**INITIAL CONSIDERATIONS:**
- Measure non-fasting full lipid profile (Total cholesterol, HDL-C, non-HDL-C, LDL-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.

**PRIMARLY PREVENTION**

<table>
<thead>
<tr>
<th>Age ≤84 &amp; QRISK ≥10% over next 10 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>
<th>CKD eGFR &lt; 60 mL/min/1.73m² and/or albuminuria</th>
<th>Age ≥85 years if appropriate consider comorbidities, frailty &amp; life expectancy</th>
</tr>
</thead>
<tbody>
<tr>
<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>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identify additional risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **SEVERE HYPERLIPIDAEMIA**

  - If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.5mmol/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 for repeat lipid profile to measure 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).

- **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 >5mmol/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.

- **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.
  - Offer Atorvastatin 80mg OD if CKD (people with GFR < 60 mL/min/1.73m²).
  - Use a lower dose of Atorvastatin if there is a potential drug interaction, high risk of or experiencing adverse effects, or patient preference.
  - Do not delay statin treatment in secondary prevention while managing modifiable risk factors. 
  - Prescribe a high intensity statin: 
    - Atorvastatin 80mg OD
  - Offer Atorvastatin 20mg if CKD or if non-HDL-C > 4.0mmol/L despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications), arrange a fasting blood test for LDL-C measurement and if PCSK9i eligibility criteria (see page 2 ‘Specialist Services’) are met, refer for confirmation and initiation of PCSK9i (NICE TA 393, 394) according to local arrangements.

- **PRIMARY PREVENTION**

  - If lifestyle modification is ineffective or inappropriate offer statin treatment.
  - Atorvastatin 20mg OD
  - **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 OD.
    - For how to increase in people with CKD see ‘Special Patient Populations’ (page 2).
  - **If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 ‘Statin Intensity Table’).**
  - **If maximum tolerated dose of statin does not achieve non-HDL-C > 40% from baseline after 3 months consider adding Ezetimibe 10mg OD (NICE TA385)**
  - **If recommended statin therapy is contraindicated or not tolerated:**
    - Ezetimibe monotherapy may be considered. Assess response after 3 months
    - See local statin intolerance guidance / pathway where available

- **SECONDARY PREVENTION**

  - Offer 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’)
  - If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value
  - High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not
  - Measure full lipid profile again after 3 months (non-fasting).

- **SECONDARY PREVENTION**

  - If non-HDL-C baseline value is not available, use target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by JBS3 consensus statement - a lower is better approach.
  - If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 ‘Statin Intensity Table’).
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 middle-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.

If statin therapy is contraindicated, not tolerated or not effective, consider ezetimibe. Do not offer a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (Check NICE CG181 for exceptions).

**PRIMARY PREVENTION RISK ASSESSMENT**

**QRS3K** is the current version of the QRSK calculator. www.qrisk.org/three
- Do not use this risk assessment tool for people with established 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 who smoke or have raised BP.

**Additional Risk Factors**

Note, standard CVD risk scores including QRSK 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 systemic lupus erythematosus, and other systemic inflammatory disorders
- impaired fasting glycaemia
- 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 QRSK < 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.

Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m².

**STATIN INTENSITY TABLE**

<table>
<thead>
<tr>
<th>Dose mg/day</th>
<th>Approximate reduction in LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Fluvacatin</td>
<td>21%</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20%</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>27%</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>37%</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>38%</td>
</tr>
<tr>
<td>Atorvastin + Ezetimibe</td>
<td>52%</td>
</tr>
</tbody>
</table>

Low/moderate intensity statins will produce a 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%

- Rosuvastatin may be used as an alternative to Atorvastatin for primary or secondary prevention if compatible with other drug therapy. Lower starting dose maybe needed in some. See BN.
- Simvastatin 80mg is not recommended (black) due to risk of muscle toxicity.
- Other statins should only be used in intolerance or drug interactions.
- Ezetimibe when combined with any statin is likely to give greater reduction in non-HDL-C/LDL-C than doubling the dose of the statin.
- PCSK9i (NICE TA393,394) alone or in combination with statins or Ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%)

**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.

Measure 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.

**TRIGLYCERIDES**

**Triglyceride concentration**

- Refer to lipid clinic for urgent specialist review if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis. 10 - 20mmol/L
- Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and review for potential secondary causes of hyperlipidaemia. 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, repeat 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 is > 4.5mmol/L.

**REFERENCES**

- http://tinyurl.com/y9emrgy4
- www.nice.org.uk/guidance/cg71
- www.nice.org.uk/guidance/TA394
- www.nice.org.uk/guidance/TA393
- www.nice.org.uk/guidance/TA385
- www.nice.org.uk/guidance/CG181
- www.nice.org.uk/guidance/TA394 Evolocumab
- NICE. 2014. CG181
- NICE. 2016. TA393 Allirocumab
- NICE. 2016. TA394 Evolocumab
- JBS3. 2014.
- NICE. 2016. TA393 Allirocumab
- NICE. 2016. TA394 Evolocumab
- JBS3. 2014.
- NICE. 2016. TA393 Allirocumab
- NICE. 2016. TA394 Evolocumab
- JBS3. 2014.

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References:
- Navarese et al. 2015. Annals of internal medicine 163(10):40-51
- NICE. 2016. TA385 www.nice.org.uk/guidance/TA385
- NICE. 2016. TA390 www.nice.org.uk/guidance/TA390
- NICE. 2016. TA393 www.nice.org.uk/guidance/TA393
- NICE. 2018. CG181 www.nice.org.uk/guidance/CG181
- NICE. 2008. CG17 www.nice.org.uk/guidance/CG17