CVD risk, lipids and statins

NICE have recently published DRAFT guidance on lipid modification, covering both primary and secondary prevention of CVD, including advice for those with diabetes and CKD (NICE Feb 2014). These draft guidelines are for consultation, with final guidance expected in late summer 2014.

The key changes are:

- CVD risk should be calculated using QRISK2, not other tools.
- The 10 year CVD risk at which treatment should be offered has been reduced from 20% to 10%.
- Atorvastatin is the first line statin, usually at 20mg for primary prevention and 80mg for secondary prevention.
- NICE refer to HDL and non-HDL cholesterol. Your non-HDL cholesterol is your total cholesterol minus your HDL cholesterol (which is not the same as your LDL!). When treating to target, NICE suggest our target should be a 40% reduction in non-HDL cholesterol. They do not focus on LDL levels because labs do not measure LDL (it is difficult-they calculate it using the Friedewald Equation).

There are 99 recommendations(!) in the draft guidance, so here is a summary of the things we need to know:

**DRAFT NICE guideline on lipid modification NICE 2014**

- Remember if you suspect familial hypercholesterolaemia, this guidance does not apply! The diagnosis and management of familial hypercholesterolaemia is discussed in the online handbook, the ‘magic’ numbers are a total cholesterol of >7.5 and LDL >4.9, but look also for a family history of premature cardiac disease. In this situation do NOT use a risk assessment tool (will significantly underestimate risk).

<table>
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<tr>
<th>PRIMARY PREVENTION OF CVD</th>
<th>SECONDARY PREVENTION OF CVD</th>
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<tbody>
<tr>
<td><strong>GENERAL POPULATION (THOSE WITHOUT DIABETES or CKD)</strong></td>
<td><strong>Offer atorvastatin 80mg (lower doses if drug interactions, risk of adverse events, patient preference).</strong> This dose is based on modelling clinical and cost effectiveness.</td>
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| • Assess CVD risk in those aged 40-74 using QRISK2.  
  o GPs should prioritise who to do a full risk assessment on by using whatever (incomplete) data they already have to calculate a ‘guestimated’ CVD risk (my term, not NICE’s!). If the ‘guestimated’ 10 year CVD risk is ≥10% do a full risk assessment (which will include a lipid profile, BP and updating smoking status etc.).  
  o NICE do not specify when CVD risks should be reassessed.  
  • If QRISK2 is ≥10%, offer a statin (atorvastatin 20mg). This dose is based on the premise that the initial big reduction in lipids reduces CVD risk significantly, but that further reductions provide only modest benefits.  
  • Those of 85y or over are at high CVD risk, based on age alone, especially if they smoke or have hypertension. NICE suggest that in those aged 85 or over we should consider offering atorvastatin 20mg (clearly after considering patient preference, co-morbidity, the harms of polypharmacy and balancing these against the potential benefits!)  
  • Remember that CVD risk assessment tools can underestimate risk in:  
    o HIV  
    o Serious mental illness  
    o CKD stage 1 & 2 (but see below)  
    o Those with autoimmune disorders (e.g. SLE, rheumatoid arthritis)  
    o Those on drugs that cause dyslipidaemia (antipsychotics, steroids, immuno-suppressants). |  |
| **TYPE 1 DIABETES** |  |
| • Do not risk use a risk assessment tool.  
  • Offer statins (start with atorvastatin 20mg)  
  o No starting age is given.  
  Lower dose suggested because lack of evidence for statins in type 1 diabetes. | **As for general population: atorvastatin 80mg (lower doses if drug interactions, risk of adverse events, patient preference).** |
| **TYPE 2 DIABETES** |  |
| • Use the UKPDS risk assessment tool to assess CVD risk (see useful websites for link to UKPDS risk engine).  
  • If 10 year CVD risk is ≥10% using the UKPDS tool, offer high intensity statins: use atorvastatin 80mg (based on clinical & cost effectiveness). NICE do not specify at what age we should start to do this risk assessment. | **As for general population: atorvastatin 80mg (lower doses if drug interactions, risk of adverse events, patient preference).** |
CHRONIC KIDNEY DISEASE

NB this advice is based mainly on consensus, as there was limited evidence (see CKD in Renal Chapter)

Lower doses of statins are recommended because of concern about adverse events plus licensing restrictions.

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<tr>
<th>In CKD 1 &amp; 2:</th>
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<tr>
<td>• Assess CVD risk using QRISK2 but do NOT tick the CKD box.</td>
<td>• Start atorvastatin 20mg. Increase dose if &lt;40% fall in non-HDL cholesterol.</td>
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<tr>
<td>• Treat only if QRISK2 is ≥10%. Use atorvastatin 20mg.</td>
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<tr>
<th>In CKD 3 or worse:</th>
<th>No guidance</th>
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<tbody>
<tr>
<td>• Do not use a CVD risk assessment tool</td>
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<tr>
<td>• In CKD 3: start atorvastatin 20mg, and increase dose if there is less than 40% reduction in non-HDL cholesterol</td>
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<tr>
<td>• In CKD 4 or 5: start atorvastatin 20mg, and increase dose only in consultation with the renal team.</td>
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So do we need to change everyone who is now on the ‘old’ treatment regimens?

• If they are on lower dose statins than now recommended, discuss this at the next medication review and offer higher doses if they wish.

