

Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease

Issued: July 2014 last modified: January 2015

NICE clinical guideline 181

guidance.nice.org.uk/cg181

Contents

Introduction	4
Drug recommendations	5
Patient-centred care	6
Key priorities for implementation	7
Identifying and assessing cardiovascular disease (CVD) risk.....	7
Lipid modification therapy for the primary and secondary prevention of CVD	7
1 Recommendations	9
1.1 Identifying and assessing cardiovascular disease (CVD) risk	9
1.2 Lifestyle modifications for the primary and secondary prevention of CVD	13
1.3 Lipid modification therapy for the primary and secondary prevention of CVD	16
2 Implementation: getting started	28
2.1 Measuring non-high density lipoprotein cholesterol when lipid profiling for the primary prevention of cardiovascular disease.....	28
2.2 Reduction of the primary prevention threshold from 20% to 10% CVD risk as calculated by QRISK2	29
2.3 Atorvastatin for the primary and secondary prevention of CVD	30
2.4 Further resources	31
3 Research recommendations	32
3.1 Simplifying risk assessment	32
3.2 Cost effectiveness using individual patient-level data	32
3.3 Statin therapy in older people	33
3.4 Lipid modification therapy in people with type 1 diabetes	33
3.5 Comparative effectiveness and risks of alternative doses of atorvastatin.....	33
4 Other information.....	35
4.1 Scope and how this guideline was developed	35
4.2 Related NICE guidance.....	35

5 The Guideline Development Group, National Collaborating Centre and NICE project team	38
5.1 Guideline Development Group	38
5.2 Co-opted GDG members and peer-reviewers	39
National Clinical Guideline Centre staff.....	40
NICE project team	40
Appendix A: Grouping of statins	42
Changes after publication.....	43
About this guideline	44
Update information	44
Strength of recommendations	52
Other versions of this guideline	54
Implementation.....	54
Your responsibility	54
Copyright.....	54

Introduction

This guideline updates and replaces NICE clinical guideline 67 and NICE technology appraisal guidance 94. The recommendations are labelled according to when they were originally published (see [about this guideline](#) for details).

Cardiovascular disease (CVD) describes disease of the heart and blood vessels caused by the process of atherosclerosis. It is the leading cause of death in England and Wales, accounting for almost one-third of deaths^[1]. In 2010, 180,000 people died from CVD – around 80,000 of these deaths were caused by coronary heart disease and 49,000 were caused by strokes. Of the 180,000 deaths, 46,000 occurred before people were aged 75 years, and 70% of those were in men. Death rates from CVD peaked in the 1970s and 1980s but have more than halved since then. Rates have fallen more rapidly in older age groups compared with younger ones, with an approximately 50% reduction in the 55–64 year age group compared with a 20% reduction in men aged 35–44 years. In spite of evidence that mortality from CVD is falling, morbidity appears to be rising. CVD has significant cost implications and was estimated to cost the NHS in England almost £6,940 million in 2003, rising to £7,880 million in 2010.

CVD shows strong age dependence and predominantly affects people older than 50 years. Risk factors for CVD include non-modifiable factors such as age, sex, family history of CVD, ethnic background and modifiable risk factors such as smoking, raised blood pressure and cholesterol. CVD is strongly associated with low income and social deprivation and shows a North–South divide, with higher rates in the north of England.

This guideline includes recommendations on risk assessment for CVD and on the use of lipid-lowering drugs. The original guideline is updated in part to allow consideration of new evidence on risk assessment tools and to reflect changes in price and availability of generic statins.

NICE has produced guidance on other modifiable risk factors for CVD and this guideline should be used in conjunction with it.

In this update the Guideline Development Group (GDG) recommend the use of non-high density lipoprotein (non-HDL) cholesterol rather than low density lipoprotein (LDL) cholesterol. Non-HDL cholesterol is total cholesterol minus HDL cholesterol. LDL cholesterol is not directly measured

but requires a calculation using a fasting sample and for triglyceride levels to be less than 4.5 mmol/litre, whereas the measurement of non-HDL cholesterol does not.

For the purpose of this guideline, statins are grouped into 3 different intensity categories according to the percentage reduction in low-density lipoprotein cholesterol they produce:

- low intensity if the reduction is 20% to 30%
- medium intensity if the reduction is 31% to 40%
- high intensity if the reduction is above 40%.

Please see [appendix A](#) for further details. This grouping was agreed by GDG consensus, informed by analyses in the literature. See also the full guideline for a discussion of this grouping.

Drug recommendations

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

^[1] [UK National Statistics](#).

Patient-centred care

This guideline offers best practice advice on the care of people at risk of cardiovascular disease.

Patients and healthcare professionals in England have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. Healthcare professionals should follow the [Department of Health's advice on consent](#). If someone does not have the capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) and the supplementary [code of practice on deprivation of liberty safeguards](#).

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#).

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Identifying and assessing cardiovascular disease (CVD) risk

- For the primary prevention of CVD in primary care, use a systematic strategy to identify people who are likely to be at high risk. **[2008, amended 2014]**
- Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is 10% or more. **[2008, amended 2014]**
- Use the QRISK2 risk assessment tool to assess CVD risk for the primary prevention of CVD in people up to and including age 84 years. **[new 2014]**
- Do not use a risk assessment tool to assess CVD risk in people with an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m² and/or albuminuria^[2]. These people are at increased risk of CVD. See recommendation 1.3.27 for advice on treatment with statins for people with chronic kidney disease. **[new 2014]**

Lipid modification therapy for the primary and secondary prevention of CVD

- Before starting lipid modification therapy for the primary prevention of CVD, take at least 1 lipid sample to measure a full lipid profile. This should include measurement of total cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol, and triglyceride concentrations. A fasting sample is not needed. **[new 2014]**
- Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. **[new 2014]**
- Start statin treatment in people with CVD with atorvastatin 80 mg^[3]. Use a lower dose of atorvastatin if any of the following apply:
 - potential drug interactions
 - high risk of adverse effects

-
- patient preference. **[new 2014]**
 - Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on high-intensity statin treatment at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved:
 - discuss adherence and timing of dose
 - optimise adherence to diet and lifestyle measures
 - consider increasing dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. **[new 2014]**

[This recommendation updates and replaces recommendation 1.10.2.7 from Type 1 diabetes (NICE clinical guideline 15).]

^[2] People on renal replacement therapy are outside the scope of this guideline.

^[3] At the time of publication (July 2014), atorvastatin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See [about this guideline](#) for details.

