BELMATT
HEALTHCARE TRAINING

# CARDIOVASCULAR DISEASE

# NICE GUIDELINES

## RECOMMENDED READIING

NICE GUIDELINES – The information in this booklet has been compiled from NICE guidelines on 20 July 2021. Please check current guidelines and local policy. The information below are guidelines and it is recommended that clinicians look at any recent updates.

## INTRODUCTION TO CARDIOVASCULAR DISEASE

Scottish Intercollegiate Guidelines Network 116 Management of Diabetes March 2010 Principles of Anatomy and Physiology Tortora; G. Grabowski, S Harper Collins Foot and Ankle Anatomy. Mc 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 according to UK National Statistics. 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.

Minn R, Hutching R, and Logan B.: Sydney, Mosby

## .1 IDENTIFYING AND ASSESSING CARDIOVASCULAR DISEASE (CVD) RISK

### IDENTIFYING PEOPLE FOR FULL FORMAL RISK ASSESSMENT

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 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**]

People older than 40 should have their estimate of CVD risk reviewed on an ongoing basis. [**2008**]

Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is 10% or more. [**2008, amended 2014**]

Discuss the process of risk assessment with the person identified as being at risk, including the option of declining any formal risk assessment. [**2008**]

Do not use opportunistic assessment as the main strategy in primary care to identify CVD risk in unselected people. [**2008**]

### FULL FORMAL RISK ASSESSMENT

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**]

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 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**]

Use the QRISK2 risk assessment tool to assess CVD risk in people with type 2 diabetes. [**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 $m^2$ and/or albuminuria. 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**]

#### PEOPLE ON RENAL REPLACEMENT THERAPY ARE OUTSIDE THE SCOPE OF THIS GUIDELINE.

Complete as many fields of the risk assessment tool as possible. [**new 2014**]

Routinely record ethnicity, BMI and family history of premature CVD in medical records. [**2008**]

Consider socioeconomic status as an additional factor that contributes to CVD risk. {20**08**]

Do not use a risk assessment tool for people with pre-existing CVD. [**2008, amended 2014**]

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

*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**]

*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**]

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**]

Severe obesity (BMI greater than 40 kg/m$^2$) increases CVD risk. Take this into account when using risk scores to inform treatment decisions in this group (see NICE's guideline on obesity: identification, assessment and management). [**2008**]

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

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 NICE's guideline on patient experience in adult NHS services. [**new 2014**]

Use every day, jargon-free language to communicate information on risk. If technical terms are used, explain them clearly. [**2008**]

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**]

Document the discussion relating to the consultation on risk assessment and the person's decision. [**2008**]

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**]

## 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]**

## LIFESTYLE MODIFICATIONS FOR THE PRIMARY AND SECONDARY PREVENTION OF CVD

### CARDIOPROTECTIVE DIET

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 on the NHS Eat well web page. **[new 2014]**

*Advise people at high risk of or with CVD to*:

- reduce their saturated fat intake.
- increase their mono-unsaturated fat intake with olive oil, rapeseed oil or spreads based on these oils and to use them in food preparation.

***FURTHER INFORMATION AND ADVICE ON HEALTHY COOKING METHODS CAN BE FOUND ON THE NHS EAT WELL WEB PAGE. [NEW 2014]***

*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 on the NHS Eat well web page. [**new 2014**]

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 on the NHS Eat well web page. [**new 2014**]

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

Advise and support people at high risk of or with CVD to achieve a healthy diet in line with NICE's guideline on behaviour change: general approaches. [**new 2014**]

## PHYSICAL ACTIVITY

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 the UK Chief Medical Officers' physical activity guidelines for more information). [**2008, amended 2014**]

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 the UK Chief Medical Officers' physical activity guidelines for more information). [**new 2014**]

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**]

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 NICE's guidelines on walking and cycling, physical activity: brief advice for adults and exercise referral schemes. [**2008**]

## COMBINED INTERVENTIONS (DIET AND PHYSICAL ACTIVITY)

Give advice on diet and physical activity in line with national recommendations (see the NHS Eat well web page). [**2008**]

## WEIGHT MANAGEMENT

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 NICE's guideline on obesity: identification, assessment and management. [**2008**]

## ALCOHOL CONSUMPTION

1.2.13 For advice on alcohol consumption, including binge drinking, see the UK chief medical officers' guidelines on low risk drinking. [**2008**]

### SMOKING CESSATION

Advise all people who smoke to stop, in line with NICE's guideline on stop smoking interventions and services. [**2008**]

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**]

If a person is unable or unwilling to accept a referral to an intensive support service, offer them pharmacotherapy in line with NICE's guideline on stop smoking interventions and services and NICE's technology appraisal guidance on varenicline for smoking cessation. [**2008**]

## PLANT STANOLS AND STEROLS

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**]

## LIPID MODIFICATION THERAPY FOR THE PRIMARY AND SECONDARY PREVENTION OF CVD

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 and low acquisition cost. [**new 2014**]

See appendix A for statin classification.

