) as recommended by Joint British Societies (JBS3).</td>
</tr>
<tr>
<td>*This scenario is not currently covered by NICE CG181. NICE will consider this as part of the guideline update with publication currently expected December 2023</td>
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**SECONDARY PREVENTION**

**If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient**

* If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects (see overleaf for recommendation). |

**SECONDARY PREVENTION**

**If non-HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider Injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA392/393, TA733).**

**Injectable therapies**

- Inclisiran - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733) |

**If not prescribed concurrently**

**- PCSK9i - see overleaf for LDL-C thresholds (TA337)** |

**Additional CV risk reduction considerations - check fasting triglycerides levels and considericosapent ethyl. See triglycerides section overleaf.**
This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. If 40% reduction of non-HDL-C has not achieved, offer intensified statin therapy. Discuss with people who are stable on a low- or medium-intensity statin the likely benefits and potential risk of side effects if changed to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

Ezetimibe, alirocumab, evolocumab or inclisiran can be added when patients’ LDL-C levels are not lowered enough with the currently tolerated dose of statins. Bempedoic acid with ezetimibe is an option when statins are contraindicated or not tolerated, and when ezetimibe alone does not control LDL-C well enough. Do not offer a fibrate or niacin except in statin intolerance with a statin-omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (check NICE CG118 and TA805 for exceptions).

### ADDITIONAL RISK FACTORS

Note, that CVD risk scores including QRISK may underestimate risk in people who have additional medical conditions or treatments. These groups include the following groups of people:

- severe obesity (BMI>40kg/m²)
- treated for HIV
- serious mental health problems
- taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
- autoimmune disorders such as SLE, and other systemic inflammatory disorders
- non-diabetic hyperglycaemia
- significant hypertriglyceridaemia (fasting triglycerides >4.5-9.9mmol/L)
- recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider socio-economic status as an additional factor contributing to CVD risk. If QRISK <10% over the next 10 years - Give lifestyle advice and ensure regular review of CVD risk in line with guidance.

### SPECIAL PATIENT POPULATIONS

#### Type 1 Diabetes

While NICE recommends offering statins to patients with Type 1 diabetes as detailed in the algorithm, it also states to consider statins in all adults with type 1 diabetes.

#### Chronic Kidney Disease

Offer atorvastatin 20mg for the primary or secondary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73 m² and/or albuminuria). Increase the dose if a greater than 40% reduction in non-HDL-C is not achieved and eGFR is 30 mL/min/1.73m² or more. Agree the higher doses of a renal specialist if eGFR is less than 30 mL/min/1.73m².

### ABBREVIATIONS

- ALT: alanine aminotransferase
- AST: aspartate aminotransferase
- CHD: coronary heart disease
- HDL-C: high density lipoprotein cholesterol
- LDL-C: low density lipoprotein cholesterol
- non-HDL-C: non-high density lipoprotein cholesterol
- PCSK9: proprotein convertase subtilisin kexin 9 monoclonal antibody inhibitor
- CKD: chronic kidney disease
- VLDL: very low density lipoprotein cholesterol
- HDL-C: high density lipoprotein cholesterol
- PLT: platelet count
- LDL-C: low density lipoprotein cholesterol
- non-HDL-C: non-high density lipoprotein cholesterol
- SPC: summary product characteristics
- TC: total cholesterol

### MANAGEMENT

**Approximate reduction in LDL-C**

<table>
<thead>
<tr>
<th>Statin dose</th>
<th>mg/day</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>40</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>20%</td>
<td>21%</td>
<td>27%</td>
<td>33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>27%</td>
<td>32%</td>
<td>37%</td>
<td>42%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Atorvastatin | 37% | 53% | 69% | 85%
| Rosuvastatin | 58% | 71% | 84% | 97% |

**Low intensity statins** will produce an LDL-C reduction of 20-30%

**Medium intensity statins** will produce an LDL-C reduction of 31-40%

**High intensity statins** will produce an LDL-C reduction above 40%

**Simvastatin 80mg** is not recommended due to risk of muscle toxicity

- Rosuvastatin may be used as an alternative to atorvastatin if compatible with other treatment. Some people may need a lower starting dose (see BNF)
- Low/middle intensity statins should only be used if intolerance or drug interactions
- Ezetimibe when combined with any statin is likely to give greater reduction in non-HDL-C or LDL-C than doubling the dose of the statin.
- PCSK9i (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%)

Bempedoic acid when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available.

