Guidelines for the Management of patients with Hypercholesterolaemia at risk of cardiovascular disease (CVD)

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Abbreviations

CVD: Cardiovascular disease
eGFR: Estimated glomerular filtration rate
HDL: High density lipoprotein
LDL: Low density lipoprotein
QOF: Quality Outcomes Framework
INTRODUCTION

Cardiovascular disease (CVD) is a major cause of morbidity and premature mortality in Scotland. Cholesterol is a major risk for CVD, and cholesterol reduction (using diet and statins) is an important component of the strategy to reduce CVD. This revised and updated Lothian guideline builds on national guidance, Risk estimation and the prevention of cardiovascular disease (SIGN 97)\(^1\) to provide a cost-effective and evidence-based approach to managing blood lipid disorders in community and hospital settings.

Guidelines published in 1998\(^2\) and 1999\(^3\) provided the first national evidence – based advice about primary and secondary prevention of CVD. Lothian Guidelines on management of blood lipid disorders for patients with established coronary heart disease were first published in 1995 (second revision 2001) and focused on secondary prevention.

This revision includes advice about patients with diabetes and primary prevention of CVD. Additionally, following publication of several large trials over the past decade, and the launch of SIGN97, this Lothian Guideline now covers CVD as a whole rather than focusing on coronary heart disease (CHD).

There are a number of modifiable risk factors for CVD including smoking, hypertension, and excess alcohol intake. Interventions to manage these risk factors are as important as cholesterol lowering treatment for patients at high risk of CVD. Indeed, the limited health economics evidence for primary and secondary prevention of CVD suggests that the cost per life year gained is substantially lower for antiplatelet therapy, antihypertensive medication, diet and smoking cessation than for statin therapy. [SIGN 97, annex 2]. Up to date advice about the management of other CVD risk factors is available in other local and national guidelines. [SIGN 97, chapter 6 – smoking], 4,5

This guideline, like the national guidelines, is based on evidence from clinical trials and studies in populations. It is important to remember that the decision to treat should be made after discussion with the patient about the risks and benefits on an individual basis. No guideline can precisely predict the risks and benefits for one individual. However, the information in this guideline is derived from the best evidence available and we hope provides useful guidance in order that the patient and the clinician can together decide on the most appropriate treatment.

Throughout this Lothian Guideline, evidence-based recommendations from SIGN97 (or JBS-2) are indicated by the term "Recommendation" (typically reflecting grade I or II evidence).

Practical advice that does not have an extensive evidence base in the published literature is indicated as follows: "Good practice point ☑️."
2 BIOCHEMICAL TESTS AND RISK ASSESSMENT

2.1 Biochemical assays
As a minimum, all patients should have the following samples checked before deciding on management of hypercholesterolaemia:
- total cholesterol (non fasting)
- high density lipoprotein (HDL) cholesterol (non fasting)
- blood glucose (non fasting)
- alanine transaminases (ALT)
- thyroid function if symptoms of thyroid disease
- creatinine (which automatically generates an estimate of glomerular filtration rate from Adult Labs in Lothian - see section 3.1)

2.1.1 Cholesterol and other lipids
Testing a random (non fasting) blood sample for total cholesterol and high density lipoprotein (HDL) cholesterol will be adequate for most patients. However, testing a full lipid profile (fasting sample) will guide management in the following circumstances:
- Familial conditions - see section 3.3
- In primary prevention, CVD risk is underestimated in patients with hypertriglyceridaemia (>1.7mmol/L) - see section 3.2
- Specialist referral for consideration of fibrate treatment if persistent hypertriglyceridaemia (>1.7mmol/L) after commencing statin therapy. (JBS-2 and SIGN97)

Good practice point
Fasting has little effect on total cholesterol, so random (non-fasting) testing is a reasonable starting point for the detection of hypercholesterolaemia. (SIGN97).

2.1.2 Blood glucose
Good practice point
A random (non-fasting) blood glucose sample should be checked at the same time as the baseline cholesterol. A blood glucose of <6.0mmol/L indicates a normal level. A value of >6.1mmol/L but <7.0mmol/L requires a repeat measurement on a fasting blood sample. If the value is >7.0mmol/L an oral glucose tolerance test should be performed.

2.1.3 Liver function
Good practice point
Liver function tests (alanine transaminases (ALT) should be checked at baseline and at 8 weeks. If liver function is within the normal range, routine tests of liver function subsequently are not indicated unless the person develops symptoms (JBS-2).

