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Quick reference guide

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Familial hypercholesterolaemia

Identification and management of familial hypercholesterolaemia

NICE clinical guideline 71
Developed by the National Collaborating Centre for Primary Care

About this booklet

This is a quick reference guide that summarises the recommendations NICE has made to the NHS in Identification and management of familial hypercholesterolaemia (NICE clinical guideline 71).

Who should read this booklet?

This quick reference guide is for GPs, nurses, consultants, dietitians, and other staff who care for people with familial hypercholesterolaemia.

Who wrote the guideline?

The guideline was developed by the National Collaborating Centre for Primary Care, which is based at the Royal College of General Practitioners. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs, nurses, dietitians and pharmacists), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

For more information on how NICE clinical guidelines are developed, go to www.nice.org.uk

Where can I get more information about the guideline?

The NICE website has the recommendations in full, reviews of the evidence they are based on, a summary of the guideline for patients and carers, and tools to support implementation (see inside back cover for more details).

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

This guidance represents the view of the Institute, 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 summary of product characteristics of any drugs they are considering.

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 avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Contents

Introduction

Familial hypercholesterolaemia (FH) is a genetic condition that causes a high cholesterol concentration in the blood. It is caused by mutations in genes of the pathway that clears low-density lipoprotein (LDL) from the bloodstream (in most cases the LDL receptor). This is present from birth and may lead to early development of atherosclerosis and coronary heart disease. The disease is transmitted from generation to generation in a dominant pattern, such that siblings and children of a person with FH have a 50% risk of inheriting FH.

The prevalence of heterozygous FH in the UK population is estimated to be 1 in 500, which means that approximately 110,000 people are affected. Having this condition leads to a greater than 50% risk of coronary heart disease in men by the age of 50 years and at least 30% in women by the age of 60 years, if left untreated.

Homozygous FH is rare, with an incidence of approximately one case per one million. Symptoms appear in childhood, and are associated with early death from coronary heart disease.

Patient-centred care

Treatment and care should take into account patients' individual needs and preferences. Good communication is essential, supported by evidence-based information, to allow patients to reach informed decisions about their care. Follow Department of Health advice on seeking consent if needed. If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care. If caring for young people in transition between paediatric and adult services refer to 'Transition: getting it right for young people' (available from www.dh.gov.uk).

Offer patients and their families written advice and information about patient support groups for people with FH.

Key priorities for implementation

Diagnosis

- A family history of premature coronary heart disease should always be assessed in a person being considered for a diagnosis of FH (see Simon Broome criteria, page 7).
- In children at risk of FH because of one affected parent, the following diagnostic tests should be carried out by the age of 10 years or at the earliest opportunity thereafter.
  - A DNA test if the family mutation is known.
  - LDL-C concentration measurement if the family mutation is not known. When excluding a diagnosis of FH a further LDL-C measurement should be repeated after puberty because LDL-C concentrations change during puberty.
- Coronary heart disease risk estimation tools such as those based on the Framingham algorithm should not be used because people with FH are already at a high risk of premature coronary heart disease.

Identifying people with FH using cascade testing

- Healthcare professionals should offer all people with FH a referral to a specialist with expertise in FH for confirmation of diagnosis and initiation of cascade testing.
- Cascade testing using a combination of DNA testing and LDL-C concentration measurement is recommended to identify affected relatives of those index individuals with a clinical diagnosis of FH. This should include at least the first- and second- and, when possible, third-degree biological relatives.
- The use of a nationwide, family-based, follow-up system is recommended to enable comprehensive identification of people affected by FH.

Management

Adults

- Healthcare professionals should consider prescribing a high-intensity statin to achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline (that is, LDL-C concentration before treatment).

Children and young people

- Healthcare professionals should offer all children and young people diagnosed with, or being investigated for, a diagnosis of FH a referral to a specialist with expertise in FH in children and young people. This should be in an appropriate child/young person-focused setting that meets the standards within the 'National service framework for children, young people and maternity services' (available from www.dh.gov.uk).

continued

Information needs and support

Information and counselling on contraception for women and girls with FH

- When lipid-modifying drug therapy is first considered for women and girls, the risks for future pregnancy and the fetus while taking lipid-modifying drug therapy should be discussed. This discussion should be revisited at least annually.

