Management of Lipids in Primary Care

(updated guidance with reference to NICE CG 181 Lipid modification)

Primary CVD prevention
All patients 40 to 85 years without known CVD, diabetes or familial hypercholesterolaemia

Primary CVD Prevention Aged 85 or over

Patients with diabetes

Type 1 DM
Offer statin if: age > 40yrs or Diabetes > 10yrs or Nephropathy or Other CVD risk

Type 2 DM
Calculate risk using QRISK 2. If > 10%

Chronic kidney disease (eGFR < 60ml/min)

Secondary CVD Prevention (all patients with clinical evidence of vascular disease or FH)

Acute Coronary Syndrome (non-ST elevation MI or unstable angina)

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Primary CVD Prevention

Aged 85 or over

Calculate CV risk using QRISK 2

Identify and address modifiable risk factors: smoking, diet, alcohol, BP control and physical activity

Offer opportunity to reassess risk after lifestyle changes after an agreed length of time

If CVD risk > 10% over next 10 years, offer patient centred discussion re statin treatment

Consider ATORVASTATIN 20mg daily

Type 2 DM

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If CVD risk > 10% over next 10 years, offer patient centred discussion re statin treatment

Consider ATORVASTATIN 40-80mg daily

Consider ATORVASTATIN 80mg daily

If there are potential drug interactions or atorvastatin is not tolerated offer a lower dose of atorvastatin, or maximum tolerated dose of alternative statin – please refer to flowchart on pg 5

Ensure baseline lipids (non-fasting) recorded pre-statin (non-HDL, HDL, Total Cholesterol, TGs) in addition to LFTs, eGFR, HbA1c & TSH. Baseline Creatinine Kinase useful if pre-existing unexplained muscle pain.

Repeat non-HDL cholesterol and LFTs 3 months after starting statin with aim of achieving 40% reduction non-HDL cholesterol.

If not achieved, discuss adherence and timing of dose, optimise adherence to diet and lifestyle measures. Consider titration of atorvastatin if that is an option.

If eGFR is <30ml/min, discuss the use of higher doses with a renal specialist. Measure CK if muscle symptoms develop (pain, tenderness, weakness)

Patients should be reviewed annually, with non-HDL monitoring to check safety, efficacy and ongoing compliance with therapy. Revisit lifestyle issues regularly.

Adapted from BSNG draft guidance by Kathryn Buchanan, Pharmacist, Swindon CCG with input from: Dr Paul Price, GWH Diabetologist, Dr Tom Hyde, GWH Cardiologist, Dr Vladimir Vaks, Lead Consultant in Community Diabetes, Swindon, Dr Michael Colley, GWH Consultant Chemical Pathologist
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Recommended Lifestyle advice

- **Stop Smoking** - via local referral pathways
- **Alcohol** - suggested limits for men: 3-4 units/day, women: 2-3 units/day
- **Weight management** - can refer to Steps to Health, Dietbusters, Weightwatchers, Slimming World etc
- **Exercise** - 150 minutes moderate intensity or 75 minutes vigorous intensity aerobic activity per week or at maximum safe capacity of the individual
- **Cardioprotective diet:**
  - To reduce saturated fat intake from animal sources (instead use olive oil, rapeseed oil or spreads based on these)
  - At least 2 portions of fish per week, including 1 portion of oily fish
  - 5 portions of fruit & vegetables per day
  - Reduced intake of sugar and foods containing refined sugars
  - 4-5 portions of unsalted nuts (25g), seeds and legumes per week

Lipid management - FAQs

**What about my existing simvastatin patients (or any other low-medium intensity statin)?**

- At next face to face review discuss likely benefits and potential risks of changing to a high intensity statin
- Agree with the individual patient whether a change is needed
- Please note: MHRA has advised that there is an increased risk of myopathy associated with simvastatin 80mg


**Treat if CVD risk over 10% - really?**

- **NICE** says to ‘consider’ treatment
- It is confident that the intervention will do more good than harm for most patients and is cost effective (Cost per QALY £4125 for atorvastatin 20mg, £4875 for atorvastatin 80mg)
- Patient centred discussions are encouraged

**How can I help my patient make the right decision for them?**

- A patient decision aid has been developed and is available at: [https://www.nice.org.uk/guidance/cg181/resources/cg181-lipid-modification-update-patient-decision-aid2](https://www.nice.org.uk/guidance/cg181/resources/cg181-lipid-modification-update-patient-decision-aid2)

**What about younger perceived ‘higher risk’ patients scoring under 10%?**

- Younger patients with multiple vascular risk factors who have a high lifetime risk of vascular disease but who do not cross the 10 year risk threshold of 10% could be considered for statin therapy in order to reduce one of the main drivers for continued atherogenesis
- Discussion with an endocrinologist or cardiologist is suggested before commencing a statin in such patients or (Swindon only) email Community Diabetes Consultant for advice with patient specific details; SWICCG.CommunityDiabetesService@nhs.net