### LIPID MEASUREMENT AND REFERRAL

Measure both total and high-density lipoprotein (HDL) cholesterol to achieve the best estimate of CVD risk. [**2008**]

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**]

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**]

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**]

### CONSIDER THE POSSIBILITY OF FAMILIAL HYPERCHOLESTEROLAEMIA AND INVESTIGATE AS DESCRIBED IN NICE'S GUIDELINE ON FAMILIAL HYPERCHOLESTEROLAEMIA IF THEY HAVE:

- a total cholesterol concentration more than 7.5 mmol/litre **and**
- a family history of premature coronary heart disease. [**new 2014**]

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**]

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**]

*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**]

*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).

There is a NICE patient decision aid to support discussions about statin therapy to reduce the risk of coronary heart disease and stroke.

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**]

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 NICE's guideline on hypertension)
- BMI or other measure of obesity (see NICE's guideline on obesity: identification, assessment and management)
- 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

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**]

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 NICE' guidelines on behaviour change: individual approaches and physical activity: exercise referral schemes.) [**new 2014**]

Offer people the opportunity to have their risk of CVD assessed again after they have tried to change their lifestyle. [**new 2014**]

If lifestyle modification is ineffective or inappropriate offer statin treatment after risk assessment. [**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**]

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

Start statin treatment in people with CVD with atorvastatin 80 mg. Use a lower dose of atorvastatin if any of the following apply:

- potential drug interactions
- high risk of adverse effects
- patient preference. [**new 2014**]

In July 2014 this was an off-label use of atorvastatin. See NICE's information on prescribing medicines.

Do not delay statin treatment in secondary prevention to manage modifiable risk factors. [**2014**]

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

Consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes. [**new 2014**]

> *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**]

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

## PRIMARY PREVENTION FOR PEOPLE WITH TYPE 2 DIABETES

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**]

## PEOPLE WITH CKD

Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD.

- 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 $m^2$ or more.
- Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/min/1.73 $m^2$. [**new 2014**]

See NICE's guideline on chronic kidney disease for CKD classification. People on renal replacement therapy are outside the scope of this guideline.

## 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 (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) 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**]

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**]

## ADVICE AND MONITORING FOR ADVERSE EFFECTS

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**]

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

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**]

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**]

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**]

Do not measure creatine kinase levels in asymptomatic people who are being treated with a statin. [**2008**]

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**]

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**]

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 NICE's guideline on preventing type 2 diabetes.) [**new 2014**]

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**]

## INTOLERANCE OF STATINS

If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose. [**new 2014**]

Tell the person that any statin at any dose reduces CVD risk. If someone reports adverse effects when taking high-intensity statin 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**]

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

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

## FIBRATES FOR PREVENTING CVD

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**]

## NICOTINIC FOR PREVENTING CVD ACID

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**]

### BILE ACID SEQUESTRANTS (ANION EXCHANGE RESINS) FOR PREVENTING CVD

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**]

### OMEGA-3 FATTY ACID COMPOUNDS FOR PREVENTING CVD

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**]

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

## COMBINATION THERAPY FOR PREVENTING CVD

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 NICE's technology appraisal guidance on ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia. [**2008**]

## TERMS USED IN THIS GUIDELINE

### HIGH-INTENSITY STATIN

The following doses for statins are high intensity, based on the percentage reduction in low density lipoprotein (LDL) cholesterol they can produce:

- atorvastatin: 20 mg to 80 mg
- rosuvastatin: 10 mg to 40 mg
- simvastatin: 80 mg.

## 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

#### 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 information on lipid profiling was updated to include details of the non-HDL cholesterol test. 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.

## REDUCTION OF THE PRIMARY PREVENTION THRESHOLD FROM 20% TO 10% CVD RISK AS CALCULATED BY QRISK2

### 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.
- There is a NICE patient decision aid 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 the lifestyle modification information in NICE's guideline on behaviour change: individual approaches.

## ATORVASTATIN FOR THE PRIMARY AND SECONDARY PREVENTION OF CVD

### 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

There are further NICE resources that may help to support implementation.

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 on NICE's Quality and Outcomes Framework indicator web page.

Uptake data about guideline recommendations and quality standard measures are available.

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# 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 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.

### 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.

### 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.

### 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.

## 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.

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

- a 20% to 30% reduction is low intensity
- a 31% to 40% reduction is medium intensity
- a reduction of more than 40% is high intensity.

This grouping was agreed by GDG consensus, informed by analyses in the literature. See the full guideline for a discussion of this grouping.

**Grouping of statins used in this guideline: reduction in LDL cholesterol by daily dose**

Fluvastatin:

- 20 mg/day, 21% reduction
- 40 mg/day, 27% reduction
- 80 mg/day, 33% reduction

Pravastatin:

- 10 mg/day, 20% reduction
- 20 mg/day, 24% reduction
- 40 mg/day, 29% reduction

Simvastatin:

- 10 mg/day, 27% reduction
- 20 mg/day, 32% reduction

- 40 mg/day, 37% reduction
- 80 mg/day, 42% reduction

Atorvastatin:

- 10 mg/day, 37% reduction
- 20 mg/day, 43% reduction
- 40 mg/day, 49% reduction
- 80 mg/day, 55% reduction

Rosuvastatin:

- 5 mg/day, 38% reduction
- 10 mg/day, 43% reduction
- 20 mg/day, 48% reduction
- 40 mg/day, 53% reduction

MHRA advice: 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

This information 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.
See the following recent American article for a summary update on recommendations for prevention of cardiovascular disease in women Journal of American Cooleage of Cardiology

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