Lifestyle for all at increased CVD risk

• Diet
  o Fat reduction: NICE suggest: reduce total fat intake to <30%, saturated fats to <10% of intake, dietary cholesterol to <300mg/d. Where possible replace saturated fats with mono-unsaturated and polyunsaturated fats. Given that won’t mean much (to me or my patients!) there are two links to useful information about fats and how to reduce fat intake in the useful websites box at the end. (Basically start using olive oil, rapeseed oil).  
  o Reduce sugar intake (especially refined sugars and fructose).  
  o Use whole grains when eating starchy foods  
  o Eat 5 portions of fruit and vegetables/day  
  o Eat at least 2 portions of fish a week, 1 of which should be oily fish: salmon, trout, mackerel, sardines, pilchards, kipper, eel(!) whitebait, herring. (Remember tuna is only counted as an oily fish when NOT tinned – in the process of canning they remove most of the good oils)  
• Alcohol: do not drink more than 3-4U alcohol/day (men) and 2-3U/d (women) and do not binge drink.  
• Exercise: in line with NICE guidance on this – that is 30mins 5x a week of moderate intensity exercise (light sweat).  
• Smoking: stop!

Starting and monitoring statins

Before starting statins:

• Modify all modifiable risk factors, with all the usual lifestyle advice (see above).

• Bloods:
  o Full lipid profile (cholesterol, HDL, LDL and TGs) – fasting is not required  
  o HbA1c  
  o Renal function  
  o Transaminase (ALT or AST)  
  o TSH

• Once on a statin, advise patients to seek medical help if they develop muscle symptoms (pain, tenderness, weakness) and if this occurs check CK. If they have been on a statin for more than 3 months, consider other causes.

Abnormalities in blood results:

• If there is significant dyslipidaemia, consider causes of this – excess alcohol, uncontrolled diabetes, hypothyroidism, liver disease, nephrotic syndrome.

• Total cholesterol >9mmol/l or non-HDL >7.5mmol/l: Refer, even in the absence of a history of a family history of premature cardiac disease.

• Triglycerides 4.5-9.9mmol/l: Look at non-HDL cholesterol – refer if non-HDL cholesterol is > 7.5mmol/l. CVD risk tools will underestimate risk.

• Triglycerides between 10-20mmol/l: repeat the sample after fasting. 30% will return to normal with a fasting sample. If still elevated, consider other causes, and seek specialist advice if remains elevated.

• Triglycerides >20mmol/l: refer urgently (if not due to excess alcohol or uncontrolled diabetes).
After 3m statin treatment:

- **Recheck lipids.**
  - Aim for a 40% or greater reduction in non-HDL cholesterol.
  - If this is not achieved discuss: compliance and timing of dose (take at night), lifestyle modification. Offer increased dose if taking less than 80mg atorvastatin.

- **Recheck ALT/AST 3m after starting statin and then at 12m. No further testing is needed.** (Note: the US FDA say no monitoring of liver function is required.)

- Do NOT routinely stop statins if AST/ALT is under 3x the upper limit of normal.

- Do NOT measure CK in asymptomatic people on statins.

If adverse events occur with high dose statins consider:

- Stopping treatment and restarting when symptoms have resolved (to ensure due to statin).
- Reducing dose within same intensity group of statins.
- Trying lower intensity statin (they don’t specify, but I think they mean simvastatin, pravastatin and fluvastatin).
- Do not stop statins because of a rising HbA1c.
- In those unable to tolerate statins, seek expert advice.

What about other treatments besides statins?

- Do NOT use/recommend the following routinely (alone or in combination with statins): plant stanols/sterols, fibrates, nicotinic acid (niacin), bile acid sequestrants, omega-3 (mainly due to lack of evidence).

- Do NOT advise co-enzyme Q10, vitamin D to help with statin compliance.

**What role for ezetimibe? (this is from NICE TA132, 2007, which NICE says still applies)**

- As monotherapy in those who should be on statins but can’t because of contraindications or intolerance (defined as potential harm to patient, not just that the patient doesn’t want to take it!).

- Alongside statins if cholesterol insufficiently lowered by statin alone.

**Auditing care**

- When auditing care, measure the proportion of people on high intensity statins rather than cholesterol levels in those with established CVD.

**Known Unknowns (where more research is needed)**

- Is age alone as effective as more complex risk stratification tools at assessing CVD risk?

- Is the benefit seen in individuals similar to the benefits seen in populations in published trials?

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**CVD risk, lipids and statins**

- In primary prevention of CVD in the general population, use QRISK2 to assess CVD risk and treat with atorvastatin 20mg if 10 year risk is ≥10%.

- In primary prevention in type 2 diabetes, use the UKPDS risk engine, and start atorvastatin 80mg if 10y CVD risk is ≥10%.

- In primary prevention of type 1 diabetes, offer 20mg of atorvastatin to all (unclear what starting age).

- In primary prevention of CKD stage 3 or worse, offer atorvastatin 20mg.

- In secondary prevention of CVD, offer 80mg of atorvastatin to all, except in CKD where lower doses are used.

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**For professionals:**

UKPDS risk engine is downloadable from: [http://tinyurl.com/GPU-UKPDS](http://tinyurl.com/GPU-UKPDS)

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**For patients:**

NHS choices information on:

Understanding fats: [www.tinyurl.com/GPU-understanding-fats](http://www.tinyurl.com/GPU-understanding-fats)

Practical advice on eating less fat: [www.tinyurl.com/GPU-eat-less-fat](http://www.tinyurl.com/GPU-eat-less-fat)

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The GP Update Course is completely free from pharmaceutical company sponsorship. This means that you can be totally reassured that there will be no biasing of the information presented to you and that there will be no reps there on the day!

Spring/Spring 2014 dates:

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<th>Location</th>
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<td>London</td>
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<td>Leeds</td>
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