Needs further discussion ....
2.1.4 **Muscle**

| Good practice point | Routine testing of creatinine kinase (CK) is not routinely required before initiating statin treatment unless the patient is at increased risk of muscle toxicity (e.g. older patients, concomitant use of drugs listed in table 2). (SIGN97). If CK level is within the normal range, routine measurement of CK subsequently is not indicated unless the person develops symptoms (JBS-2). |

2.1.5 **Thyroid function**

| Good practice point | Consider thyroid disease as a secondary cause of dyslipidaemia and check thyroid function if there is clinical suspicion of hypothyroidism or hyperthyroidism. |

2.2 **Lipid measurement and CVD risk estimation for primary prevention of CVD**

The decision to use a statin for primary prevention of CVD is based on the estimation of absolute 10-year CVD risk (sum of Framingham algorithms for CHD risk and stroke risk). A statin should be considered if the 10-year CVD risk ≥ 20%.

The Framingham algorithms require the following information:
- Age
- Sex
- Pre-treatment systolic and diastolic blood pressure
- Ratio of total cholesterol and HDL cholesterol
- Smoking status
- In addition the Framingham algorithm includes diabetes and presence of left ventricular hypertrophy on electrocardiogram – most people with these CVD risk factors should be managed as for secondary prevention (see section 2.1).

An estimate of CVD risk can be obtained using either published charts (JBS-2)\(^6\), or a computer program \(^7,8\). Use of a computer program to estimate CVD risk is preferable as the CVD risk charts overestimate CVD risk in younger people. Framingham algorithms should not be used to estimate CVD risk in people with pre-existing symptomatic CVD, diabetes or familial hypercholesterolaemia (see section 3.3). Framingham algorithms underestimate CVD risk in the following groups: British Asians, people with a strong family history, or people from a lower socio-economic background (SIGN97). Accordingly, SIGN97 proposes the use of a computer programme (ASSIGN) that estimates risk for the Scottish population taking account of socio-economic status, and including family history in the assessment (which has the additional benefit of providing some adjustment for ethnicity) but the tool is still under development.\(^7\)

| Good practice point | When assessing a patient for primary prevention of CVD, 10-year CVD risk should be estimated using a computer program based on the Framingham algorithm (such as [http://cvrisk.mvm.ed.ac.uk/calculator.htm](http://cvrisk.mvm.ed.ac.uk/calculator.htm)). |
| Good practice point | CVD risk assessment should not be attempted for patients with pre-existing CVD or patients with diabetes. |
2.3 Lipid measurement in secondary prevention of CVD and diabetes

The decision to commence a statin for secondary prevention or for patients with diabetes should no longer be based on whether the patient's cholesterol level exceeds a particular threshold (SIGN97 and JBS-2). Nonetheless, cholesterol checks should be performed for secondary prevention and for patients with diabetes both at baseline and to assess the response to treatment.

**Baseline testing:** All patients with cardiovascular disease or diabetes should have their total cholesterol documented for the Quality Outcomes Framework (QOF) in the General Medical Services contract for primary care (appendix 1). Samples taken during an admission with acute coronary syndrome are likely to underestimate lipid levels and should be repeated two to three months after hospital admission.

**Follow up testing:** Once statin treatment is commenced, total cholesterol should be checked annually to monitor response to statin treatment as indicated for QOF.

<table>
<thead>
<tr>
<th>Good practice point</th>
<th>For patients with acute coronary syndrome (particularly myocardial infarction), repeat full lipid profile 8 to 12 weeks after hospital admission, testing for familial hypercholesterolaemia and assessing response to statin treatment. (JBS-2)</th>
</tr>
</thead>
</table>

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3 WHO TO CONSIDER FOR STATIN TREATMENT

JBS-2 recommends that the following indications for statin treatment are given equal priority:

- secondary prevention of CVD
- people with diabetes
- people at high absolute risk of CVD (10-year CVD risk > 20%)

The management of people with Familial Hypercholesterolaemia is discussed at the end of this section.

3.1 Primary prevention

Statins are also effective in the primary prevention of major coronary events with the best evidence to date provided by the WOSCOPS trial (men aged 45 to 64 years) and AFCAPS/TexCAPS trial (men aged 45-73 years and women aged 55-73 years).

**Recommendation**

All adults over the age of 40 years who are assessed as having a ten year risk of having a first cardiovascular event > 20% should be considered for statin treatment following an informed discussion of risks and benefits between the patient and responsible clinician. (SIGN97)

**Good practice point**

Framingham equations may underestimate CVD risk for individuals with one or more of the following additional risk factors. The decision to commence a statin in individuals with one or more of the following risk factors should be made on a case by case basis, and should be accompanied by lifestyle advice:

- Cholesterol >8.0mmol/L (but see also section 3.3 for familial conditions)
- Systolic BP>160mmHg/ Diastolic BP>100mmHg
- People from deprived socio-economic groups
- People from the south Asian subcontinent
- Abdominal obesity – waist circumference: men=102cm (=90cm for men of south Asian origin), women=88cm (=80cm for women of south Asian origin)
- Impaired glucose tolerance (see section 2.4.1)
- Raised fasting triglyceride level (>1.7mmo/L)

Family history of premature CVD (coronary disease or stroke in parents or siblings below age 60 or in several close relatives). SIGN97 and JBS-2.