1.1 Identifying and assessing cardiovascular disease (CVD) risk

Identifying people for full formal risk assessment

- 1.1.1 For the primary prevention of CVD in primary care, use a systematic strategy to identify people who are likely to be at high risk. **[2008, amended 2014]**
- 1.1.2 Prioritise people on the basis of an estimate of their CVD risk before a full formal risk assessment. Estimate their CVD risk using CVD risk factors already recorded in primary care electronic medical records. **[2008]**
- 1.1.3 People older than 40 should have their estimate of CVD risk reviewed on an ongoing basis. **[2008]**
- 1.1.4 Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is 10% or more. **[2008, amended 2014]**
- 1.1.5 Discuss the process of risk assessment with the person identified as being at risk, including the option of declining any formal risk assessment. **[2008]**
- 1.1.6 Do not use opportunistic assessment as the main strategy in primary care to identify CVD risk in unselected people. **[2008]**

Full formal risk assessment

- 1.1.7 Be aware that all CVD risk assessment tools can provide only an approximate value for CVD risk. Interpretation of CVD risk scores should always reflect informed clinical judgement. **[2008]**
- 1.1.8 Use the QRISK2 risk assessment tool to assess CVD risk for the primary prevention of CVD in people up to and including age 84 years. **[new 2014]**
- 1.1.9 Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes. See recommendations 1.3.23, 1.3.24 and 1.3.25 for advice on treatment with statins for people with type 1 diabetes. **[new 2014]** [This recommendation updates and replaces recommendation 1.10.1.2 from [Type 1 diabetes](#) (NICE clinical guideline 15).]
- 1.1.10 Use the QRISK2 risk assessment tool to assess CVD risk in people with type 2 diabetes. **[new 2014]** [This recommendation updates and replaces recommendations 1.9.1, 1.9.2 and 1.9.3 from [Type 2 diabetes](#) (NICE clinical guideline 87).]
- 1.1.11 Do not use a risk assessment tool to assess CVD risk in people with an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m² and/or albuminuria^[4]. These people are at increased risk of CVD. See recommendation 1.3.27 for advice on treatment with statins for people with chronic kidney disease (CKD). **[new 2014]**
- 1.1.12 Complete as many fields of the risk assessment tool as possible. **[new 2014]**
- 1.1.13 Routinely record ethnicity, body mass index and family history of premature CVD in medical records. **[2008]**
- 1.1.14 Consider socioeconomic status as an additional factor that contributes to CVD risk. **[2008]**
- 1.1.15 Do not use a risk assessment tool for people with pre-existing CVD. **[2008, amended 2014]**

1.1.16 Do not use a risk assessment tool for people who are at high risk of developing CVD because of familial hypercholesterolaemia (see [Familial hypercholesterolaemia](#) [NICE clinical guideline 71]) or other inherited disorders of lipid metabolism. **[2008, amended 2014]**

1.1.17 When using the risk score to inform drug treatment decisions, particularly if it is near to the threshold for treatment, take into account other factors that:

- may predispose the person to premature CVD **and**
- may not be included in calculated risk scores. **[2008, amended 2014]**

1.1.18 Recognise that standard CVD risk scores will underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include:

- people treated for HIV
- people with serious mental health problems
- people taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
- people with autoimmune disorders such as systemic lupus erythematosus, and other systemic inflammatory disorders. **[2008, amended 2014]**

1.1.19 Recognise that CVD risk will be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking. Use clinical judgement to decide on further treatment of risk factors in people who are below the CVD risk threshold for treatment. **[2008, amended 2014]**

1.1.20 Severe obesity (body mass index greater than 40 kg/m²) increases CVD risk. Take this into account when using risk scores to inform treatment decisions in this group (see [Obesity](#) [NICE clinical guideline 43]). **[2008]**

- 1.1.21 Consider people aged 85 or older to be at increased risk of CVD because of age alone, particularly people who smoke or have raised blood pressure. **[2008, amended 2014]**

Communication about risk assessment and treatment

- 1.1.22 NICE has produced guidance on the components of good patient experience in adult NHS services. These include recommendations on the communication of risk. Follow the recommendations in [Patient experience in adult NHS services](#) (NICE clinical guidance 138). **[new 2014]**
- 1.1.23 Use everyday, jargon-free language to communicate information on risk. If technical terms are used, explain them clearly. **[2008]**
- 1.1.24 Set aside adequate time during the consultation to provide information on risk assessment and to allow any questions to be answered. Further consultation may be required. **[2008]**
- 1.1.25 Document the discussion relating to the consultation on risk assessment and the person's decision. **[2008]**
- 1.1.26 Offer people information about their absolute risk of CVD and about the absolute benefits and harms of an intervention over a 10-year period. This information should be in a form that:
- presents individualised risk and benefit scenarios **and**
 - presents the absolute risk of events numerically **and**
 - uses appropriate diagrams and text. **[2008]**
- 1.1.27 To encourage the person to participate in reducing their CVD risk:
- find out what, if anything, the person has already been told about their CVD risk and how they feel about it
 - explore the person's beliefs about what determines future health (this may affect their attitude to changing risk)

- assess their readiness to make changes to their lifestyle (diet, physical activity, smoking and alcohol consumption), to undergo investigations and to take long-term medication
- assess their confidence in making changes to their lifestyle, undergoing investigations and taking medication
- inform them of potential future management based on current evidence and best practice
- involve them in developing a shared management plan
- check with them that they have understood what has been discussed. **[2008, amended 2014]**

1.1.28 If the person's CVD risk is at a level where intervention is recommended but they decline the offer of treatment, advise them that their CVD risk should be reassessed again in the future. Record their choice in their medical notes. **[2008, amended 2014]**

1.2 Lifestyle modifications for the primary and secondary prevention of CVD

Cardioprotective diet

1.2.1 Advise people at high risk of or with CVD to eat a diet in which total fat intake is 30% or less of total energy intake, saturated fats are 7% or less of total energy intake, intake of dietary cholesterol is less than 300 mg/day and where possible saturated fats are replaced by mono-unsaturated and polyunsaturated fats. Further information and advice can be found at [NHS Choices](#). **[new 2014]**

1.2.2 For people at high risk of or with CVD:

- Tell them that reducing their saturated fat intake from animal sources also reduces their mono-unsaturated fat levels.
- Advise them to replace their saturated and mono-unsaturated fat intake with olive oil, rapeseed oil or spreads based on these oils.

- Advise them to use olive oil, rapeseed oil or spreads based on these oils in food preparation.

Further information and advice on healthy cooking methods can be found at [NHS Choices](#). **[new 2014]**

1.2.3 Advise people at high risk of or with CVD to do all of the following:

- choose wholegrain varieties of starchy food
- reduce their intake of sugar and food products containing refined sugars including fructose
- eat at least 5 portions of fruit and vegetables per day
- eat at least 2 portions of fish per week, including a portion of oily fish
- eat at least 4 to 5 portions of unsalted nuts, seeds and legumes per week.