**What tests do I order and when? (effective from January 2016)**

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>What needs to be tested</th>
<th>Fasting (F) or non-fasting (NF)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRISK assessment</td>
<td>TC &amp; HDL</td>
<td>NF</td>
<td>Non HDL will be routinely calculated &amp; reported by lab. Can be repeated within 1 year but must state ‘post lifestyle changes’</td>
</tr>
<tr>
<td>About to start statin</td>
<td>TC &amp; HDL PLUS TGs, LFTs, HbaA1c, eGFR, TSH</td>
<td>NF</td>
<td>Non HDL will be routinely calculated &amp; reported by lab. If cholesterol tests already done (within last year) e.g. for QRISK, they will not routinely be redone without justification</td>
</tr>
<tr>
<td>3 month post statin check</td>
<td>TC, HDL &amp; LFTs</td>
<td>NF</td>
<td>Needs to be at least 6 weeks post statin initiation</td>
</tr>
<tr>
<td>Statin annual review</td>
<td>TC &amp; HDL</td>
<td>NF</td>
<td>TGs are not routinely needed. Lipid review will be the same whether diabetic, hypertension, CHD or CKD. More frequent than annual requests will not be routinely done without justification e.g. change in therapy</td>
</tr>
<tr>
<td>Non fasting TGs &gt; 10</td>
<td>TGs</td>
<td>F</td>
<td></td>
</tr>
</tbody>
</table>
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What if triglycerides are high?

- If non-fasting TGs > 20mmol/L, refer for urgent specialist review (if it is not due to excess alcohol or poor glycaemia control). In the absence of any existing lipid treatment, consider starting bezafibrate if specialist review is delayed.
- If non-fasting TGs 10-20mmol/L, repeat with a fasting test 5-14 days later. Refer if >10mmol/L
- If non-fasting TGs 4.5-9mmol/L, be aware that Qrisk may underestimate CVD risk, optimise management of other CVD risk factors and offer statin in accordance with CVD risk. Additional lipid lowering treatment is not necessarily indicated. If non-HDL-C is also significantly raised, > 7.5mmol/L, seek specialist advice.
- Consider specialist referral if TGs remain high (>5mmol/L non diabetic, >10mmol/L for diabetic) despite statin / lifestyle changes.

Why have we recommended 40mg or 80mg Atorvastatin? How do I choose?

- NICE recommends 80mg for secondary prevention of CVD but to consider a lower dose if drug interactions, risk of adverse events or patient preference.
- Lipid lowering difference between the two is relatively small (6% on average) and there is a higher risk of adverse effects present in the elderly, those with low muscle mass or impaired renal function.
- Adverse effects of LFTs are more common with an 80mg dose.

Risk of new onset diabetes with statins?

- There is some data to support an association between atorvastatin 80mg and new onset diabetes, mainly in patients already at risk of developing diabetes.
- Level of risk may vary between statins and dose but insufficient evidence to confirm or exclude.
- For the group of patients who would be receiving atorvastatin 80mg (ACS) the reduced vascular risk outweighs the risk of diabetes and not a reason for stopping statin treatment.

How do I manage suspected Familial Hypercholesterolemia (FH)?

- If a person has a combination of a family history of premature coronary heart disease (<50 years in 1st degree relative) and total cholesterol above 7.5mmol/l consider FH or total cholesterol above 9mmol/l on its own (Near normal TGs will increase the suspicion).
- Exclude secondary causes of dyslipidaemia – might include hypothyroidism, excess alcohol, poorly controlled diabetes, liver and renal disease (nephrotic syndrome) before referral.
- Refer to endocrinology initially - onward referral to specialist centres in Bath or Oxford may be required.
- Statins are 1st line treatment in FH as per NICE CG 71 (2008).

What do I do if my patient is intolerant to statins?

- If a person is not able to tolerate a high intensity statin aim to treat with the maximum tolerated dose – any statin at any dose will reduce CVD risk. (See locally agreed flow chart on p5).
- If adverse effects reported from taking a high intensity statin discuss the following strategies:
  - Stop the statin and try again once symptoms have resolved to check that symptoms are related to statin.
  - Reduce the dose within the same intensity group e.g. atorvastatin 40mg to 20mg (see table on pg5).
  - Change the statin to a lower intensity group e.g. atorvastatin 20mg to simvastatin (see table on pg 5).
  - Ezetimibe may then be an option for high risk patients who are intolerant to 3 statins.
- Seek specialist advice for people at high risk of CVD who are intolerant to 3 different statins.

What about rosuvastatin / pravastatin?