**Good practice point**

People who do not meet the criteria for primary prevention with a statin should be given general advice about lifestyle (e.g. diet, weight, alcohol intake, exercise, smoking) and have their risk assessed again in ~ 5 years.

3.2 Secondary prevention and diabetes

Statins are effective in the secondary prevention of:

- CHD events
- Coronary revascularisation
- Strokes and transient ischaemic events
- Combined major vascular events (including peripheral vascular disease).
Additionally, JBS-2 identifies patients with target organ damage as being at sufficiently high risk to warrant treatment without estimation of cardiovascular risk, even in the absence of symptomatic atherosclerotic disease.

People with diabetes aged over 40 years also benefit from statin therapy\(^{11}\), and some younger people with diabetes may also benefit from treatment (e.g. those with end organ damage, hypertension, metabolic syndrome or family history, but trial evidence for these groups remains limited). (p43, JBS-2)

| Recommendation | All patients with established symptomatic atherosclerotic CVD (CHD, stroke or TIA, peripheral vascular disease) should be considered for statin therapy following an informed discussion of risks and benefits between the patient and responsible clinician. (SIGN97) |
| Good practice point | Patients with target organ damage should also be considered for statin treatment, even in the absence of symptomatic atherosclerotic CVD. Target organ damage includes:  
  - Heart failure  
  - Abnormal renal function (elevated serum creatinine, reduced estimated glomerular filtration rate \(\text{eGFR}^*\leq 60\text{ml/min/1.73m}^2\) or proteinuria/microalbuminuria)  
  - Hypertensive or diabetic retinopathy  
  - Left ventricular hypertrophy on ECG or echocardiography (SIGN97 and JBS-2) |

\(^*\text{eGFR can be provided by the biochemistry lab using the following information: serum creatinine concentration, age and sex. If the patient is of African-Caribbean origin, then multiply eGFR by 1.21.}\)

| Good practice point | In order to meet the requirements of the Quality and Outcomes Framework (QOF)\(^{12}\), GP practices should keep a register of patients with:  
  - Coronary heart disease  
  - Stroke or TIA  
  - Diabetes (see appendix 1)  

In addition, although not included in QOF, GP practices may wish to keep a register of patients with peripheral vascular disease in order to monitor their response to statin treatment. |
3.3 Familial conditions
Patients with suspected familial hypercholesterolaemia or familial combined hyperlipidaemia should be referred to a specialist for investigation and management.

**Familial hypercholesterolaemia** should be considered if total cholesterol > 7.5mmol/L or low density lipoprotein (LDL) cholesterol > 4.9mmol/L.

Definite familial hypercholesterolaemia is diagnosed using Simon Broome criteria, with total cholesterol/ LDL cholesterol exceeding the values above plus tendon xanthomata in the person or a 1st or 2nd degree relative.

Possible familial hypercholesterolaemia is defined as total cholesterol/LDL cholesterol exceeding the values above plus a family history of MI before 60 years in a first-degree relative or a cholesterol of > 7.5 mmol/L in a first or second-degree relative.

**Familial combined hyperlipidaemia** should be considered in patients with a family history of hyperlipidaemia or premature coronary heart disease (CHD) not due to familial hypercholesterolaemia, and moderate to severe mixed hyperlipidaemia - typically serum total cholesterol 6.5-8.0 mmol/l and serum triglycerides 2.3-5.0 mmol/l. HDL levels are often low (< 1mmol/L) in these individuals.
4 AIMS OF TREATMENT AND TARGETS

The aims of treatment are to reduce morbidity and mortality from CVD by reducing total cholesterol.

4.1 Primary prevention

The most recent SIGN guideline differs from the most recent Joint British Society guidelines on the issue of treatment to target for primary prevention of CVD. There is little evidence to support aggressive treatment to arbitrary cholesterol targets in primary prevention. Additionally, there is no QOF indicator for cholesterol levels in the primary prevention of CVD with statins.

Good practice point
Once the patient is on a therapeutic dose of statin (e.g. generic simvastatin 40mg) it is not necessary to escalate treatment to achieve target cholesterol levels in primary prevention of CVD.

4.2 Secondary prevention and diabetes

QOF uses a total cholesterol treatment target of <5mmol/L for secondary prevention of CHD, cerebrovascular disease and diabetes; there is no equivalent target for peripheral vascular disease (see appendix 1). SIGN97 and JBS-2 use a target of <5mmol/L as the minimum standard of care. More research evidence is required before making a decision about more aggressive cholesterol lowering (see appendix 2).