**Inclisiran (TA733)** alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

### TITRATION THRESHOLD / TARGETS

**Primary prevention**

- Intensively lowering therapy if non-HDL-C reduction from baseline is less than 40%
- **Secondary Prevention**
  - Intensively lowering therapy if at least 50% reduction in LDL-C (or non-HDL-C)

**FLH**

- Optimise lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C)

If baseline cholesterol is unknown in the setting of secondary prevention use the joint British Societies’ JBS3 consensus recommendation.

- **JBS3**
  - LDL-C = TC minus HDL-C
  - **LDL-C = non-HDL-C (total triglycerides)/2.2**

- **Valid** only when fasting triglycerides are less than 4.5 mmol/L

### SPECIAL SERVICES

Scope of specialist service available locally may include; lipid clinic, PCSK9i clinic (offering initiation and subsequent follow up), FH genetic diagnosis and cascade testing, Lipoprotein apheresis service. NICE eligibility criteria for PCSK9i and fasting triglycerides thresholds are summarised below.

**NICE**

**TA393 Alirocumab**

**TA394 Evolocumab**

- **Widow without CVD**
  - LDL-C > 4.0 mmol/L
  - LDL-C > 3.5 mmol/L

- **With CVD**
  - LDL-C > 4.0 mmol/L
  - LDL-C > 3.5 mmol/L

History of any of the following: ACS; coronary or other arterial revascularisation procedures; CHD, ischaemic stroke, PAD. * Recurrent CV events or CV events in more than 1 vascular bed (that is, ischaemic stroke and PAD) for people with Type 2 diabetes.

Bempedoic acid/ezetimibe and inclisiran are available in primary care and do not require initiation by specialist services. ’PCS7Kii may be available for prescribing in primary care: see local initiation pathways.

### TRIGLYCERIDES

- **Triglyceride concentration**
  - No treatment if <400 mmol/L
  - 400 mmol/L - 4.99 mmol/L refer to specialist
  - ≥ 5.0 mmol/L refer to specialist

- **Action**
  - Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and report for potential secondary causes of hypertriglyceridaemia. Seek specialist advice if the TG concentration remains > 10mmol/litre. At risk of acute pancreatitis

- **If non-fasting triglycerides are greater than 4.5mmol/L**, refer with a fasting TG measurement. Be aware that the CVD risk may be underestimated by risk assessment tools, optimise the management of other CVD risk factors present and seek specialist advice if non- HDL-C concentration > 7.8 mmol/L.

- **Icosapent ethyl (TA805)**
  - Check fasting triglycerides levels.
  - Manage secondary causes of hypertriglyceridaemia.
  - Consider icosapent ethyl (TA805) if patient has established cardiovascular disease (secondary prevention) and
  - on statins and fasting TG ≥ 1.7mmol/L and LDL-C≥ between 1.84 and ≤2.6mmol/L.
  - See table above and refer as appropriate.

**LDL-C** cannot be calculated using Friedewald’s formula (TG >4.5). Discuss with your lab. Consider using an alternative equation (eg Sampson, doi: 10.1001/jamacardio.2020.0013) or beta-quantification.

* I talk doesn’t represent calculated LDL-C beyond one decimal point.

### STATIN INTOLERANCE

Statin intolerance is defined as the presence of clinically significant adverse effect from statin therapy that is considered to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised.

For people who are intolerant of the recommended statin treatment see the NHSE AAC statin intolerance algorithm, available on the NHSE AAC page

**References:**


Navarese et al. 2015. Annuals of internal medicine 163(1):40-51


NICE 2016. TA385 www.nice.org.uk/guidance/TA385

NICE 2016. TA393 www.nice.org.uk/guidance/TA393

NICE 2018. CG71 www.nice.org.uk/guidance/CG71

NICE 2021. TA694 www.nice.org.uk/guidance/TA694

NICE 2021. TA733 www.nice.org.uk/guidance/TA733

NICE 2022. TA805 www.nice.org.uk/guidance/TA805

NICE confirmed that its guidance is accurately represented, Nov 2022.