UKMi North West

NICE Bites

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A summary of prescribing recommendations from NICE guidance

Lipid modification

NICE CG181; 2014

This guideline includes recommendations on risk assessment for CVD and on the use of lipid-lowering drugs in adults.

Definition of terms

CVD	cardiovascular disease
FH	familial hypercholesterolaemia
LDL	low density lipoprotein
HDL	high density lipoprotein
CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
CK	creatine kinase

See **NICE pathway: Cardiovascular disease prevention**

Identifying people for cardiovascular risk assessment in primary care

- For primary prevention of CVD use a systematic strategy to identify people who are likely to be at high risk.
- **Do NOT** use opportunistic assessment as the main strategy to identify CVD risk in unselected people.
- Prioritise people based on an estimate of their CVD risk using CVD risk factors already recorded in electronic medical records before a full formal risk assessment.
- Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is ≥10%.
- People aged >40 years should have their estimate of CVD risk reviewed on an ongoing basis.

Full formal risk assessment

- Discuss the process of risk assessment with the person including the option of declining any formal risk assessment.
- Use the QRISK2 risk assessment tool to assess CVD risk:
  - for primary prevention of CVD in people ≤84 years,
  - in people with type 2 diabetes.
- **Do NOT** use a risk assessment tool to assess CVD risk in people:
  - with type 1 diabetes,
  - with an eGFR <60ml/min/1.73m^2 and/or albuminuria: these people are at increased risk of CVD*,
  - pre-existing CVD,
  - at high risk of developing CVD because of FH.
- Complete as many fields of the risk assessment tool as possible.
- Routinely record ethnicity, body mass index and family history of premature CVD in medical records.
- All CVD risk assessment tools provide only an approximate value for CVD risk. Interpretation of CVD risk scores should always reflect informed clinical judgement.
- Consider socioeconomic status as an additional factor that contributes to CVD risk.
- When using the risk score to inform drug treatment decisions, particularly if near the threshold for treatment, take account of other factors that may not be included in calculated risk scores and may predispose the person to premature CVD.
- Recognise that standard CVD risk scores will underestimate risk in people with underlying medical conditions or treatments including:
  - HIV infection,
  - serious mental health problems,
  - taking medicines that can cause dyslipidaemia e.g. antipsychotics, corticosteroids or immunosuppressant drugs,
  - autoimmune disorders e.g. systemic lupus erythematosus, and other systemic inflammatory disorders.
- Recognise that CVD risk will be underestimated in people already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking.
- Severe obesity (body mass index >40kg/m^2) increases CVD risk. Take this into account when using risk scores to inform treatment decisions.
- Use clinical judgement to decide on further treatment of risk factors in people below the CVD risk threshold for treatment.
- Consider people aged ≥85 years to be at increased risk of CVD because of age alone, particularly people who smoke or have raised blood pressure.

Communication about risk assessment and treatment

- Use everyday, jargon-free language to communicate information on risk. Clearly explain any technical terms.
- Set aside adequate time to provide information on risk assessment and allow any questions to be answered. Further consultation may be required.
- Document the discussion relating to CVD risk assessment and the person's decision.
- Offer people information about their absolute risk of CVD and the absolute benefits and harms of an intervention over a 10-year period in a form that:
  - presents individualised risk and benefit scenarios,
  - presents the absolute risk of events numerically,
  - uses appropriate diagrams and text.
- To encourage the person to reduce their CVD risk:
  - find out what, if anything, they have 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 and confidence to make changes to their lifestyle (diet, physical activity, smoking and alcohol consumption), to undergo investigations and to take long-term medication,
  - inform them of potential future management based on current evidence and best practice,
  - involve them in developing a shared management plan,
  - check that they have understood what has been discussed.

* People on renal replacement therapy are outside the scope of this guideline.

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- If a person declines treatment record their choice and advise them that their CVD risk should be reassessed again in the future.

Lifestyle modifications

Alcohol consumption

- Men should not regularly drink more than 3 to 4 units a day and women should not regularly drink more than 2 to 3 units a day. Binge drinking should be avoided.

Diet

- Advise people with CVD or at high risk to eat a diet in which total fat intake is ≤30% of total energy intake, saturated fats are ≤7% of total energy intake, intake of dietary cholesterol is <300mg/day and where possible saturated fats are replaced by monounsaturated and polyunsaturated fats.
- For people with CVD or at high risk, advise:
  - that reducing saturated fat intake from animal sources also reduces their monounsaturated fat levels,
  - to replace their saturated and monounsaturated fat intake with olive oil, rapeseed oil or spreads based on these oils and to use these in food preparation.
- Advise people with CVD or at high risk to do all of the following:
  - choose wholegrain varieties of starchy food,
  - reduce their intake of 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.
- Advise pregnant women to limit their oily fish to no more than 2 portions per week and avoid marlin, shark and swordfish.
- Take account of a person's individual circumstances when giving dietary advice e.g. drug therapy, comorbidities and other lifestyle modifications.
- Advise and support people with CVD or at high risk to achieve a healthy diet.