Ongoing assessment and monitoring

Review

- All people with FH should be offered a regular structured review that is carried out at least annually.

Definition of terms used in this guideline

Adult: a person who is 16 years and older.

Cascade testing: a method for identifying people at risk of a genetic condition by a process of family tracing.

Child/young person: 'child' refers to anyone younger than 10 years of age; 'young person' refers to anyone from the age of 10 years up to the age of 15 years.

First-degree relative: a person's biological parent, sister, brother or child.

Heterozygous FH: people who have inherited a defective gene from only one parent.

High-intensity statin: statins are classified as high intensity if they produce greater low-density lipoprotein cholesterol (LDL-C) reductions than simvastatin 40 mg (for example, simvastatin 80 mg and appropriate doses of atorvastatin and rosuvastatin).

Homozygous FH: people who have inherited a defective gene from both parents. This may be the same or a different defective gene and the term homozygous FH will be used to cover both conditions in this guideline.

Index individual: the original patient who is the starting point for follow-up of other members of a family when investigating possible genetic factors that are responsible for the presenting condition.

Second-degree relative: a person's biological grandparent, grandchild, aunt, uncle, niece, nephew, half sister or half brother.

Third-degree relative: a person's biological great grandparent, great grandchild, great aunt, great uncle, first cousin, grand niece or grand nephew.

Urgent referral: as soon as possible but within a maximum time frame of 14 days.

Diagnosis

- Consider the possibility of familial hypercholesterolaemia (FH) in adults who have raised total cholesterol concentrations (typically greater than 7.5 mmol/l), especially if there is a personal or family history of premature coronary heart disease.
- Exclude secondary causes of hypercholesterolaemia before considering a diagnosis of FH.
- Use the Simon Broome criteria (see below) to make a diagnosis of FH.
- Absence of clinical signs (for example, tendon xanthomata) does not exclude a diagnosis of FH.
- To confirm a diagnosis of FH, take two measurements of low-density lipoprotein cholesterol (LDL-C) concentration.
- Provide clear and appropriate information about FH, the process of family testing, DNA testing and measuring LDL-C concentration.

Simon Broome diagnostic criteria for index individuals*

Diagnose a person with **definite** FH if they have:

- cholesterol concentrations as defined in table 1 and tendon xanthomas, or evidence of these signs in first- or second-degree relative

or

- DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.

Diagnose a person with **possible** FH if they have cholesterol concentrations as defined in table 1 **and** at least one of the following.

- Family history of myocardial infarction: aged younger than 50 years in second-degree relative or aged younger than 60 years in first-degree relative.
- Family history of raised total cholesterol: greater than 7.5 mmol/l in adult first- or second-degree relative or greater than 6.7 mmol/l in child, brother or sister aged younger than 16 years.

Table 1 Cholesterol levels to be used as diagnostic criteria for the index individual[1]

	Total cholesterol	LDL-C
Child/young person	> 6.7 mmol/l	> 4.0 mmol/l
Adult	> 7.5 mmol/l	> 4.9 mmol/l

[1] Levels either pre-treatment or highest on treatment.
LDL-C, low-density lipoprotein cholesterol.

* Marks D, Thorogood M, Neil HA, Humphries SE (2003) A review on the diagnosis, natural history, and treatment of familial hypercholesterolaemia. Atherosclerosis 168 (1): 1–14.

Family history

- When considering a diagnosis of FH, always take a family history of premature coronary heart disease.

- When considering a diagnosis of FH, healthcare professionals with expertise in FH should use standardised pedigree terminology to record, when possible, at least a three-generation pedigree, including relatives':
  - age of onset of coronary heart disease
  - lipid concentrations
  - smoking history.
- If relatives are deceased, record:
  - age and cause of death
  - smoking history.
- Ask the patient to verify this information with other family members if possible.

Clinical diagnosis of FH

- If a person has a diagnosis of FH based on the Simon Broome criteria (see page 7), inform them that they have a clinical diagnosis of FH.
- Consider a clinical diagnosis of homozygous FH in:
  - adults with an LDL-C concentration greater than 13 mmol/l
  - children/young people with an LDL-C concentration greater than 11 mmol/l.
- Offer all people with a clinical diagnosis of homozygous FH a referral to a specialist centre.