Further information and advice can be found at [NHS Choices](#). **[new 2014]**

1.2.4 Advise pregnant women to limit their oily fish to no more than 2 portions per week and to avoid marlin, shark and swordfish. Further information and advice on oily fish consumption can be found at [NHS Choices](#). **[new 2014]**

1.2.5 Take account of a person's individual circumstances – for example, drug therapy, comorbidities and other lifestyle modifications when giving dietary advice. **[new 2014]**

1.2.6 Advise and support people at high risk of or with CVD to achieve a healthy diet in line with [Behaviour change: the principles for effective interventions](#) (NICE public health guidance 6). **[new 2014]**

Physical activity

1.2.7 Advise people at high risk of or with CVD to do the following every week:

- at least 150 minutes of moderate intensity aerobic activity **or**

- 75 minutes of vigorous intensity aerobic activity or a mix of moderate and vigorous aerobic activity

in line with national guidance for the general population (see [Physical activity guidelines for adults](#) at NHS Choices). **[2008, amended 2014]**

- 1.2.8 Advise people to do muscle-strengthening activities on 2 or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders and arms) in line with national guidance for the general population (see [Physical activity guidelines for adults](#) at NHS Choices). **[new 2014]**
- 1.2.9 Encourage people who are unable to perform moderate-intensity physical activity because of comorbidity, medical conditions or personal circumstances to exercise at their maximum safe capacity. **[2008, amended 2014]**
- 1.2.10 Advice about physical activity should take into account the person's needs, preferences and circumstances. Agree goals and provide the person with written information about the benefits of activity and local opportunities to be active, in line with [Four commonly used methods to increase physical activity](#) (NICE public health guidance 2). **[2008]**

Combined interventions (diet and physical activity)

- 1.2.11 Give advice on diet and physical activity in line with national recommendations (see [NHS Choices](#)). **[2008]**

Weight management

- 1.2.12 Offer people at high risk of or with CVD who are overweight or obese appropriate advice and support to work towards achieving and maintaining a healthy weight, in line with [Obesity](#) (NICE clinical guideline 43). **[2008]**

Alcohol consumption

- 1.2.13 Be aware that men should not regularly drink more than 3–4 units a day and women should not regularly drink more than 2–3 units a day. People should avoid binge drinking. Further information can be found at [NHS Choices](#). **[2008]**

Smoking cessation

- 1.2.14 Advise all people who smoke to stop, in line with [Smoking cessation services](#) (NICE public health guidance 10). **[2008]**
- 1.2.15 Offer people who want to stop smoking support and advice, and referral to an intensive support service (for example, the NHS Stop Smoking Services). **[2008]**
- 1.2.16 If a person is unable or unwilling to accept a referral to an intensive support service, offer them pharmacotherapy in line with [Smoking cessation services](#) (NICE public health guidance 10) and [Varenicline for smoking cessation](#) (NICE technology appraisal guidance 123). **[2008]**

Plant stanols and sterols

- 1.2.17 Do not advise any of the following to take plant stanols or sterols for the prevention of CVD:
- people who are being treated for primary prevention
 - people who are being treated for secondary prevention
 - people with CKD
 - people with type 1 diabetes
 - people with type 2 diabetes. **[new 2014]**

1.3 Lipid modification therapy for the primary and secondary prevention of CVD

- 1.3.1 Be aware that when deciding on lipid modification therapy for the prevention of CVD, drugs are preferred for which there is evidence in clinical trials of a beneficial effect on CVD morbidity and mortality. **[2008]**
- 1.3.2 When a decision is made to prescribe a statin use a statin of high intensity^[3] and low acquisition cost. **[new 2014]**

Lipid measurement and referral

Recommendations in this section update and replace recommendation 1.9.4 from [Type 2 diabetes](#) (NICE clinical guideline 87).

- 1.3.3 Measure both total and high-density lipoprotein (HDL) cholesterol to achieve the best estimate of CVD risk. **[2008]**
- 1.3.4 Before starting lipid modification therapy for the primary prevention of CVD, take at least 1 lipid sample to measure a full lipid profile. This should include measurement of total cholesterol, HDL cholesterol, non-HDL cholesterol and triglyceride concentrations. A fasting sample is not needed. **[new 2014]**

For information about implementing this recommendation, see [Implementation: getting started](#).

- 1.3.5 Use the clinical findings, lipid profile and family history to judge the likelihood of a familial lipid disorder rather than the use of strict lipid cut-off values alone. **[new 2014]**
- 1.3.6 Exclude possible common secondary causes of dyslipidaemia (such as excess alcohol, uncontrolled diabetes, hypothyroidism, liver disease and nephrotic syndrome) before referring for specialist review. **[new 2014]**
- 1.3.7 Consider the possibility of familial hypercholesterolaemia and investigate as described in [Familial hypercholesterolaemia](#) (NICE clinical guideline 71) if they have:
- a total cholesterol concentration more than 7.5 mmol/litre **and**
 - a family history of premature coronary heart disease. **[new 2014]**
- 1.3.8 Arrange for specialist assessment of people with a total cholesterol concentration of more than 9.0 mmol/litre or a non-HDL cholesterol concentration of more than 7.5 mmol/litre even in the absence of a first-degree family history of premature coronary heart disease. **[new 2014]**

- 1.3.9 Refer for urgent specialist review if a person has a triglyceride concentration of more than 20 mmol/litre that is not a result of excess alcohol or poor glycaemic control. **[new 2014]**
- 1.3.10 In people with a triglyceride concentration between 10 and 20 mmol/litre:
- repeat the triglyceride measurement with a fasting test (after an interval of 5 days, but within 2 weeks) **and**
 - review for potential secondary causes of hyperlipidaemia **and**
 - seek specialist advice if the triglyceride concentration remains above 10 mmol/litre. **[new 2014]**
- 1.3.11 In people with a triglyceride concentration between 4.5 and 9.9 mmol/litre:
- be aware that the CVD risk may be underestimated by risk assessment tools **and**
 - optimise the management of other CVD risk factors present **and**
 - seek specialist advice if non-HDL cholesterol concentration is more than 7.5 mmol/litre. **[new 2014]**

Statins for the prevention of CVD

Recommendations in this section update and replace those in [Statins for the prevention of cardiovascular events](#) (NICE technology appraisal guidance 94)].

- 1.3.12 The decision whether to start statin therapy should be made after an informed discussion between the clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as potential benefits from lifestyle modifications, informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy. **[new 2014]**
- 1.3.13 Before starting statin treatment perform baseline blood tests and clinical assessment, and treat comorbidities and secondary causes of dyslipidaemia. Include all of the following in the assessment:
- smoking status

- alcohol consumption
- blood pressure (see [Hypertension](#) [NICE clinical guideline 127])
- body mass index or other measure of obesity (see [Obesity](#) [NICE clinical guideline 43])
- total cholesterol, non-HDL cholesterol, HDL cholesterol and triglycerides
- HbA_{1c}
- renal function and eGFR
- transaminase level (alanine aminotransferase or aspartate aminotransferase)
- thyroid-stimulating hormone. **[new 2014]**

Primary prevention

- 1.3.14 Before offering statin treatment for primary prevention, discuss the benefits of lifestyle modification and optimise the management of all other modifiable CVD risk factors if possible. **[new 2014]**
- 1.3.15 Recognise that people may need support to change their lifestyle. To help them do this, refer them to programmes such as exercise referral schemes. (See [Behaviour change: individual approaches](#) [NICE public health guidance 49].) **[new 2014]**
- 1.3.16 Offer people the opportunity to have their risk of CVD assessed again after they have tried to change their lifestyle. **[new 2014]**
- 1.3.17 If lifestyle modification is ineffective or inappropriate offer statin treatment after risk assessment. **[new 2014]**
- 1.3.18 Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. **[new 2014]**

For information about implementing this recommendation, see [Implementation: getting started](#).