Plant stanols and sterols

- **Do NOT** advise taking plant stanols or sterols for the prevention of CVD for people:
  - who are being treated for primary or secondary prevention of CVD,
  - with CKD, type 1 or type 2 diabetes.

Weight management

- Offer people with CVD or at high risk who are overweight or obese appropriate advice and support to work towards achieving and maintaining a healthy weight. See NICE pathway: obesity.

Stopping Smoking

- Advise all people who smoke to stop.
- Offer people who want to stop smoking support and advice, and referral to an intensive support service e.g. NHS Stop Smoking Services.
- If a person is unable or unwilling to accept a referral to an intensive support service, offer pharmacotherapy. See NICE pathway: smoking cessation.

Physical activity

- Give advice on diet and physical activity** See NICE pathway: diet.

** in line with national recommendations for the general population.

- Advise people with CVD or at high risk 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.
- 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),**
- 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.
- Advice on physical activity should take account of the person's needs, preferences and circumstances. Agree goals and provide written information about the benefits of activity and local opportunities to be active.

Lipid measurement and referral

Lipid measurement

This guideline recommends the use of non-HDL cholesterol rather than LDL cholesterol.

Non-HDL cholesterol = total cholesterol – HDL cholesterol

A fasting sample is NOT required

- Measure both total and HDL cholesterol to achieve the best estimate of CVD risk.
- Before starting treatment for primary prevention of CVD, take at least one sample for a full lipid profile; measure total cholesterol, HDL and non-HDL cholesterol, and triglyceride concentrations. A fasting sample is not needed.
- Use clinical findings, lipid profile and family history to judge the likelihood of a familial lipid disorder rather than use of strict lipid cut-off values alone.
- Exclude possible common secondary causes of dyslipidaemia (e.g. excess alcohol, uncontrolled diabetes, hypothyroidism, liver disease and nephrotic syndrome) before referring for specialist review.
- Consider the possibility of FH and investigate as described in NICE CG71 if they have:
  - total cholesterol >7.5mmol/litre, **AND**
  - a family history of premature coronary heart disease.
- Arrange specialist assessment of people with a total cholesterol >9.0mmol/litre or a non-HDL cholesterol >7.5mmol/litre, even in the absence of a first-degree family history of premature coronary heart disease.
- Refer for urgent specialist review if a person has a triglyceride concentration of >20mmol/litre that is not a result of excess alcohol or poor glycaemic control.
- In people with a triglyceride concentration between 10 and 20mmol/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 >10mmol/litre.
- In people with a triglyceride concentration between 4.5 and 9.9mmol/litre:
  - be aware that CVD risk may be underestimated by risk assessment tools, **AND**
  - optimise management of other CVD risk factors, **AND**
  - seek specialist advice if non-HDL cholesterol concentration is >7.5mmol/litre.

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Table 1: Statin groupings

Drug	Daily dose (mg)				
	5	10	20	40	80
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%¤
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	

20 - 30%	Low intensity
30 - 40%	Medium intensity
Above 40%	High intensity

Table 1: Notes

% = percentage reduction in LDL cholesterol

¤ Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80mg) simvastatin. This dose should only be considered 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 table is based on: Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. BMJ 2003; 326: 1423.

Pharmacological treatment

In this guideline statins are grouped into 3 different intensity categories - see **Table 1**

Lipid modification therapy

- Drugs are preferred for which there is evidence in clinical trials of a beneficial effect on CVD morbidity and mortality.
- When a decision is made to prescribe a statin use a statin of high intensity and low acquisition cost.

Before starting treatment for primary prevention

- Discuss the benefits of lifestyle modification and optimise the management of all other modifiable CVD risk factors.
- Recognise that people may need support to change their lifestyle. Refer them to programmes such as exercise referral schemes. See NICE pathway: behaviour change.
- Offer people the opportunity to have their CVD risk assessed again after making lifestyle changes.
- If lifestyle modification is ineffective or inappropriate offer statin treatment after risk assessment.

Also see **Baseline monitoring and follow-up**

Primary prevention

- Offer atorvastatin 20mg[α] to people with a ≥10% 10-year risk of developing CVD estimated using the QRISK2 assessment tool.
- For people ≥85 years consider atorvastatin 20mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction. Be aware of factors that may make treatment inappropriate.