DNA testing

- Offer a DNA test to people with a clinical diagnosis of FH.
- Inform all people who have an identified mutation diagnostic of FH that they have an unequivocal diagnosis of FH even if their LDL-C concentration does not meet the diagnostic criteria for index individuals (see Simon Broome criteria, page 7) or their relatives (see tables 2 and 3, pages 11 and 12).
- When DNA testing has excluded a diagnosis of FH in a member of a family, manage the person's risk of coronary heart disease as in the general population[1].

What not to do

- Do not use ultrasonography of the Achilles tendon.
- Do not use coronary heart disease risk estimation tools, such as those based on the Framingham algorithm, because people with FH are already at a high risk of premature coronary heart disease.

[1] See 'Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease' (NICE clinical guideline 67).

Diagnosing FH in children

In children at risk of FH because of:	
One affected parent	By the age of 10 years or as soon as possible after this: • offer a DNA test if the family mutation is known • measure LDL-C concentration if the family mutation is not known. Repeat after puberty before excluding a diagnosis of FH.
Two affected parents or the presence of clinical signs (for example, cutaneous lipid deposits)	By the age of 5 years or as soon as possible after this: • measure LDL-C concentration • if LDL-C concentration is greater than 11 mmol/l, consider a clinical diagnosis of homozygous FH.

Referral

Offer a referral to a specialist with expertise in FH to:

- all people for confirmation of diagnosis and initiation of cascade testing (see page 10)
- any child or young person being investigated for FH, or who has a diagnosis of FH – refer to an appropriate child/young person-focused setting[2]
- an adult with FH for consideration for further treatment if they are assessed to be at very high risk of a coronary event, that is, if they have any of the following.
  - Established coronary heart disease.
  - A family history of premature coronary heart disease.
  - Two or more other cardiovascular risk factors (for example, they are male, they smoke, or they have hypertension or diabetes).

Offer a referral to a cardiologist for evaluation of coronary heart disease to:

- all people diagnosed with homozygous FH
- a person with FH who has symptoms or signs of possible coronary heart disease that are:
  - **not** immediately life threatening – refer urgently (see page 6; a low threshold for referral is recommended)
  - immediately life threatening – refer to hospital as an emergency.
- Consider offering a referral to a cardiologist if there is a family history of coronary heart disease in early adulthood or two or more other cardiovascular risk factors (for example, they are male, they smoke, or they have hypertension or diabetes).
- Do not routinely offer referral to asymptomatic children or young people with heterozygous FH.

[2] This should be an appropriate child/young person-focused setting that meets the standards within the 'National service framework for children, young people and maternity services' (available from www.dh.gov.uk).