Good practice point
The existing total cholesterol target of <5mmol/L in individuals with established symptomatic atherosclerotic disease should be regarded as the minimum standard of care. (SIGN97)
5 TREATMENT

5.1 Dietary advice
SIGN97 provides a useful summary of the evidence supporting dietary advice. A Cochrane review of the effect of reduction/modification of dietary fats found a reduction in cardiovascular events of 24% in studies with follow up of two years or more\textsuperscript{14}. Evidence for dietary management of familial hypercholesterolaemia is limited\textsuperscript{15}. Lifestyle advice should be given simultaneously with drug treatment (for primary and secondary prevention of CVD). Further information about diet is given in appendix 3.

| Good practice point | Lifestyle measures to reduce cholesterol levels should be encouraged, irrespective of the need for pharmacological treatment. |

5.2 Statin treatment
The Lothian Joint Formulary recommends simvastatin as first choice and atorvastatin as second choice statin.

There are large differences in costs between branded and generic statins as shown in table 1. However, different types of statins have broadly similar beneficial outcomes.\textsuperscript{16} (SIGN97). A comparison of the different cost of statins available in the UK is shown in table 1.

Table 1. Prices of branded and generic statins - (atorva, fluva and rosuva) are from BNF53, September 2007, while those generic statins (prava and simva) are from the Scottish Drug Tariff (November 2007 prices).\textsuperscript{17}

<table>
<thead>
<tr>
<th>Statin</th>
<th>Dose</th>
<th>Cost for 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10mg</td>
<td>£18.03</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>40mg</td>
<td>£15.26</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40mg</td>
<td>£7.54</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>20mg</td>
<td>£26.02</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>40mg</td>
<td>£1.31</td>
</tr>
</tbody>
</table>

Based on considerations of cost and effectiveness, simvastatin 40mg is the first choice statin. Also consider titration of the dose up from 10mg or 20mg simvastatin in older patients, and if there are concerns about liver function, alcohol excess or anxiety about side effects (in the absence of contraindications) or co-prescribing of drugs that may interact. If patient is taking medication that affects the cytochrome P450 3A4 pathway then consider pravastatin 40mg.

SIGN97 reports that there is considerable uncertainty about the cost effectiveness of statins in primary prevention. For this reason only generic simvastatin is recommended and the use of branded statins is probably not a cost effective approach in primary prevention.
The Lothian Joint Formulary recommends simvastatin as first choice and atorvastatin as second choice statin.

Different statins may be considered in the following circumstances.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Indication for trying alternative statin</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° prevention, 2° prevention or diabetes</td>
<td>Patient does not tolerate simvastatin or pravastatin due to side effects</td>
<td>Try atorvastatin 10mg in first instance (or fluvastatin 20mg if on medication that affects the cytochrome P450 3A4 pathway)</td>
</tr>
<tr>
<td>Secondary prevention, diabetes or Familial Hypercholesterolaemia</td>
<td>Total cholesterol remains above 5mmol/L after three months of treatment with simvastatin 40mg or pravastatin 40mg</td>
<td>Try atorvastatin 10mg (or rosuvastatin 10mg if on medication that affects the cytochrome P450 3A4 pathway) and increase dose according to response to treatment</td>
</tr>
</tbody>
</table>

5.3 Other drug treatments

Other drugs are available that have been shown to lower cholesterol levels. They can be useful in some specific situations, see below.

**Ezetimibe** is a drug with a different mode of action from statins. Ezetimibe is a cholesterol absorption inhibitor, and lowers cholesterol to a modest degree (15-20% when prescribed as 10mg monotherapy). Ezetimibe lowers cholesterol but there is no evidence to show that ezetimibe produces beneficial clinical outcomes.

The Lothian Formulary Committee recommend that ezetimibe should be reserved for patients who are statin intolerant* or when a statin is contraindicated in secondary prevention. Ezetimibe is not recommended in primary prevention. The Formulary Committee do not recommend the use of ezetimibe in combination with a statin.

**Fibrates** are primarily used for lowering triglycerides and raising low HDL levels. A fibrate should be initiated on specialist advice.

**Nicotinic acid** raises HDL levels and can be a useful therapy in patients with raised triglycerides and low HDL levels. Nicotinic acid should be initiated on specialist advice.

*The National Institute for Health and Clinical Excellence (NICE) define intolerance to statin therapy as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in compliance with therapy being compromised. Adverse effects include evidence of new onset muscle pain (often associated with levels of muscle enzymes in the blood indicative of muscle damage), significant gastrointestinal disturbance or alterations of LFTs. (NICE TA132)
6 COMPLIANCE, SIDE EFFECTS AND COMPLICATIONS WITH STATIN TREATMENT

6.1 Compliance
Three non-trial-based UK studies estimated compliance, identifying that between 64% and 86% of patients were compliant with therapy (defined as taking more than 70% or 80% of therapy).\textsuperscript{18} This estimate is likely to better reflect compliance in the general population than findings from randomised controlled trials.