- 1.3.19 For people 85 years or older consider atorvastatin 20 mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction. Be aware of factors that may make treatment inappropriate (see recommendation 1.3.12). **[new 2014]**

Secondary prevention

- 1.3.20 Start statin treatment in people with CVD with atorvastatin 80 mg^[6]. Use a lower dose of atorvastatin if any of the following apply:
- potential drug interactions
 - high risk of adverse effects
 - patient preference. **[new 2014]**

For information about implementing this recommendation, see [Implementation: getting started](#).

- 1.3.21 Do not delay statin treatment in secondary prevention to manage modifiable risk factors. **[2014]**
- 1.3.22 If a person has acute coronary syndrome, do not delay statin treatment. Take a lipid sample on admission and about 3 months after the start of treatment. **[2008, amended 2014]**

Primary prevention for people with type 1 diabetes

Recommendations in this section update and replace recommendations 1.10.1.3, 1.10.1.4, 1.10.1.5 and 1.10.2.4 from [Type 1 diabetes](#) (NICE clinical guideline 15).

- 1.3.23 Consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes. **[new 2014]**
- 1.3.24 Offer statin treatment for the primary prevention of CVD to adults with type 1 diabetes who:
- are older than 40 years **or**

- have had diabetes for more than 10 years **or**
- have established nephropathy **or**
- have other CVD risk factors. **[new 2014]**

1.3.25 Start treatment for adults with type 1 diabetes with atorvastatin 20 mg. **[new 2014]**

Primary prevention for people with type 2 diabetes

1.3.26 Offer atorvastatin 20 mg for the primary prevention of CVD to people with type 2 diabetes who have a 10% or greater 10-year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. **[new 2014]** [This recommendation updates and replaces recommendations 1.10.1.2, 1.10.1.3, and 1.10.1.5 from [Type 2 diabetes](#) (NICE clinical guideline 87).]

People with CKD

1.3.27 Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD^[7].

- Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved (see recommendation 1.3.28) and eGFR is 30 ml/min/1.73 m² or more.
- Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/min/1.73 m². **[new 2014]**

Follow-up of people started on statin treatment

1.3.28 Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on high-intensity statin treatment at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved:

- discuss adherence and timing of dose
- optimise adherence to diet and lifestyle measures

- consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. [new 2014]

[This recommendation updates and replaces recommendation 1.10.2.7 from [Type 1 diabetes](#) (NICE clinical guideline 15) and recommendation 1.10.1.6 from [Type 2 diabetes](#) (NICE clinical guideline 87).]

1.3.29 Provide annual medication reviews for people taking statins.

- Use these reviews to discuss medicines adherence and lifestyle modification and address CVD risk factors.
- Consider an annual non-fasting blood test for non-HDL cholesterol to inform the discussion. [new 2014]

1.3.30 Discuss with people who are stable on a low- or middle-intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed. [new 2014]

For information about implementing this recommendation, see [Implementation: getting started](#).

Advice and monitoring for adverse effects

1.3.31 Advise people who are being treated with a statin:

- that other drugs, some foods (for example, grapefruit juice) and some supplements may interfere with statins **and**
- to always consult the patient information leaflet, a pharmacist or prescriber for advice when starting other drugs or thinking about taking supplements. [new 2014]

1.3.32 Remind the person to restart the statin if they stopped taking it because of drug interactions or to treat intercurrent illnesses. [new 2014]

- 1.3.33 Before offering a statin, ask the person if they have had persistent generalised unexplained muscle pain, whether associated or not with previous lipid-lowering therapy. If they have, measure creatine kinase levels.
- If creatine kinase levels are more than 5 times the upper limit of normal, re-measure creatine kinase after 7 days. If creatine kinase levels are still 5 times the upper limit of normal, do not start statin treatment.
 - If creatine kinase levels are raised but less than 5 times the upper limit of normal, start statin treatment at a lower dose. **[new 2014]**
- 1.3.34 Advise people who are being treated with a statin to seek medical advice if they develop muscle symptoms (pain, tenderness or weakness). If this occurs, measure creatine kinase. **[2008]**
- 1.3.35 If people report muscle pain or weakness while taking a statin, explore other possible causes of muscle pain or weakness and raised creatine kinase if they have previously tolerated statin therapy for more than 3 months. **[new 2014]**
- 1.3.36 Do not measure creatine kinase levels in asymptomatic people who are being treated with a statin. **[2008]**
- 1.3.37 Measure baseline liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) before starting a statin. Measure liver transaminase within 3 months of starting treatment and at 12 months, but not again unless clinically indicated. **[2008]**
- 1.3.38 Do not routinely exclude from statin therapy people who have liver transaminase levels that are raised but are less than 3 times the upper limit of normal. **[2008]**
- 1.3.39 Do not stop statins because of an increase in blood glucose level or HbA_{1c}. (See the recommendations on assessing for risk of diabetes mellitus in [Preventing type 2 diabetes](#) [NICE public health guidance 38].) **[new 2014]**
- 1.3.40 Statins are contraindicated in pregnancy:

- Advise women of childbearing potential of the potential teratogenic risk of statins and to stop taking them if pregnancy is a possibility.

Advise women planning pregnancy to stop taking statins 3 months before they attempt to conceive and to not restart them until breastfeeding is finished. **[new 2014]**

[This recommendation updates and replaces recommendation 1.10.1.7 from [Type 2 diabetes](#) (NICE clinical guideline 87).]

Intolerance of statins

- 1.3.41 If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose. **[new 2014]**
- 1.3.42 Tell the person that any statin at any dose reduces CVD risk. If someone reports adverse effects when taking high-intensity statins discuss the following possible strategies with them:
- stopping the statin and trying again when the symptoms have resolved to check if the symptoms are related to the statin
 - reducing the dose within the same intensity group
 - changing the statin to a lower intensity group. **[new 2014]**
- 1.3.43 Seek specialist advice about options for treating people at high risk of CVD such as those with CKD, type 1 diabetes, type 2 diabetes or genetic dyslipidaemias, and those with CVD, who are intolerant to 3 different statins. Advice can be sought for example, by telephone, virtual clinic or referral. **[new 2014]**

Adherence to statin therapy

- 1.3.44 Do not offer coenzyme Q10 or vitamin D to increase adherence to statin treatment. **[new 2014]**

Fibrates for preventing CVD

1.3.45 Do not routinely offer fibrates for the prevention of CVD to any of the following:

- people who are being treated for primary prevention
- people who are being treated for secondary prevention
- people with CKD
- people with type 1 diabetes

people with type 2 diabetes. **[new 2014]**

[This recommendation updates and replaces recommendations 1.10.2.3 and 1.10.2.4 from [Type 2 diabetes](#) (NICE clinical guideline 87) and recommendations 1.10.2.5 and 1.10.2.6 from [Type 1 diabetes](#) (NICE clinical guideline 15).]

