**Cardiovascular Risk**

Patients needing lipid lowering intervention should be identified by calculating absolute cardiovascular (CV) (rather than just coronary heart disease [CHD]) risk taking account of multiple risk factors and not lipid levels only. Framingham-based scoring systems are the most widely accepted method of doing this but tend to overestimate risk in low and medium risk groups and underestimate risk in an individual with a lower socioeconomic status, a family history of premature CHD and in certain ethnic subgroups. Framingham-based scoring systems are also not applicable in very young (age less than 40 years) and elderly (75 years and over) individuals. The ASSIGN score addresses some of these limitations and may be a more accurate risk scoring system in Scotland.

Non-fasting samples are suitable for measurement of total cholesterol (TC) and HDL-C, but not for triglycerides (TG) and measurement or calculation of LDL-C. Secondary causes of dyslipidaemia (hypothyroidism, renal impairment, liver disease, alcohol excess and diabetes, particularly when glycaemic control is poor) should always be excluded. Very high levels should prompt screening for familial hyperlipidaemia. HDL-C levels should be used to help estimate risk but should not be a target for treatment on the basis of current evidence. Patients on antihypertensive therapy should have their risk estimated using their pre-treatment blood pressure.

All individuals aged 40 years or more and younger patients with a family history of premature CV disease or familial hypercholesterolaemia should ideally have their risk assessed at least every five years. Patients likely to have a high estimated risk (including those aged 40 years or more who smoke, are of South Asian descent or have a family history of premature CV disease) should have their risk assessed without delay. Patients with established CV disease should ideally have risk factor monitoring every 3-6 months. Asymptomatic individuals at high CV disease risk should ideally have their risk factors monitored every 6-12 months. These frequencies of risk factor monitoring are taken from SIGN 97 (Risk estimation and the prevention of cardiovascular disease).

Individuals at high risk are defined as asymptomatic individuals with a risk of a first cardiovascular event of ≥20% over 10 years. Most patients with diabetes (see below), patients with familial hypercholesterolaemia, chronic kidney disease and all patients with a previous cardiovascular event should be assumed to be at high risk. Patients at high risk should be considered for treatment with lipid lowering drugs. Individuals with extreme cholesterol levels (TC ≥ 8mmol/l or a TC to HDL-C ratio ≥ 6.0) but no other risk factors should also be considered for intervention. Individuals at high risk should receive intervention for all reversible risk factors and be commenced on aspirin 75mg once daily. Clopidogrel 75mg once daily should be considered instead of aspirin in patients with a previous cardiovascular event who have aspirin hypersensitivity or intolerance despite acid suppression therapy.
**Lipid Lowering**

Women of potentially childbearing age taking statins require adequate contraception. In the elderly the decision to start drug therapy should be based on individual CVD risk, life expectancy and quality of life.

Lipid lowering intervention includes lifestyle changes as well as pharmacological treatment. A diet low in total and saturated fat should be recommended to all individuals. Other lifestyle changes including reduction of salt intake, increased fruit and vegetable consumption, weight reduction, moderately intense physical activity and smoking cessation should also be recommended. This lifestyle advice should be particularly intensive for individuals at high and intermediate (10-20% over 10 years) CV disease risk.

The relative CVD risk reduction observed with cholesterol lowering is independent of the presenting level. There is little evidence for treating individuals to any specific cholesterol target. There is evidence, however, for treating specific groups of patients with specific drugs at specific doses. At the same time, it is inevitable that targets and the Quality and Outcomes framework target in particular will influence prescribing.

There is evidence of benefit of intensive rather than conservative lipid lowering in patients with established CHD. There is less evidence of benefit in patients with other forms of CV disease or in asymptomatic individuals at high risk of CVD. Treating all patients with CHD intensively is not affordable. It is therefore important to identify CHD patients at the highest risk. Patients with acute coronary syndromes (ACS) are at higher risk than patients with stable CHD. Patients with familial hypercholesterolaemia should also be treated intensively.

**Simvastatin 40mg should be the first choice statin for most individuals requiring lipid lowering drug treatment.**

**Acute Coronary Syndromes**

Atorvastatin 80mg for at least 2 years should be considered instead of simvastatin 40mg for patients presenting with ACS. The statin should be commenced during the ACS hospital admission and lipid measurement should be repeated after at least 8 weeks. After 2 years simvastatin 40mg may be substituted. Atorvastatin 80mg should not be used in non-selected chest pain admissions but reserved for patients with suspected or proven ACS ie patients with elevated cardiac markers, ischaemic ECG changes and/or a classical history of prolonged or recurrent cardiac ischaemic chest pain at rest. Simvastatin 40mg may be more suitable than atorvastatin 80mg for elderly or frail patients, particularly if statin naive. NHSL ACS guidelines can be found at: http://www.nhsdots.org/meded/clinicalgpp/index_gpp.asp?hospsite=wg&dept/Cardiology
Diabetes

Diabetic patients with established cardiovascular disease or microalbuminuria / proteinuria have a particularly high cardiovascular risk. The vast majority of diabetic patients aged 40 years or more should be assumed to be at moderately high risk. Exceptions are patients without established cardiovascular disease and microalbuminuria / proteinuria who also do not have any conventional cardiovascular risk factors (smoking, hypertension, dyslipidaemia, south Asian ethnicity and family history of cardiovascular disease) and who are not overweight. Most diabetic patients under the age of 40 years are at lower risk although statins should be considered when microalbuminuria or conventional cardiovascular risk factors are present. The presence of more than one risk factors indicates a relatively higher cardiovascular risk.