6.2 Side effects
Statins appear to be well tolerated in the majority of patients. Statins may cause mild effects including (BNF53, SIGN97):

- **Headache**
- **Paraesthesia**
- **Gastro-intestinal** effects including abdominal pain, flatulence, constipation, diarrhoea, nausea and vomiting.
- **Minor muscle discomfort** (reversible myalgia and myositis – incidence varies). Other causes of muscle pain/raised CK should also be considered, including increased physical activity, trauma, falls, accidents, seizure, shaking chills, hypothyroidism, infections, carbon monoxide poisoning, polymyositis, dermatomyositis, alcohol abuse, drug abuse (cocaine, amphetamines, or heroin and others).

6.3 Complications
More serious complications are uncommon, but may include (SIGN97):

- **Altered liver function** (~1% of those treated), rarely progressing to hepatitis. More common with atorvastatin 80mg, or with concomitant use of ezetimibe. Consider withdrawal of statin (or reducing dose) if ALT is more than 3 times the upper limit of reference range. The clinician should be alert to patient reports of jaundice, malaise, fatigue, lethargy and signs of hepatomegaly. Increased bilirubin level and elevated prothrombin time are more reliable indicators of hepatotoxicity than simple elevations in liver transaminase levels.
- **Myopathy** with CK raised to more than 10 times upper normal limit (rare: 1/1000) - seek specialist advice. Rhabdomyolysis is defined as myopathy with end organ (renal) damage (very rare: 1 in 10,000 per year of exposure to statins) - requires emergency specialist review.
- **Peripheral neuropathy** (rare, exclude other causes in first instance)
- **Rash and hypersensitivity reactions** (including angioedema and anaphylaxis) have also been reported (rare).

**Good practice point**

Patients should be advised to report unexplained muscle pains or other adverse effects promptly, especially if associated with fever or malaise.

If such effects are mild, a different statin may be tried and/or the statin dose reduced after discussing the risks involved with the patient.

If severe side-effects are experienced, statin therapy should be discontinued.
7 CAUTIONS AND CONTRAINDICATIONS TO STATIN TREATMENT

The following cautions and contraindications are listed in JBS-2, SIGN97 and/or BNF 5419. More detailed information about interactions with specific drugs is provided in table 2.

Cautions
1. Non-alcoholic steatohepatitis
2. Untreated hypothyroidism
3. Significant chronic renal impairment (creatinine ≥ 160 mmol/l)
4. Certain drugs metabolised through cytochrome P450 (especially atorvastatin and simvastatin which are metabolised through 3A4 pathway). Note: Fluvastatin is metabolised by a different cytochrome P450 enzyme, while pravastatin and rosuvastatin are not substantially metabolised by cytochrome P450.
5. Excess alcohol intake
6. Grapefruit juice (in large amount) with statins metabolised through P450 3A4 pathway
7. Porphyria (though rosuvastatin may be safe, with specialist supervision)

Contraindications
1. Gemfibrozil co-prescription
2. Significant liver disease (moderate transaminase elevation up to 3 times upper limit of normal may represent fatty change and not be a contraindication)
3. Pregnancy (adequate contraception required during treatment and for 1 month afterwards)
4. Breast-feeding

Good practice point

Patients who are using medications that influence cytochrome P450 metabolism should avoid concomitant use of atorvastatin or simvastatin. In such cases, pravastatin is an acceptable alternative lipid lowering therapy.
Table 2. Interactions between statins and other medication (BNF 54, 2007). See also Committee on Safety of Medicines\textsuperscript{20}. Some of these medications may be given concomitantly with statins, but this will require specialist advice and support. E.g. BNF 54 recommends a maximum dose of simvastatin 10mg if patient taking ciclosporin or danazol, and simvastatin 20mg if patient taking amiodarone or verapamil.

<table>
<thead>
<tr>
<th>Statin</th>
<th>Atorva (1)</th>
<th>Fluva</th>
<th>Prava</th>
<th>Rosuva</th>
<th>Simva</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Amiodarone</td>
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<td>Antifungals, Imidazole</td>
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<td>* (even small volume)</td>
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</table>

1 - plasma concentration of statin increased with concomitant use  
2 - plasma concentration of statin reduced with concomitant use  
3 - concomitant use of statin possibly increases concentration of other drug  
4 - may transiently reduce anticoagulant effect of warfarin  
5 - increases anticoagulant effect of warfarin and other coumarins  
6 - combination may increase plasma concentration of either drug (or both)  
7 - absorption of rosuvastatin reduced by antacids  
* - increased risk of myopathy - avoid concomitant use  
† - possible increased risk of myopathy  
\textsuperscript{20} Committee on Safety of Medicines.
8 SPECIALIST ADVICE

Advice about assessing CVD risk, commencing or increasing therapy, and how to manage potential interactions can be obtained through the following clinics:

- Lipid Clinic – Royal Infirmary: RIE.LipidClinicAdvice@luht.scot.nhs.uk
- Cardiovascular risk clinic WGH: WGH.CardiovascRiskAdvice@luht.scot.nhs.uk
- Lipid Clinic – St John’s Hospital: (01506) 419666 (ext 2110)
There are a number of QOF indicators that are relevant to this guideline.

