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/medication interactions.
- If non-fasting triglyceride above 4.5mmol/L see page 2.

**PRIMARY PREVENTION**
Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, ‘Primary Prevention Risk Assessment’).

<table>
<thead>
<tr>
<th>Age ≥85 years</th>
<th>Type 2 diabetes &amp; QRISK ≥10% over next 10 years</th>
<th>Type 1 diabetes, if they have one or more of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 mLMin/1.73m² and/or albuminuria</td>
<td>Over 40 years</td>
<td>Had diabetes for &gt;10 years</td>
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<tr>
<td>Frailty &amp; life expectancy</td>
<td>Established nephropathy</td>
<td>Have other CVD risk factors</td>
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</table>

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

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).

If lifestyle modification is ineffective or inappropriate offer statin treatment.
Atorvastatin 20mg daily

- **Measure full lipid profile again after 3 months (non-fasting).**
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months:
  - Discuss treatment adherence, timing of dose, diet and lifestyle
  - If at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 ‘Additional Risk Factors’) consider increasing the dose every 2-3 months up to a maximum dose of atorvastatin 80mg daily.
  - For how to increase in people with CKD see ‘Special Patient Populations’ (page 2).

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements.

**SEVERE HYPERLIPIDAEMIA**
If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH)
Do not use QRISK risk assessment tool

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

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

Do not delay statin treatment in secondary prevention while managing modifiable risk factors.
Prescribe a high intensity statin.
Atorvastatin 80mg daily

- Use a lower dose of atorvastatin if there is a potential drug interaction, high risk of or experiencing adverse effects, or patient preference.
- Offer atorvastatin 20mg if CKD (people with GFR < 60 mL/min/1.73m²).

**TREATMENT TARGETS IN FH**
If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH. BUT aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline.

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy if:
- they are assessed to be at very high risk of a coronary event**
- OR therapy is not tolerated
- OR LDL-C remains >5.0mmol/L (primary prevention)
- OR LDL-C remains >3.5mmol/L (secondary prevention) despite maximal tolerated statin and ezetimibe therapy.

**Defined as any of the following:**
- Established coronary heart disease
- Two or more other CVD risk factors

If non-FH-C remain >3.5mmol/L despite other lipid lowering therapies consider injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA393/394, TA733)

**If recommended statin treatment is contraindicated or not tolerated - follow ACC Statin Intolerance Algorithm for advice regarding adverse effects (click here).**

If statin intolerance is confirmed, consider:
- Ezetimibe 10mg monotherapy, Assess response after 3 months (TA385)
- Ezetimibe 10mg/bempedoic acid 180 mg combination when ezetimibe alone does not control non-HDL-C sufficiently, (NICE TA694)

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 (TA393/394, TA733)

Injectable therapies**
- If non-FH-C > 2.5mmol/L; Arrange fasting blood test to measure LDL-C to assess eligibility:
  - Inclisiran - if fasting LDL-C ≥ 2.5mmol/L despite maximum tolerated lipid lowering therapy (TA733) OR
  - PCSK9i - see overleaf for LDL-C thresholds. (TA393/4)

* See overleaf for information to support shared decision making
** Inclisiran and PCSK9 should not be prescribed concurrently

If eligibility criteria are not met, consider ezetimibe 10mg daily (if not previously considered)

**SEVERE HYPERLIPIDAEMIA**
If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH)
Do not use QRISK risk assessment tool

**DIAGNOSIS AND REFERRAL**
Take fasting blood test to profile LDL-C.
Use the Simon Broome or Dutch Lipid Clinic Network (DLCN) criteria to make a clinical diagnosis of FH.

Refer to Lipid Clinic for further assessment if clinical diagnosis of FH or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides >10mmol/L (regardless of family history) (page 2).

**SECONDARY PREVENTION**
Prescribe a high intensity statin:
Atorvastatin 80mg daily

- OR LDL-C remains >3.5mmol/L
- OR LDL-C remains >5mmol/L
- OR therapy is not tolerated

Arrange fasting blood test to measure LDL-C for LDL-C thresholds.