- Rosuvastatin has considerably higher cost compared to atorvastatin and no evidence of greater effectiveness therefore not recommended by NICE. Locally, we consider it may be appropriate for 3rd line use in secondary prevention patients only.
- Pravastatin seems to have similar side effect profile to rosuvastatin (they are both hydrophilic) although not as potent so it may be useful 3rd line for primary prevention patients.
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What about ezetimibe?

• People with primary hypercholesterolaemia should be considered for ezetimibe in line with latest NICE TA i.e. statin contra-indicated or not tolerated (see above)
• The IMPROVE-IT trial has been published (June 15), showing a benefit of simvastatin 40 + ezetimibe over simvastatin 40 alone on death from (cardiovascular disease, a major coronary or nonfatal stroke) in ACS patients. This suggests that benefit is due to LDL lowering rather than any special ezetimibe effect
• Please note: Atorvastatin at doses suggested here is already more intense LDL lowering that simvastatin 40mg in those patients so current advice hasn’t changed at all

What if LFTs are raised?

• Do not exclude people who have liver transaminase levels which are raised but are less than 3 x the upper limit of normal

What if Creatinine Kinase levels are raised?

• If CK levels are more than 5 x the upper limit of normal, re-measure after 7 days. If still more than 5 x upper limit of normal, do not start statin treatment.
• If CK levels are raised but less than 5 x the upper limit of normal, start or reduce to a lower dose of statin once symptoms have resolved

What about other treatments for prevention of CVD?

• NICE states do NOT offer;
  • Fibrates (routinely, alone or in combination)
  • Nicotinic acid; niacin
  • Bile acid sequestrants; cholestyramine, colestipol, colesvelam
  • Omega-3 fatty acid compounds; Omacor, Prestylon, Maxepa
• This applies to treatment for primary and secondary prevention, including people with diabetes and CKD
• Existing patients may be on for dyslipidaemia under specialist guidance but there may be opportunities to review
• Do not offer coenzyme Q10 or Vitamin D to increase adherence to statin treatment

When to refer and who to refer to?

Consider referring;

• High risk patients who do not reach non-HDL reductions of 40% despite maximal statin therapy
• High risk patients who are intolerant to at least 3 statins and ezetimibe
• Suspected familial hypercholesterolemia
• Severe hypertriglyceridemia (>10mmol/L fasting)
• Severe hypercholesterolemia (TC >9 or non-HDL-C >7.5mmol)

Refer to endocrinology or cardiology at GWH

Further information

QRISK 2 – CVD risk calculator – http://qintervention.org

Non–HDL–Cholesterol target ready reckoner for rechecking levels at 3 months

<table>
<thead>
<tr>
<th>Baseline</th>
<th>40% reduction</th>
</tr>
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<tbody>
<tr>
<td>8</td>
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</tr>
<tr>
<td>7.5</td>
<td>4.5</td>
</tr>
<tr>
<td>7</td>
<td>4.2</td>
</tr>
<tr>
<td>6.5</td>
<td>3.9</td>
</tr>
<tr>
<td>6</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Note that non-HDL-cholesterol may vary by up to 1mmol/L from day to day and this target reduction is merely a guide for discussion with patient before deciding to increase the dose

References: NICE CG 181: Lipid modification

Management of Lipids in Primary Care November 2015 Review due November 2017

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INTOLERABLE SIDE EFFECTS FROM STATIN

Non-muscular

CK<5 ULN

Stop statin for 2-4 weeks

Symptoms persist

Symptoms improve

RECHALLENGE

Lower dose same intensity group of statin e.g. atorvastatin 40mg -> 20mg, 80mg -> 40mg. If patients on atorvastatin 20mg see below *

Symptoms persist

Symptoms improve

Continue

Muscular

Measure CK

CK>5 ULN +/- rhabdomyolysis

STOP STATIN

Retest after 7 days

Normal (<5 ULN)

Low dose alternative statin, see below * (start when symptoms resolve)

Symptoms improve

Avoid statin and discuss with specialist if high risk patient

High (>5 ULN)

Aim for maximally tolerated dose of statin (ideally increasing every 4 weeks)

Symptoms persist after 3 statin trials

Ezetimibe

Symptoms persist

Refer to specialist

Symptoms improve

CONTINUE

*Alternative statin options to consider in order of preference (start low dose and titrate up if possible)

Statin

Rationale

Smrfastatin

Cost effective, reasonably potent & good chance of being tolerated

Pravastatin

Cost effective, well tolerated but less potent

(secondary prevention)

Rosuvastatin

Well tolerated, potent but expensive

(secondary prevention)

Fluvastatin

Well tolerated, less potent & expensive

Rosuvastain twice weekly

Well tolerated, less potent but lacking in evidence base and 'off label' use