A GP practice should be able to produce a register of patients with:
- Stroke or TIA (STROKE 1)
- Coronary heart disease (CHD 1)
- Diabetes mellitus (DM 1)

A GP practice should have a record of total cholesterol (measured in the last 15 months) for patients with:
- Stroke or TIA (STROKE 7)
- Coronary heart disease (CHD 7)
- Diabetes mellitus (DM 16)

A GP practice should have a record of the percentage of patients with the following condition whose last measured total cholesterol (measured in last 15 months) is 5mmol/l or less:
- Stroke or TIA (STROKE 8)
- Coronary heart disease (CHD8)
- Diabetes mellitus (DM 17)
10 EVIDENCE FOR AND AGAINST MORE AGGRESSIVE CHOLESTEROL LOWERING

There has been a long running debate about optimal levels for cholesterol reduction. The three main approaches to cholesterol lowering are described below.

Fixed dose: Large randomised controlled trials of lipid lowering have compared the effect of fixed dose statins with placebo, and meta-analysis of these trials has demonstrated large reductions in cardiovascular end points and all cause mortality.\textsuperscript{10} These studies provide the strongest evidence for statins.

High dose: More recently several large randomised controlled trials have compared standard dose to high dose statins, but while a meta-analysis of the latter studies demonstrated a reduction in composite cardiovascular outcomes with high dose statin treatment, it did not identify a statistically significant reduction in all cause mortality.\textsuperscript{21}

Titrating dose: Few studies have looked at aggressive treatment to a specified total or LDL cholesterol, and while some guideline groups have attempted to extrapolate benefits of lipid lowering from observational studies, there are hazards with this approach.\textsuperscript{22}

There is therefore little evidence to support the optimal treatment targets quoted in JBS-2 (total cholesterol <4mmol/L or a 25% reduction, whichever is greatest; and LDL cholesterol, 2mmol/L or a 30% reduction, whichever is greatest) or the more aggressive lipid lowering recommended in American guidelines.\textsuperscript{23}

SIGN97 does not specify optimal treatment targets for primary prevention. (See also good practice point in section 4.2.)
DIETARY MANAGEMENT

While this dietary advice is designed for use in secondary prevention of CVD, many of the principles can be extended to primary prevention.

11.1 Reduce total fat intake (particularly saturated fats)
Advised:
- Reduce animal fats e.g. butter, cheese, red meats
- Replace with unsaturated fats e.g. rapeseed, canola or olive oils or spread
- Use low fat/reduced fat products e.g. reduced fat margarines, low fat yoghurts, semi-skimmed milk
- Use alternative cooking methods that do not add fat e.g. grill, bake, steam, microwave
- Reduce processed foods e.g. fatty and processed meats, cakes, biscuits and pastries.

11.2 Increase fruit & vegetable intake
Aim for 5 portions per day minimum, aim to incorporate into every meal and snack.

<table>
<thead>
<tr>
<th>What is a portion?</th>
<th>Healthy suggestions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 apple, orange or banana</td>
<td>use fresh, frozen, tinned or dried fruit and vegetables</td>
</tr>
<tr>
<td>3 tablespoonfuls of cooked vegetables, 1 dessert bowlful of salad</td>
<td>add vegetables to soups, stews, curries and stir-fries, or have salad with your main meal</td>
</tr>
<tr>
<td>2 plums, kiwis or satsumas or a cupful of grapes, strawberries or raspberries</td>
<td>try snacking on fresh or dried fruit</td>
</tr>
<tr>
<td>1 glass of fruit juice (150mls)</td>
<td></td>
</tr>
<tr>
<td>1 tablespoon of dried fruit</td>
<td></td>
</tr>
</tbody>
</table>

11.3 Increase Omega-3 fat intake

General population/ people suffering from CVD (but not previous MI)
- 2 portions fish per week, one of which should be oily fish

Post-MI:
- 2-3 portions of oily fish per week     OR
- equivalent 0.5 – 1.0g Omega-3 or Fish Body/Marine Oil supplements per day
  Portion size = 4oz or 120g

Oily fish:
Mackerel, Pilchards, fresh Tuna, Trout, Salmon, Sardines.

Non-fish Sources of Omega-3 fats:
- Rapeseed/Canola/Walnut oil
- Seeds and Nuts e.g. flax seeds, linseeds, walnuts, almonds
- Omega-3 enriched foods
11.4 Encourage Mediterranean-style diet
This includes:
- Increase Omega-3 intake
- Increase fruit & veg
- Increase wholegrains, nuts and pulses
- Increase fresh foods
- Decrease processed foods
- Decrease saturated fat intake

11.5 Reduce salt intake
Advise:
- Use small amounts in cooking, try to avoid adding salt at the table
- Use pepper, herbs and spices, vinegar and lemon juice to flavour food
- Do not rely too heavily on ready meals, tinned and processed foods, as they contain much higher amounts of salt.