If non-HDL-C > 2.5mmol/L;
- Ezetimibe 10mg/bempedoic acid 180 mg combination when ezetimibe alone does not control non-HDL-C sufficiently, (NICE TA694)

If non-HDL-C > 2.5mmol/L;
- Ezetimibe 10mg daily

- 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 - page 2 ‘Additional Risk Factors’), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see ‘Special Patient Populations’ (page 2).

If non-HDL-C baseline value is not available*, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3)

Additional Risk Factors:
Type 2 diabetes & QRISK ≥10% over next 10 years
Type 1 diabetes, if they have one or more of the following:
- Over 40 years
- Had diabetes for >10 years
- Have established nephropathy
- Have other CVD risk factors

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements.

> Refer to Lipid Clinic for further assessment if clinical diagnosis of FH or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides >10mmol/L (regardless of family history) (page 2).

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy if:
- they are assessed to be at very high risk of a coronary event**
- OR therapy is not tolerated
- OR LDL-C remains >5.0mmol/L (primary prevention)
- OR LDL-C remains >3.5mmol/L (secondary prevention) despite maximal tolerated statin and ezetimibe therapy.

**Defined as any of the following:**
- Established coronary heart disease
- Two or more other CVD risk factors

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.

Ezetimibe 10mg daily
(NICE TA385). Reassess after three months. If non-HDL-C remains > 2.5mmol/L, consider injectable therapies arrange a fasting blood test and assess eligibility

* See overleaf for information to support shared decision making
** Inclisiran and PCSK9 should not be prescribed concurrently

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 (TA393/394, TA733)
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 not achieved, offer high intensity statins. Discuss with people who are stable on a low- or medium-intensity with 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 maximally 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, nicotinic acid, bile acid binder or omega-3 fatty acid supplement or combination with statin, for the prevention of CVD (Check NICE CG181 for exceptions).

**PRIMARY PREVENTION RISK ASSESSMENT**

QRIK3 is the current version of the QRIK calculator. [www.qrik.org/three](http://www.qrik.org/three)

- Do not use this risk assessment tool for people established with CVD or those who are at high risk of developing CVD because of FH or other inherited disorders of lipid metabolism.
- Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes, or eGFR less than 60 mL/min/1.73 m² and/or albuminuria.
- Consider people aged > 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.

**Additional Risk Factors**

Note, standard CVD risk grading including QRIK3 may underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include the following groups of people;

- severe obesity (BMI>40kg/m²) increases CVD risk
- 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 QRIK < 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/1.73m² 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. Agreed the use of higher doses with a renal specialist if eGFR is less than 30 mL/ min/1.73m²

**ABBREVIATIONS**

ALT: alanine aminotransferase  
LDL-C: low density lipoprotein cholesterol  
AST: aspartate aminotransferase  
non-HDL-C: non-high density lipoprotein cholesterol  
CHD: coronary heart disease  
PCSK9: proprotein convertase subtilisin kexin 9 monoclonal antibody inhibitor  
CVD: cardiovascular disease  
SC: systemic lupus erythematosus  
FH: familial hypercholesterolaemia  
SFC: summary of product characteristics  
TC: total cholesterol

**MONITORING**

Baseline Measurements

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and Hba1c to exclude secondary causes and co-morbidities.

Monitor baseline liver transaminase (ALT or AST) before starting a statin. Measure CK if unexplained muscle pain before starting a statin. CK should not be measured routinely especially if a patient is asymptomatic.

**EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES**

The extent of lipid lowering with available therapies is summarised below.

**TITRATION THRESHOLD / TARGETS**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>TITRATION THRESHOLD / TARGETS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C &lt; 2.5mmol/L (200mg/dL)</td>
<td>Primary prevention</td>
</tr>
<tr>
<td>LDL-C &lt; 1.8mmol/L (70mg/dL)</td>
<td>Secondary Prevention</td>
</tr>
</tbody>
</table>

**REFERENCES**

NICE TA393 Atorvastatin  
NICE TA394 Evolocumab  
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NICE 2021. TA733 www.nice.org.uk/guidance/TA733

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**AUTHORS**