Although the evidence is limited, current practice with regard to cholesterol lowering in diabetic patients usually endorses treating to a target of TC < 4.0mmol/L or a LDL-C < 2.0mmol/L. Switching to atorvastatin 40-80mg or rosuvastatin should be considered when diabetic patients have lipid levels higher than these values, particularly if they also have established CV disease or microalbuminuria / proteinuria. These guidelines apply equally to both type 1 and type 2 diabetic patients. The treatment of hypertriglyceridaemia is discussed below.

Other Groups

For other groups of patients in whom more intensive lipid lowering is desired, atorvastatin 40-80mg and rosuvastatin 10-20mg (starting dose 5mg for some individuals – see below) are both suitable options. Atorvastatin has the greatest evidence for patients with stable CHD, stroke or TIA. Rosuvastatin is more cost effective in terms of cholesterol lowering however and may also be more suitable for patients taking medications that influence cytochrome P450. Ezetimibe is also a cost effective alternative but unlike the statins has no clinical outcome data. It is therefore recommended that statin therapy is switched and/or the dose uptitrated before the initiation of ezetimibe is considered. Ezetimibe 10mg once daily is suitable for patients intolerant of even low dose statin. It is also suitable in combination with low dose statins for patients intolerant of higher doses, and in combination with high dose statins when very intensive lipid lowering is desirable.

Practical Points

Patients using medications that influence cytochrome P450 should avoid concomitant use of simvastatin and atorvastatin. Common examples include amiodarone, diltiazem and verapamil. Pravastatin 40mg is a suitable alternative in these individuals. Individuals taking simvastatin or atorvastatin should also avoid drinking large quantities of grapefruit juice for similar reasons.

Doses of simvastatin, atorvastatin and pravastatin less than 40mg should be avoided except when there are problems with tolerability or potential drug interaction.

Rosuvastatin should be started at a dose of 5mg rather than 10mg for individuals aged over 70 years, those of Asian ancestry and individuals with moderate renal
impairment or other predisposing factors to myopathy including alcohol excess. The
dose of rosvastatin should only be increased after at least 4 weeks.

Hypertriglyceridaemia

If hypertriglyceridaemia is suspected, measurement of a full fasting lipid profile is
required. If confirmed secondary causes as listed above should be sought. Hypertriglyceridaemia (TG > 4.5mmol/L) and mixed dyslipidaemias should be
treated with bezafibrate m/r 400mg once daily, usually in addition to a statin. When
severe hypertriglyceridaemia is present bezafibrate m/r may need to be started before a
statin because of the risk of pancreatitis. Bezafibrate m/r should also be considered
when TG is moderately elevated (2.3 - 4.5mmol/L) and CV risk is high. The
prescribing of the combination of a statin and fibrate requires particular care because
of the greater risk of myopathy.

Toxicity

It is not usually necessary to obtain a baseline CK level or to measure CK levels in
asymptomatic patients. Patients on a statin should be advised to report unexplained
muscle pains promptly, especially if associated with fever or malaise. If such effects
are mild, a reduced dose or a different statin should be tried. If severe side effects are
experienced the statin should be stopped. Patients with CK > 10 times the upper limit
of normal should stop statin therapy.

Transaminase levels should be measured before starting therapy, after 12 weeks, after
a dose increase and periodically thereafter. Bilirubin is a better indicator of liver
injury. Statins should be stopped when there is evidence of significant liver injury. When a transaminase level is 3 times the upper limit of normal and the patient is
asymptomatic, the test should be repeated. If still elevated a dose reduction and
discontinuation should be considered. Patients with chronic liver disease and non-
alcoholic steatohepatitis may safely receive statins.

References

SIGN 97  Risk estimation and the prevention of cardiovascular disease  A national
clinical guideline  February 2007
JBS2: Joint British Societies’ guidelines on prevention of cardiovascular disease in
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NICE Clinical Guideline GC66
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Lewis Vickers
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LIPID LOWERING SUMMARY

- SIMVASTATIN 40 MG is the drug of choice for most patients
- Consider ATORVASTATIN 80 MG for patients with ACS
- Consider ATORVASTATIN 40-80 MG or ROSUVASTATIN 10'-20 MG when more aggressive lipid lowering is desired
- Consider PRAVASTATIN 40 MG and ROSUVASTATIN 10'-20 MG rather than simvastatin and atorvastatin respectively when patients are prescribed drugs that influence cytochrome P450
- Only use lower doses of the drugs above if intolerant of high doses
- Consider EZETIMIBE 10 MG as monotherapy if intolerant of low dose statin
- Consider adding EZETIMIBE 10 MG to statin only when taking most potent statin tolerated at highest dose tolerated
- Consider BEZAFIBRATE MR 400 MG to treat hypertriglyceridaemia

5 MG for patients aged over 70 years, Asians, patients with renal impairment or at risk of myopathy