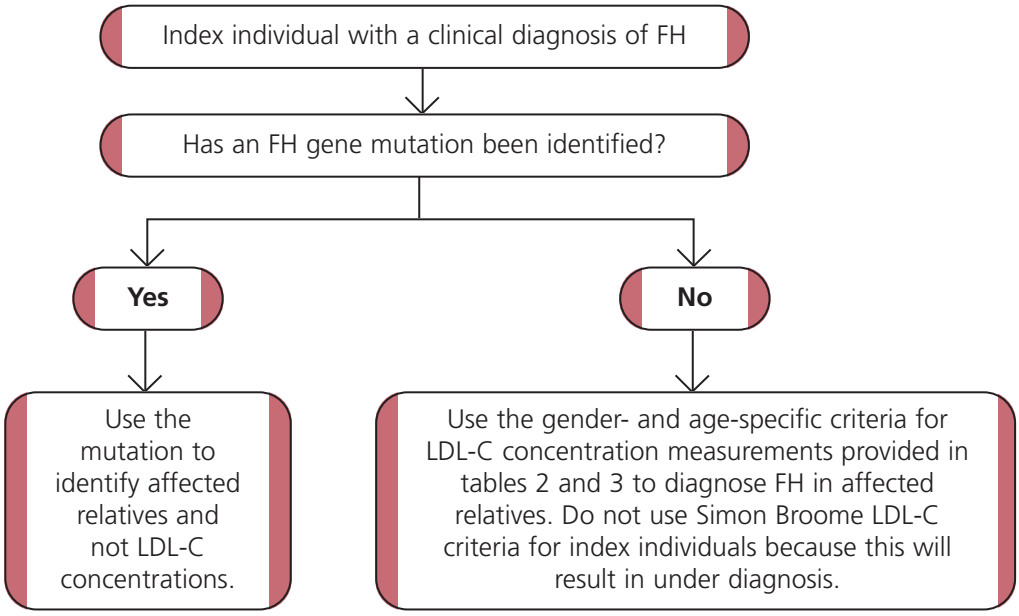
Information and support

Healthcare professionals with expertise in FH should:

- provide information to patients about their specific level of risk of coronary heart disease, its implications for the patient and their families, lifestyle advice (see page 16) and treatment options (see pages 13–17)
- when considering cascade testing (see below), offer to help with sharing of information about FH with family members
- encourage patients to contact their relatives to inform them of their potential risk and so that cascade testing can take place.

Cascade testing

- Explain what cascade testing is and discuss implications with the patient.
- Use a nationwide, family-based, follow-up system to enable comprehensive identification of affected people.
- Use a combination of DNA testing and LDL-C concentration measurement to identify affected relatives of index individuals with a clinical diagnosis of FH (see below).



- Include at least first- and second-degree relatives. Include third-degree relatives if possible.
- Be aware of the latest guidance on data protection.

Table 2 Gender- and age-specific LDL-C criteria for the diagnosis of FH in female relatives of an index individual*

Age (years)					
0 to 14	15 to 24	25 to 34	35 to 44	45 to 54	55 and older
5.3	5.3	5.3	5.3	5.3	5.3
5.2	5.2	5.2	5.2	5.2	5.2
5.1	5.1	5.1	5.1	5.1	5.1
5.0	5.0	5.0	5.0	5.0	5.0
4.9	4.9	4.9	4.9	4.9	4.9
4.8	4.8	4.8	4.8	4.8	4.8
4.7	4.7	4.7	4.7	4.7	4.7
4.6	4.6	4.6	4.6	4.6	4.6
4.5	4.5	4.5	4.5	4.5	4.5
4.4	4.4	4.4	4.4	4.4	4.4
4.3	4.3	4.3	4.3	4.3	4.3
4.2	4.2	4.2	4.2	4.2	4.2
4.1	4.1	4.1	4.1	4.1	4.1
4.0	4.0	4.0	4.0	4.0	4.0
3.9	3.9	3.9	3.9	3.9	3.9
3.8	3.8	3.8	3.8	3.8	3.8
3.7	3.7	3.7	3.7	3.7	3.7
3.6	3.6	3.6	3.6	3.6	3.6
3.5	3.5	3.5	3.5	3.5	3.5
3.4	3.4	3.4	3.4	3.4	3.4
3.3	3.3	3.3	3.3	3.3	3.3
3.2	3.2	3.2	3.2	3.2	3.2

*Values given are LDL-C concentrations (mmol/l). This table is taken from Starr B, et al. (2008) Development of sensitive and specific age- and gender-specific low density lipoprotein cholesterol cutoffs for diagnosis of first-degree relatives with familial hypercholesterolaemia in cascade testing. Clinical Chemistry and Laboratory Medicine 46 (6): 791–803.

LDL-C, low-density lipoprotein cholesterol.

Key to tables 2 and 3:

Likely to have a clinical diagnosis of FH.

Uncertain: carry out a further measurement of LDL-C concentration and, if level is still in the grey zone, repeat annually. If LDL-C concentration remains in the grey zone, manage risk of coronary heart disease as in the general population[3].

Unlikely to have FH: manage risk of coronary heart disease as in the general population[3].

[3] See 'Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease' (NICE clinical guideline 67).