11.6 Alcohol: drink within sensible limits
Men: no more than 3-4 units per day, no more than 21 units per week
Women: no more than 2-3 units per day, no more than 14 units per week
One unit of alcohol is:
- a pub measure of spirits
- a small glass (125mls) of wine
- ½ pint of beer, lager or cider.

You should aim to keep your intake within these limits, and have 2 alcohol-free days per week.

11.7 Achieve and maintain a healthy body weight
Overweight and obese patients will require additional advice regarding total calorie intake e.g. restricting fat/sugar, controlling portion sizes.

11.8 Plant Stanols & Sterols

Plant Stanols/Sterols e.g. Benecol, Danecol, Flora Proactiv may have additional benefit in lowering LDL in addition to following the dietary advice given here.
11.9 Dietetic Referral Pathway for patients with established CVD

Established Cardiovascular Disease/Secondary Prevention
Post ME, Post Rehab, Post CABG Post rehab
Ischaemic Stroke. TIA. PVD. Angina. Diabetes

At GP practice / Chronic Disease Management clinic
Discuss the benefits of lifestyle changes/reinforce previous education for reduction of further risk, prevention of further events and improving health.
• Provide healthy eating, increased physical activity, and behavioural change advice
• Dietary information web addresses: Ref help, CHD/stroke MCN and NHS Lipid guidelines

Agree dietary/lifestyle outcomes based on the following:
• reduction of fat especially saturated fats
• increase fruit and vegetables, reduction in salt
• weight management (Counterweight Programme offered if appropriate)
• Mediterranean diet
• 2 portions of fish/week (one of which should be oily fish), post MI encourage 2-3 portions oily fish per week
• increase in activity: 30 minutes moderate activity no less than 5 days/week

Practice to review at 3 months: Achieving agreed outcomes

YES
Refer to Dietician for dietetic assessment if patient is willing to make changes and;
• Has difficulties making dietary changes
• Has BMI >30 or underweight <18.9
• Waist circumference of:
  ➢ >102cm men
  ➢ >88cm women
  ➢ >90cm Asian men
  ➢ >80cm Asian women
• has difficulties controlling or reducing weight
• is commencing anti-obesity medication
• has difficulties controlling cholesterol or triglycerides
• unwilling or unable to take lipid lowering medication
• any of the above and diabetes

NO
Continue to monitor at Practice as recommended
Locality Dietician Contact details:

<table>
<thead>
<tr>
<th>LHP</th>
<th>ADDRESS</th>
<th>TEL NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Central</td>
<td>Blackford Pavilion Astley Ainslie Hospital 133 Grange Loan EDINBURGH, EH9 2HL</td>
<td>0131 537 9258</td>
</tr>
<tr>
<td>South East</td>
<td>Gracemount Medical Centre 24 Gracemount Drive EDINBURGH, EH16 6RN</td>
<td>0131 672 9530</td>
</tr>
<tr>
<td>South East (Healthy Living Initiative)</td>
<td>Healthy Eating development worker Unit 2 Block B Gracemount Business Pavilions Captains Road, Edinburgh EH17 8QF</td>
<td>0131 664 0555</td>
</tr>
<tr>
<td>South West</td>
<td>Sighthill Health Centre 380 Calder Road EDINBURGH, EH11 4AU</td>
<td>0131 537 7132</td>
</tr>
<tr>
<td></td>
<td>Wester Hailes Health Agency 40 Dumbryden Drive, EH14 2QR</td>
<td>0131 453 4786</td>
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<tr>
<td>North East</td>
<td>CTC, Junction Place, Leith, EH6 5JQ</td>
<td>0131 536 6281</td>
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<tr>
<td>North West</td>
<td>Craigroyston Health Centre 1b Pennywell Road, Edinburgh, EH4 4PH</td>
<td>0131 315 2202</td>
</tr>
<tr>
<td>North East. Khush Dil Project</td>
<td>Allander House 141 Leith Walk Edinburgh EH6 8NP</td>
<td>0131 537 4585</td>
</tr>
<tr>
<td>East Lothian</td>
<td>Roodlands Hospital Haddington, EH39</td>
<td>0131 536 8318</td>
</tr>
<tr>
<td>Midlothian</td>
<td>Bonnyrigg Health Centre 109-111 High St Bonnyrigg EH19 2ET</td>
<td>0131 537 9884</td>
</tr>
<tr>
<td>West Lothian</td>
<td>Nutrition and Dietetic Dept St Johns Hospital Howden Livingston</td>
<td>01506 419 666 ext: 2306</td>
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## 11.11 Dietary Information Leaflets For Secondary Prevention