Nicotinic acid for preventing CVD

1.3.46 Do not offer nicotinic acid (niacin) for the prevention of CVD to any of the following:

- people who are being treated for primary prevention
- people who are being treated for secondary prevention
- people with CKD
- people with type 1 diabetes

people with type 2 diabetes. **[new 2014]**

[This recommendation updates and replaces recommendations 1.10.2.5 from [Type 1 diabetes](#) (NICE clinical guideline 15) and 1.10.3.1 from [Type 2 diabetes](#) (NICE clinical guideline 87).]

Bile acid sequestrants (anion exchange resins) for preventing CVD

1.3.47 Do not offer a bile acid sequestrant (anion exchange resin) for the prevention of CVD to any of the following:

- people who are being treated for primary prevention
- people who are being treated for secondary prevention
- people with CKD
- people with type 1 diabetes
- people with type 2 diabetes. **[new 2014]**

[This recommendation updates and replaces recommendation 1.10.2.5 from [Type 1 diabetes](#) (NICE clinical guideline 15).]

Omega-3 fatty acid compounds for preventing CVD

Recommendations in this section update and replace recommendations 1.10.4.1 and 1.10.4.2 from [Type 2 diabetes](#) (NICE clinical guideline 87).

1.3.48 Do not offer omega-3 fatty acid compounds for the prevention of CVD to any of the following:

- people who are being treated for primary prevention
- people who are being treated for secondary prevention
- people with CKD
- people with type 1 diabetes
- people with type 2 diabetes. **[new 2014]**

1.3.49 Tell people that there is no evidence that omega-3 fatty acid compounds help to prevent CVD. **[new 2014]**

Combination therapy for preventing CVD

1.3.50 Do not offer the combination of a bile acid sequestrant (anion exchange resin), fibrate, nicotinic acid or omega-3 fatty acid compound with a statin for the primary or secondary prevention of CVD. **[new 2014]**

Ezetimibe

1.3.51 People with primary hypercholesterolaemia should be considered for ezetimibe treatment in line with [Ezetimibe for the treatment of primary \(heterozygous-familial and non-familial\) hypercholesterolaemia](#) (NICE technology appraisal guidance 132). **[2008]**

^[4] People on renal replacement therapy are outside the scope of this guideline.

^[5] See [appendix A](#) for statin classification.

^[6] At the time of publication (July 2014), atorvastatin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

^[7] See the forthcoming updated guideline on CKD (publication expected 23 July 2014) for CKD classification. People on renal replacement therapy are outside the scope of this guideline.

2 Implementation: getting started

This section highlights some important changes to practice that may result from implementing this guideline identified at publication in July 2014. With input from stakeholders, experts and health professionals, 3 areas have been identified that may have a big impact on practice or could be challenging to implement. However, other changes to practice may be needed to fully implement the guideline.

2.1 Measuring non-high density lipoprotein cholesterol when lipid profiling for the primary prevention of cardiovascular disease

See recommendation 1.3.4.

Potential impact of implementation

Non-high density lipoprotein (non-HDL) cholesterol is seen to be a better cardiovascular disease (CVD) risk indicator than low-density lipoprotein (LDL) cholesterol. It is more accurate, more practical and cost effective. A fasting blood sample is not needed. This is more convenient for patients and may reduce the need for additional blood samples. Those requesting lipid profiles for their patients – such as GPs, practice nurses and community pharmacists – may need to change their practice. Laboratories may also need to change their reporting procedures.

Challenges for implementation

- The United Kingdom National External Quality Assessment Service (UKNEQAS) estimated that less than 10% of laboratories included non-HDL cholesterol in their reports; however, this was primarily due to lack of demand.
- Healthcare workers may need educating in what the non-HDL cholesterol test means, how to interpret the laboratory results, and how it compares with the previously used LDL cholesterol test.

Support for implementation

- The Association of Clinical Biochemistry and Laboratory Medicine disseminated the updated guidance to their members – specifically clinical scientists at the laboratories – to request

that they routinely include non-HDL cholesterol in their lipid profile reports. No additional equipment is needed for the non-HDL cholesterol test, other than a change to the software used when producing the report, and no extra time is needed to produce the lipid profile. Local organisations may wish to contact the laboratory they use to ensure it has this information.

- Lab Tests Online UK updated their website to include details of the non-HDL cholesterol test in their information on [lipid profiling](#). The information on this site explains what the test is, why it is carried out, what it involves and how to interpret the results. The website is a resource for both professionals and the public.

2.2 Reduction of the primary prevention threshold from 20% to 10% CVD risk as calculated by QRISK2

See recommendation 1.3.18.

Potential impact of implementation

It is expected that there will be a reduction in the number of deaths and hospital-related admissions due to CVD events. Because the price of statins has fallen, using statins to reduce the risk of CVD at a lower threshold than NICE previously recommended is cost effective. Primary healthcare professionals may need to change their practice.

Challenges for implementation

The number of people eligible to take statins for the primary prevention of CVD will increase because of the reduction in the treatment threshold from a 20% to a 10% 10-year risk of a CVD event. The challenge is to ensure that statin treatment is presented as a patient choice in addition to lifestyle modification to avoid unnecessarily 'medicalising' this group of people. To help patients make an informed decision, healthcare professionals will need an effective way of briefly but clearly communicating the pros and cons of the various options available.

Support for implementation

- The guideline does not propose that statins should be used instead of the lifestyle adjustments that people at risk need to make. It encourages GPs to fully explore with their

patients all the options promoted by the guidance, including lifestyle changes, blood pressure control, avoidance of diabetes and cholesterol (lipid) lowering.

- A NICE [patient decision aid](#) is available to support primary healthcare professionals in discussing the pros and cons of statin therapy with their patients so they can make an informed choice.
- Expert opinion suggests that around 20% of these people will choose not to take statins after discussions with their healthcare professional.
- Health practitioners may wish to refer to NICE's guideline on [behaviour change](#) for further support on lifestyle modification.

2.3 Atorvastatin for the primary and secondary prevention of CVD

See recommendations 1.3.18, 1.3.20 and 1.3.30.

Potential impact of implementation

Since the 2008 guideline on lipid modification was published, atorvastatin has come off-patent and is available at a reduced cost, therefore making it more cost effective. Atorvastatin is more potent than other non-generic statins and has a lower risk of adverse interactions with other drugs. There is also greater compatibility with other cardiovascular and lipid modifying therapies. In addition, atorvastatin does not have to be taken at night, which may increase convenience.

Challenges for implementation

- The rationale for recommending atorvastatin over other statins may not be well understood, both when starting treatment for people with a 10% CVD risk or greater and when prescribing statins for people with existing CVD.
- Prescribers may be uncertain about switching existing patients to atorvastatin from other statins, and may perceive there to be an impact on their workload in doing so.

Support for implementation

- A meta-analysis of studies with statins was conducted after statins were classified into high-, medium- and low-efficacy groups based on their efficacy in lowering LDL cholesterol levels.

High-efficacy statins at low acquisition cost (for example, atorvastatin 20 mg or greater) were more effective than moderate-intensity statins (simvastatin 20 mg or atorvastatin 10 mg) in reducing cardiovascular outcomes. This increment in therapy was cost effective, with high-intensity statin therapy reducing CVD events by an extra 9–12 per thousand fatal and non-fatal heart attacks and stroke events in this comparison.