Table 3 Gender- and age-specific LDL-C criteria for the diagnosis of FH in male relatives of an index individual*

Age (years)					
0 to 14	15 to 24	25 to 34	35 to 44	45 to 54	55 and older
5.3	5.3	5.3	5.3	5.3	5.3
5.2	5.2	5.2	5.2	5.2	5.2
5.1	5.1	5.1	5.1	5.1	5.1
5.0	5.0	5.0	5.0	5.0	5.0
4.9	4.9	4.9	4.9	4.9	4.9
4.8	4.8	4.8	4.8	4.8	4.8
4.7	4.7	4.7	4.7	4.7	4.7
4.6	4.6	4.6	4.6	4.6	4.6
4.5	4.5	4.5	4.5	4.5	4.5
4.4	4.4	4.4	4.4	4.4	4.4
4.3	4.3	4.3	4.3	4.3	4.3
4.2	4.2	4.2	4.2	4.2	4.2
4.1	4.1	4.1	4.1	4.1	4.1
4.0	4.0	4.0	4.0	4.0	4.0
3.9	3.9	3.9	3.9	3.9	3.9
3.8	3.8	3.8	3.8	3.8	3.8
3.7	3.7	3.7	3.7	3.7	3.7
3.6	3.6	3.6	3.6	3.6	3.6
3.5	3.5	3.5	3.5	3.5	3.5
3.4	3.4	3.4	3.4	3.4	3.4
3.3	3.3	3.3	3.3	3.3	3.3
3.2	3.2	3.2	3.2	3.2	3.2
3.1	3.1	3.1	3.1	3.1	3.1
3.0	3.0	3.0	3.0	3.0	3.0

*Values given are LDL-C concentrations (mmol/l). This table is taken from Starr B, et al. (2008) Development of sensitive and specific age- and gender-specific low density lipoprotein cholesterol cutoffs for diagnosis of first-degree relatives with familial hypercholesterolaemia in cascade testing. Clinical Chemistry and Laboratory Medicine 46 (6): 791–803.

LDL-C, low-density lipoprotein cholesterol.

Management

Drug treatment

- When deciding on drug treatment (see table 4), discuss options with the adult or child/young person and their parent/carer and consider concomitant medication, comorbidities, safety and tolerability.
- When offering lipid-modifying drug therapy, inform the adult or child/young person and their parent/carer that this treatment should be lifelong.
- If the patient has any side effects that compromise concordance with lipid-modifying drug therapy, offer referral to a specialist with expertise in FH.

Adults

- If treatment with the maximum tolerated dose of a high-intensity statin and ezetimibe does not reduce LDL-C concentrations by greater than 50% from baseline, offer a referral to a specialist in FH.
- Prescribe drugs for the treatment of homozygous FH in a specialist centre.

Children and young people

- Consider lipid-modifying drug therapy by the age of 10 years.
- When deciding to defer or offer lipid-modifying drug therapy, take into account:
  - their age
  - age of onset of coronary heart disease within the family, and
  - the presence of other cardiovascular risk factors, including their LDL-C concentration.
- In exceptional circumstances (for example, when there is family history of coronary heart disease in early adulthood), consider offering:
  - a higher dose of statin than is licensed for use in the appropriate age group, and/or
  - more than one lipid-modifying drug therapy, and/or
  - lipid-modifying drug therapy before the age of 10 years.
- In children and young people with homozygous FH, consider lipid-modifying drug therapy to lower LDL-C concentrations before LDL apheresis (see page 17).
- Routinely monitor growth and pubertal development.