<table>
<thead>
<tr>
<th>Information Leaflet</th>
<th>Cost</th>
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| Eat for the Beat               | £9.22 (£9.22 = 20) | Scottish Nutrition and Diet Resource Initiative | Room MS 010, Milton Street Building, Glasgow Caledonian University, Glasgow, G4 0BA         | Tel: 0141 331 8479  
|                                |               |                                                   |                                                                                             | Fax: 0141 331 3208  
|                                |               |                                                   |                                                                                             | E-mail: Leona.O'Reilly@gcal.ac.uk                                           |
| Eat Fish                       | See Price List | BDA, UK Heart Health Dietitians                  | Comic Company                                                                              | Tel: 020 8675 1007  
|                                |               |                                                   |                                                                                             | Fax: 020 8675 7486  
|                                |               |                                                   |                                                                                             | E-mail: heartfood@comiccompany.co.uk                                        |
| Good Heart Food                | See Price List | BDA, UK Heart Health Dietitians                  | Comic Company                                                                              | Tel: 020 8675 1007  
|                                |               |                                                   |                                                                                             | Fax: 020 8675 7486  
|                                |               |                                                   |                                                                                             | E-mail: heartfood@comiccompany.co.uk                                        |
| Heart Disease and Omega-3s     |               | BDA, UK Heart Health Dietitians                  | Can be downloaded from BDA website                                                          | [www.bda.uk.com](http://www.bda.uk.com)  
|                                |               |                                                   |                                                                                             | ➔ Educational & Training ➔ Continuous Professional Development ➔ Specialist Groups ➔ UK Heart Health & Thoracic Dieticians |
| Eating For Your Heart          | By Donation   | British Heart Foundation                         | 14 Fitzhardinge Street, London W1H 6DH (can be ordered via website)                          | Tel: 0207 935 0185  
|                                |               |                                                   |                                                                                             | Website: [www.bhf.org.uk](http://www.bhf.org.uk)                           |
| Cut the Saturated Fat from your Diet | By Donation   | British Heart Foundation                         | 14 Fitzhardinge Street, London W1H 6DH (can be ordered via website)                          | Tel: 0207 935 0185  
|                                |               |                                                   |                                                                                             | Website: [www.bhf.org.uk](http://www.bhf.org.uk)                           |
| Omega-3 and your health        | £7 = 50  
|                                |               |                                                  | Fish Foundation                                                                            | Tel: 01884 257547  
|                                |               |                                                  |                                                                                             | Fax: 01884 259929  
|                                |               |                                                  |                                                                                             | E-mail: rayrice@eclips.co.uk                                               |
| Enjoy Healthy Eating: The Balance of Good Health | Free | Food Standards Agency | c/o EC Logistics  
|                                |               |                                                   | Swallowfield Way, Hayes, Middlesex UB3 1DQ                                                  | Tel: 0845 606 0667  
|                                |               |                                                   |                                                                                             | Fax: 020 8867 3225  
|                                |               |                                                   |                                                                                             | E-mail: foodstandards@eclogistics.co.uk                                    |
| Eating For Health              | Free          | HEBS                                             | Lothian NHS Board Library Resource Centre, Deaconess House, 148 Pleasance, Edinburgh, EH8 9RS | Tel: 0131 536 9451  
|                                |               |                                                   |                                                                                             | Fax: 0131 536 9246                                                      |
### Dietary Information Leaflets For Weight Reduction

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<tr>
<td>So You Want To Lose Weight .... For Good</td>
<td>By Donation</td>
<td>British Heart Foundation</td>
<td>14 Fitzhardinge Street London W1H 6DH (can be ordered via website)</td>
<td>Tel: 0207 935 0185&lt;br&gt;Website: <a href="http://www.bhf.org.uk">www.bhf.org.uk</a></td>
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<tr>
<td>Weight Loss On A Plate</td>
<td>20 = £6.40&lt;br&gt;Meal Planner (50) = £0.94</td>
<td>Scottish Nutrition and Diet Resource Initiative</td>
<td>Room MS 010, Milton Street Building, Glasgow Caledonian University, Glasgow, G4 OBA</td>
<td>Tel: 0141 331 8479&lt;br&gt;Fax: 0141 331 3208&lt;br&gt;Email: Leona.O'<a href="mailto:Reilly@gcal.ac.uk">Reilly@gcal.ac.uk</a></td>
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### Miscellaneous Leaflets

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<td>Guide to Food Labelling</td>
<td>By Donation</td>
<td>British Heart Foundation</td>
<td>14 Fitzhardinge Street London W1H 6DH (can be ordered via website)</td>
<td>Tel: 0207 935 0185&lt;br&gt;Website: <a href="http://www.bhf.org.uk">www.bhf.org.uk</a></td>
</tr>
</tbody>
</table>
12 REFERENCES


3. SIGN guideline 40. Lipids and the Primary Prevention of Coronary Heart Disease. A national clinical guideline. SIGN 1999


13 Members of Lothian Lipid Guideline Group

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Fiona Black
Dr Peter Bloomfield
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Dr Simon Walker
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