- People admitted for acute coronary syndromes are likely to have been prescribed atorvastatin 80 mg on the basis of recommendations made in the 2008 guideline. Therefore, only people with chronic CVD would need to be considered for conversion to high-dose, high-intensity statin (atorvastatin 80 mg).
- There is no time restriction on implementing recommendation 1.3.30 with existing patients. There is no anticipated increase in workload as discussion could take place at the time of their next annual review.

2.4 Further resources

Further [resources](#) are available from NICE that may help to support implementation.

The [NICE online learning module](#) addresses the underpinning evidence behind key recommendations and explains how and why NICE made the recommendations. It also covers: the whole pathway for primary prevention; the change to non-HDL cholesterol testing; and consultation skills in relation to using the patient decision aid and discussing lifestyle modification.

The UK National Screening Committee has agreed to reflect the 10% risk threshold in The NHS Health Check programme in line with the NICE recommendations.

NICE produces indicators annually for use in the Quality and Outcomes Framework (QOF) for the UK. The process for this and the NICE menu can be found [here](#).

[Uptake data](#) about guideline recommendations and quality standard measures are available on the NICE website.

3 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline.

3.1 Simplifying risk assessment

What is the effectiveness of age alone and other routinely available risk factors compared with the formal structured multifactorial risk assessment to identify people at high risk of developing CVD?

Why this is important

Current risk assessment tools rely on a complex set of data derived from demographic, lifestyle, physiological and biochemical parameters. The principal determinant of CVD risk is age, and this may be sufficient to identify high-risk populations. However, focusing on age alone may result in people being missed who are at higher risk as a result of other factors that do not require access to intensive resources, such as smoking status, family history and deprivation. It is important therefore to assess age against validated simplified and complex CVD risk tools when predicting people at high risk.

3.2 Cost effectiveness using individual patient-level data

What is the improvement in the cost-effectiveness metrics for statin therapy in reducing CVD that can be obtained when using a complete individual patient-based outcomes meta-analysis data set compared with using published outcomes data?

Why this is important

This guideline development process uses published summary data from trials in a meta-analysis to inform the clinical efficacy of statins. This use of aggregate data has limitations. The use of individual patient data would allow use of time to event statistics and allow investigation of interaction with baseline risk. Such an approach can be used to validate the current approach and would provide useful information on limitations of use of summary data.

3.3 Statin therapy in older people

What is the effectiveness of statin therapy in older people?

Why this is important

The UK population is ageing and atherosclerosis is an age-associated process. Few trials assessing cardiovascular outcomes have recruited many people older than 80 years yet the important effect of age on CVD risk suggests that all people in this group should be offered statin therapy. However, there is no evidence to validate the CVD benefits and side effects of statin therapy such as effect on muscle and renal function in this age group. Controversy also exists about the efficacy of statins in preventing or promoting other chronic diseases of ageing such as dementia, Parkinson's disease, or age-related macular degeneration.

3.4 Lipid modification therapy in people with type 1 diabetes

What is the effectiveness of statins and/or other LDL-cholesterol-lowering treatment in people with type 1 diabetes?

Why this is important

People with type 1 diabetes have increased CVD risk derived from age, sex, glycaemia, blood pressure, renal function and lipid levels as identified in epidemiological studies. Long-term glycaemic control is associated with better outcomes but no trial has investigated the efficacy of statin therapy or other LDL-cholesterol-lowering therapies exclusively in people with type 1 diabetes.

3.5 Comparative effectiveness and risks of alternative doses of atorvastatin

What is the clinical effectiveness and rate of adverse events of statin therapy using atorvastatin 20 mg per day compared with atorvastatin 40 mg per day and atorvastatin 80 mg per day in people without established CVD?

Why this is important

This guideline has established that atorvastatin 20 mg is clinically and cost effective for the primary prevention of CVD and should be recommended for those at 10% risk of cardiovascular events as assessed using the QRISK2 calculator. However, this analysis looked at the effectiveness of treatment shown by 'high-intensity' statins as a group, as it was not possible to establish the relative effectiveness of atorvastatin 20 mg, 40 mg and 80 mg using trial data. Trial data with clinical outcomes exists for atorvastatin 80 mg against atorvastatin 10 mg only. The rates of adverse events resulting from different doses of atorvastatin in routine clinical practice are also uncertain and would need to be considered in combination with effectiveness in assessing the relative costs and benefits of different doses of atorvastatin.

4 Other information

4.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group ([see section 5](#)), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

4.2 Related NICE guidance

Details are correct at the time of publication of the guideline (July 2014). Further information is available on the [NICE website](#).

Published

General

- [Patient experience in adult NHS services](#). NICE clinical guidance 138 (2012).
- [Medicines adherence](#). NICE clinical guidance 76 (2009).

Condition-specific

- [Behaviour change: individual approaches](#). NICE public health guidance 49 (2014).
- [Myocardial infarction: secondary prevention](#). NICE clinical guideline 172 (2013).
- [Myocardial infarction with ST-segment elevation](#). NICE clinical guideline 167 (2013).
- [Lower limb peripheral arterial disease](#). NICE clinical guideline 147 (2012).

- [Preventing type 2 diabetes - risk identification and interventions for individuals at high risk.](#) NICE public health guidance 38 (2012).
- [Hypertension: clinical management of primary hypertension in adults.](#) NICE clinical guideline 127 (2011).
- [Type 2 diabetes: the management of type 2 diabetes.](#) NICE clinical guideline 87 (2009).
- [Familial hypercholesterolaemia: identification and management of familial hypercholesterolaemia.](#) NICE clinical guideline 71 (2008).
- [Reducing the rate of premature deaths from cardiovascular disease and other smoking-related diseases: finding and supporting those most at risk and improving access to services.](#) NICE public health guidance 15 (2008).
- [Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities.](#) NICE public health guidance 10 (2008).
- [Behaviour change: the principles for effective interventions.](#) NICE public health guidance 6 (2007).
- [Ezetimibe for the treatment of primary \(heterozygous-familial and non-familial\) hypercholesterolaemia.](#) NICE technology appraisal guidance 132 (2007).
- [Varenicline for smoking cessation.](#) NICE technology appraisal guidance 123 (2007).
- [Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children.](#) NICE clinical guideline 43 (2006).
- [Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling.](#) NICE public health intervention guidance 2 (2006).
- [Brief interventions and referral for smoking cessation in primary care and other settings.](#) NICE public health intervention guidance 1 (2006).

Under development

NICE is developing the following guidance (details available from the [NICE website](#)):

-
- Chronic kidney disease (update). NICE clinical guideline (publication expected July 2014).
 - Type 1 diabetes (update). NICE clinical guideline (publication expected August 2015).
 - Type 2 diabetes (update). NICE clinical guideline (publication expected August 2015).

5 The Guideline Development Group, National Collaborating Centre and NICE project team

5.1 Guideline Development Group

The Guideline Development Group members listed are those for the 2014 update. For the composition of the previous Guideline Development Group, see the full guideline.