Adults with type 1 diabetes

- Consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes.
- Offer statin treatment for the primary prevention of CVD to adults with type 1 diabetes who:
  - Are aged >40 years, **OR**
  - have had diabetes for >10 years, **OR**
  - have established nephropathy, **OR**
  - have other CVD risk factors.
- Start treatment with atorvastatin 20mg.[α]

α See Summary of Product Characteristics for full prescribing information.

Adults with type 2 diabetes

- Offer atorvastatin 20mg[α] for the primary prevention of CVD to people with type 2 diabetes with a ≥10% 10-year risk of developing CVD estimated using the QRISK2 assessment tool.

Adults with CKD

- Offer atorvastatin 20mg for[α] the primary or secondary prevention of CVD to people with CKD:
  - increase the dose if a >40% reduction in non-HDL cholesterol is not achieved and eGFR is ≥30ml/min/1.73m^2,
  - agree the use of higher doses with a renal specialist if eGFR is <30ml/min/1.73m^2.

Secondary prevention

- **Do NOT** delay statin treatment for secondary prevention to manage modifiable risk factors.
- 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.
- Start treatment in people with CVD with atorvastatin 80mg **U**.
- Use a lower dose of atorvastatin if any of the following apply:
  - potential drug interactions,
  - high risk of adverse effects,
  - patient preference.

Cautions and counselling

- 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 CK levels:
  - if CK levels are >5 times the upper limit of normal, re-measure CK after 7 days. If CK levels are still 5 times the upper limit of normal, do not start statin treatment.

U Unlicensed indication. Obtain and document informed consent.

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- if CK levels are raised but <5 times the upper limit of normal, start statin treatment at a lower dose.

- Advise people being treated with a statin:
  - that other drugs, some foods (e.g. 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.
- Remind the person to restart the statin if they stopped taking it because of drug interactions or to treat intercurrent illnesses.
- 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 CK.
- If people report muscle pain or weakness while taking a statin, explore other possible causes of muscle pain or weakness and raised CK if they have previously tolerated statin therapy for >3 months.
- 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 not to restart them until breastfeeding is finished.

Baseline monitoring and follow-up

- 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,
  - body mass index or other measure of obesity,
  - total cholesterol, non-HDL cholesterol, HDL cholesterol and triglycerides,
  - HbA1c,
  - renal function and eGFR,
  - transaminase level (alanine aminotransferase or aspartate aminotransferase),
  - thyroid-stimulating hormone.
- **Do NOT** routinely exclude from statin therapy people who have liver transaminase levels that are raised but are <3 times the upper limit of normal.
- Measure liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) within 3 months of starting treatment and at 12 months, but not again unless clinically indicated.
- **Do NOT** measure CK levels in asymptomatic people who are being treated with a statin.
- **Do NOT** stop statins because of an increase in blood glucose level or HbA1c.
- For people stable on a low- or middle-intensity statin discuss the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person if a change is needed.
- 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 >40% reduction in non-HDL cholesterol.

  If this 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 80mg and the person is at higher risk because of comorbidities, risk score or using clinical judgement.
- Provide annual medication reviews for people taking statins:
  - use these reviews to discuss medicines adherence and lifestyle modification and address CVD risk factors.
  - consider taking a non-fasting blood test for non-HDL cholesterol to inform the discussion.

Statin intolerance

- If a person cannot tolerate a high-intensity statin aim to treat with the maximum tolerated dose.
- Tell the person that any statin at any dose reduces CVD risk. If someone reports adverse effects when taking statins discuss the following possible strategies with them:
  - stop the statin and try again when symptoms have resolved to check if symptoms are related to the statin,
  - reduce the dose within the same intensity group,
  - change the statin to a lower intensity group (see Table 1).
- Seek specialist advice about options for treating people at high risk of CVD such as those with CKD, type 1 or type 2 diabetes, genetic dyslipidaemias, and those with CVD, who are intolerant to three different statins. Advice can be sought by telephone, virtual clinic or referral.

Ezetimibe

- For the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia ezetimibe can be considered as a treatment option in line with the recommendations in NICE TA132.

Treatments NOT to use

- **Do NOT** routinely offer fibrates, nicotinic acid (niacin), a bile acid sequestrant (anion exchange resin) or omega-3 fatty acid compounds for the prevention of CVD to any of the following:
  - people being treated for primary or secondary prevention,
  - people with CKD, type 1 or type 2 diabetes.
- Tell people that there is no evidence that omega-3 fatty acid compounds help to prevent 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.
- **Do NOT** offer coenzyme Q10 or vitamin D to increase adherence to statin treatment.

See **NICE pathway: Cardiovascular disease prevention**