Anthony Wierzbicki (Chair)

Consultant in Chemical Pathology/Honorary Professor, Guy's & St Thomas' Hospitals, London

Rajai Ahmad

Consultant Interventional Cardiologist, Sandwell and West Birmingham Hospitals NHS Trust

Lindsay Banks

Medicines Information Pharmacist, Liverpool

Liz Clark

Patient/carer member, Exeter

Martin Duerden

General Practitioner and Clinical Senior Lecturer, Centre for Health Economics and Medicines Evaluation, Bangor University

Eleanor Grey (until December 2013)

Patient/carer member, London

Michael Khan

Consultant Diabetologist, University Hospitals of Coventry and Warwickshire NHS Trust

Emma McGowan

Familial Hypercholesterolaemia (FH) Cascade Nurse Specialist, University Hospitals of Coventry and Warwickshire NHS Trust

Dermot Neely

Consultant in Clinical Biochemistry and Metabolic Medicine, Newcastle upon Tyne Hospitals NHS Foundation Trust

Nadeem Qureshi

General Practitioner and Clinical Professor of Primary Care, School of Medicine, University of Nottingham

Alan Rees

Consultant Physician with a Special Interest in Diabetes, Endocrinology and Clinical Lipidology, University Hospital of Wales, Cardiff

David Wald (until September 2013)

Professor in Cardiology and Honorary Consultant Cardiologist, Queen Mary University of London

5.2 Co-opted GDG members and peer-reviewers

Gary Collins

Senior Medical Statistician, University of Oxford

Jo Farrington

Public Health Specialist and Cardiovascular Dietitian, Oldham PCT

David Wheeler

Reader, Centre for Nephrology, University College London

The following people provided peer-review comments during the development of the guideline

Joan Morris

Professor of Medical Statistics, Queen Mary University of London

Mark Simmonds

Research Fellow, Centre for Reviews and Dissemination, University of York

Liam Smeeth

Head of the Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine

Rod Jackson

Professor of Epidemiology and Biostatistics, University of Auckland, New Zealand

National Clinical Guideline Centre staff

Angela Cooper

Senior Research Fellow

Lina Gulhane

Joint Head of Information Science

Martin Harker

Health Economist

Norma O'Flynn

Clinical Director and Guideline Lead

Silvia Rabar

Senior Research Fellow and Project Manager

NICE project team

Sarah Willett

Guideline Lead

Phil Alderson

Clinical Adviser

Caroline Keir

Guideline Commissioning Manager

Margaret Ghلامي

Guideline Coordinator

Judith Thornton

Technical Lead

Bhash Naidoo

Health Economist

Annette Mead

Editor

Appendix A: Grouping of statins

For the purpose of this guideline, statins are grouped into 3 different intensity categories according to the percentage reduction in low-density lipoprotein cholesterol (see table 1). This grouping was agreed by GDG consensus, informed by analyses in the literature. See the full guideline for a discussion of this grouping.

Table 1 Grouping of statins used in this guideline

Dose (mg/day)	Reduction in low-density lipoprotein cholesterol				
	5	10	20	40	80
Fluvastatin	–	–	21% ¹	27% ¹	33% ²
Pravastatin	–	20% ¹	24% ¹	29% ¹	–
Simvastatin	–	27% ¹	32% ²	37% ²	42% ^{3,4}
Atorvastatin	–	37% ²	43% ³	49% ³	55% ³
Rosuvastatin	38% ²	43% ³	48% ³	53% ³	–

¹ 20%–30%: low intensity.
² 31%–40%: medium intensity.
³ Above 40%: high intensity.
⁴ Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.

The information used to make the table is from Law MR, Wald NJ, Rudnicka AR (2003) Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. *BMJ* 326: 1423.

Changes after publication

January 2015: New section Implementation: getting started added.

January 2015: Minor change to [Appendix B](#) of the full guideline.

September 2014: Minor maintenance.

About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions.

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

This guideline was developed by the National Clinical Guideline Centre, which is based at the Royal College of Physicians. The Collaborating Centre worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

Update information

This guideline updates and replaces NICE clinical guideline 67 (published September 2008). It also updates and replaces recommendations relating to risk assessment and lipids management for type 1 and type 2 diabetes and chronic kidney disease, and statin therapy for people at increased risk of developing cardiovascular disease or those with established cardiovascular disease:

- [Type 1 diabetes](#) (2004) NICE guideline CG15 sections 1.10.1 and 1.10.2
- [Type 2 diabetes](#) (2006) NICE guideline CG87 sections 1.9 and 1.10

- [Chronic kidney disease](#) (2008) NICE guideline CG73 recommendations 1.8.19 and 1.8.20
- [Statins for the prevention of cardiovascular events](#) (2006) NICE guideline TA94

Recommendations are marked as [new 2014], [2014], [2008] or [2008, amended 2014]:

- [new 2014] indicates that the evidence has been reviewed and the recommendation has been added or updated
- [2014] indicates that the evidence has been reviewed but no change has been made to the recommended action
- [2008] indicates that the evidence has not been reviewed since 2008
- [2008, amended 2014] indicates that the evidence has not been reviewed since 2008, but changes have been made to the recommendation wording that change the meaning (see below).

Recommendations from NICE clinical guideline 67 that have been amended

Recommendations are labelled **[2008, amended 2014]** if the evidence has not been reviewed since 2008 but changes have been made to the recommendation wording that change the meaning.

Recommendation in 2008 guideline	Recommendation in current guideline	Reason for change
----------------------------------	-------------------------------------	-------------------

<p>1.1.1 For the primary prevention of CVD in primary care, a systematic strategy should be used to identify people aged 40–74 who are likely to be at high risk.</p>	<p>1.1.1 For the primary prevention of CVD in primary care, use a systematic strategy to identify people who are likely to be at high risk. [2008, amended 2014]</p>	<p>The tools available for estimating CVD risk in 2008 had an upper age range of 74 years. QRISK2 has an upper age range of 84 years. The age range was therefore removed for clarity.</p>
<p>1.1.4 People should be prioritised for a full formal risk assessment if their estimated 10-year risk of CVD is 20% or more.</p>	<p>1.1.4 Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is 10% or more. [2008, amended 2014]</p>	<p>The threshold for treatment has been changed from 20% to 10% because of new health economics results.</p>
<p>1.1.10 Risk equations should not be used for people with pre-existing:</p> <ul style="list-style-type: none"> • peripheral vascular disease. 	<p>1.1.15 Do not use a risk assessment tool for people with pre-existing CVD. [2008, amended 2014]</p>	<p>The GDG made this recommendation more general to include all CV diseases.</p>

<p>1.1.11 Risk equations should not be used for people who are already considered at high risk of CVD because of:</p> <ul style="list-style-type: none"> • diabetes, see 'Type 2 diabetes: the management of type 2 diabetes (update)' (NICE clinical guideline 66). 	<p>1.1.16 Do not use a risk assessment tool for people who are at high risk of developing CVD because of familial hypercholesterolaemia (see Familial hypercholesterolaemia [NICE clinical guideline 71]) or other inherited disorders of lipid metabolism. [2008, amended 2014]</p>	<p>The bullet point about type 2 diabetes has been deleted because the GDG made separate specific recommendations for this subgroup.</p>
<p>1.1.13 When using the risk score to inform drug treatment decisions, particularly if it is near to the threshold of 20%, healthcare professionals should consider other factors that:</p> <ul style="list-style-type: none"> • may not be included in calculated risk scores. 	<p>1.1.17 When using the risk score to inform drug treatment decisions, particularly if it is near to the threshold for treatment, take into account other factors that:</p> <ul style="list-style-type: none"> • may predispose the person to premature CVD and • may not be included in calculated risk scores. [2008, amended 2014] 	<p>The threshold for treatment has been changed because of new health economics results.</p> <p>'healthcare professionals should consider' has been amended to: 'take into account' in line with current NICE style for recommendations in clinical guidelines.</p>

<p>1.1.20 CVD risk may be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking. Clinical judgement should be used to decide on further treatment of risk factors in people who are below the 20% CVD risk threshold.</p>	<p>1.1.19 Recognise that CVD risk will be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking. Use clinical judgement to decide on further treatment of risk factors in people who are below the CVD risk threshold for treatment. [2008, amended 2014]</p>	<p>The threshold for treatment has been changed because of new health economics results.</p>
<p>1.1.21 CVD risk scores may not be appropriate as a way of assessing risk in people who are at increased CVD risk because of underlying medical conditions or treatments. These include people treated for HIV or with antipsychotic medication, people with chronic kidney disease and people with autoimmune disorders such as systemic lupus erythematosus (SLE) and rheumatoid arthritis.</p>	<p>1.1.18 Recognise that standard CVD risk scores will underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include:</p>	<p>The list of underlying medical conditions had been updated.</p>

<p>1.1.22 People aged 75 or older should be considered at increased risk of CVD, particularly people who smoke or have raised blood pressure. They are likely to benefit from statin treatment. Assessment and treatment should be guided by the benefits and risks of treatment, informed preference and comorbidities that may make treatment inappropriate.</p>	<p>1.1.21 Consider people aged 85 or older to be at increased risk of CVD because of age alone, particularly people who smoke or have raised blood pressure. [2008, amended 2014]</p>	<p>'should be considered' has been amended to: 'consider' in line with current NICE style for recommendations in clinical guidelines.</p> <p>The age value has been changed to 85, as this is the upper limit of the QRISK2 assessment tools.</p> <p>The part on treatment has been deleted, as recommendations on treatment are listed in section 1.3.</p>
--	--	---

<p>1.2.5 In order to encourage the person to participate in reducing their CVD risk, the healthcare professional should:</p> <ul style="list-style-type: none"> • find out what, if anything, the person has already been told about their CVD risk and how they feel about it • explore the person's beliefs about what determines future health (this may affect their attitude to changing risk) • assess their readiness to make changes to their lifestyle (diet, physical activity, smoking and alcohol consumption), to undergo investigations and to take medication • assess their confidence in making changes to their lifestyle, undergoing investigations and taking medication • inform them of potential future management based on current evidence and best practice • involve them in developing a shared management plan • check with them that they have understood what has been discussed. 	<p>1.1.27 To encourage the person to participate in reducing their CVD risk:</p> <ul style="list-style-type: none"> • find out what, if anything, the person has already been told about their CVD risk and how they feel about it • explore the person's beliefs about what determines future health (this may affect their attitude to changing risk) • assess their readiness to make changes to their lifestyle (diet, physical activity, smoking and alcohol consumption), to undergo investigations and to take long-term medication • assess their confidence in making changes to their lifestyle, undergoing investigations and taking medication • inform them of potential future management based on current evidence and best practice • involve them in developing a shared management plan • check with them that they have understood what has 	<p>The words 'long-term' have been added to the third bullet in relation to medication to emphasise the need to discuss people's views about taking medication long term.</p>
---	---	---

	been discussed. [2008, amended 2014]	
1.2.7 If the person's CVD risk is considered to be at a level that merits intervention but they decline the offer of treatment, they should be advised that their CVD risk should be considered again in the future.	1.1.28 If the person's CVD risk is at a level where intervention is recommended but they decline the offer of treatment, advise them that their CVD risk should be reassessed again in the future. Record their choice in their medical notes. [2008, amended 2014]	The GDG considered it important that people's involvement in decision-making and their choices are adequately recorded.
1.3.7 People at high risk of CVD or with CVD should be advised to take 30 minutes of physical activity a day, of at least moderate intensity, at least 5 days a week, in line with national guidance for the general population. (see Physical activity guidelines for adults) [2008,]	1.2.7 Advise people at high risk of or with CVD to do the following every week: <ul style="list-style-type: none"> • at least 150 minutes of moderate intensity aerobic activity or • 75 minutes of vigorous intensity aerobic activity or • a mix of moderate and vigorous aerobic activity <p>in line with national guidance for the general population (see Physical activity guidelines for adults at NHS Choices). [2008, amended 2014]</p>	This recommendation has been updated because the chief medical officer issued changes to recommendations on physical activity in 2011.

<p>1.3.8 People who are unable to perform moderate-intensity physical activity at least 5 days a week because of co-morbidity, medical conditions or personal circumstances should be encouraged to exercise at their maximum safe capacity. [2008]</p>	<p>1.2.9 Encourage people who are unable to perform moderate-intensity physical activity because of comorbidity, medical conditions or personal circumstances to exercise at their maximum safe capacity. [2008, amended 2014]</p>	<p>This recommendation has been updated because the chief medical officer issued changes to recommendations on physical activity in 2011.</p>
<p>1.4.18 If a person has acute coronary syndrome, statin treatment should not be delayed until lipid levels are available. A fasting lipid sample should be taken about 3 months after the start of treatment.</p>	<p>1.3.22 If a person has acute coronary syndrome, do not delay statin treatment. Take a lipid sample on admission and about 3 months after the start of treatment. [2008, amended 2014]</p>	<p>The GDG considered that a fasting sample is not necessary if non-HDL cholesterol is measured (see recommendation 1.3.4). The GDG wished to highlight the importance of taking a lipid sample also on admission.</p>

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also [Patient-centred care](#)).

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation wording in guideline updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2008] (see 'Update information' above for details about how recommendations are labelled). In particular, for recommendations labelled [2008], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Other versions of this guideline

The full guideline, [Lipid modification](#), contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guideline Centre.

The recommendations from this guideline have been incorporated into a [NICE Pathway](#).

We have produced [information for the public](#) about this guideline.

Implementation

[Implementation tools and resources](#) to help you put the guideline into practice are also available.

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Copyright

© National Institute for Health and Care Excellence 2014. All rights reserved. NICE copyright material can be downloaded for private research and study, and may be reproduced for educational and not-for-profit purposes. No reproduction by or for commercial organisations, or for commercial purposes, is allowed without the written permission of NICE.

ISBN: 978-1-4731-0638-3