Table 4 When to offer drug treatment and special considerations

<table>
<tr><th>Drug therapy</th><th colspan="2">Adults with FH</th><th>Children/young people with FH</th></tr>
<tr><td>Statins</td><td colspan="2">• Use as initial treatment.
• To achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline:
– consider prescribing a high-intensity statin
– increase to the maximum licensed or tolerated dose.
• When an adult, who does not have coronary heart disease, is diagnosed with FH after the age of 60 years, offer a statin with a low acquisition cost.</td><td>• Use as initial treatment.
• Choose the statin licensed for use in the appropriate age group.
• Prescribe at the doses specified in the BNF for children.</td></tr>
<tr><td></td><td colspan="3">• Measure baseline liver and muscle enzymes (including transaminases and creatine kinase) before starting treatment.
• Raised liver or muscle enzymes should not routinely exclude a person from therapy.
• Do not routinely monitor creatine kinase levels in asymptomatic patients.</td></tr>
<tr><td>Ezetimibe</td><td colspan="2">• Is an option for adults with heterozygous FH if statins are contraindicated or not tolerated[1,2].
• Is an option for adults with heterozygous FH when coadministered with initial statin therapy[1,3] if:
– serum total or LDL-C concentration is not appropriately controlled[4] with initial statin therapy after appropriate dose titration or because of intolerance[2] to the statin, and
– consideration is being given to changing from initial statin therapy to an alternative statin.</td><td>• Consider if statins are not tolerated.</td></tr>
<tr><td>Bile acid sequestrant (resin)</td><td>• For long-term treatment, consider offering fat-soluble vitamins (A, D and K) and folic acid supplementation.</td><td rowspan="3">• Consider if statins or ezetimibe are contraindicated or not tolerated.
• Offer a referral to a specialist in FH for consideration of this treatment.
• The specialist should make the decision as to whether any of these treatments should be added to initial statin therapy[5].</td><td>• Consider if statins are not tolerated.
• For long-term treatment, consider offering fat-soluble vitamins (A, D and K) and folic acid supplementation.</td></tr>
<tr><td>Fibrate</td><td>• Do not use gemfibrozil and statins together.</td><td>• Consider if statins are not tolerated.</td></tr>
<tr><td>Nicotinic acid</td><td>• Offer advice on strategies that reduce flushing, including taking:
– low initial doses with meals, and/or
– aspirin 30 minutes before the first daily dose.</td><td>• There is no recommendation on the use of nicotinic acid in this age group.</td></tr>
</table>

BNF, British national formulary; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol.

[1] These recommendations are from 'Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia' (NICE technology appraisal guidance 132). They have been incorporated into this guideline in line with NICE procedures for developing clinical guidelines.
[2] Intolerance is defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in compliance with therapy being compromised. Adverse effects include evidence of new-onset muscle pain, significant gastrointestinal disturbance or alterations of liver function tests.
[3] When prescribing ezetimibe, choose the agent with the lowest acquisition cost.
[4] Base the decision as to whether or not cholesterol concentrations are appropriately controlled on individualised risk assessment in accordance with national guidance on the management of cardiovascular disease for the relevant population.
[5] Exercise caution when adding nicotinic acid or a fibrate to a statin because of the risk of muscle-related side effects (including rhabdomyolysis).

Information for women and girls with FH

- Give specific information that is tailored to their needs. Offer a choice of effective contraceptive methods.
- When first considering lipid-modifying drug therapy (see pages 13 and 14), discuss the risks of taking such medication for future pregnancy and the risks to the fetus. Revisit at least once a year.
- For women and girls with FH who are receiving treatment with lipid-modifying drug therapy:
  - combined oral contraceptives are not generally contraindicated (refer to the relevant summary of product characteristics for contraindications)
  - because there is a potential small increased risk of cardiovascular events with the use of combined oral contraceptives, consider other forms of contraception.

Pregnancy in women with FH

- Be aware that, in general, there is no reason to advise against pregnancy or breastfeeding in women with FH.
- Advise women that, because of the potential risk of fetal abnormality, if they are planning to conceive or are pregnant they should not take lipid-modifying drug therapy.
- Advise women to stop taking lipid-modifying drug therapy 3 months before attempting to conceive.
- Advise women who conceive while taking statins or other systemically absorbed lipid-modifying drug therapy to stop treatment immediately. Offer an urgent referral to an obstetrician for fetal assessment. Inform the woman fully about the nature and purpose of this assessment.
- If a woman has conceived while taking statins or other systemically absorbed lipid-modifying drug therapy and has had a fetal assessment, give her the time, opportunity and full information that she needs to consider her options (including the advantages and disadvantages) of continuing with the pregnancy.
- Organise shared-care arrangements, including expertise in cardiology and obstetrics, for women with FH who are considering pregnancy or are pregnant. Assess coronary heart disease risk, particularly to exclude aortic stenosis. This is essential for women with homozygous FH.
- Do not routinely measure serum cholesterol concentrations during pregnancy.
- Advise women with FH who are pregnant on the potential risks and benefits of re-starting lipid-modifying drug therapy for them and the breastfed infant.
- During lactation, do not use any lipid-modifying drug therapy except for bile acid sequestrants (resins).

Lifestyle advice

Regard lifestyle advice as a component of medical management and not as a substitute for lipid-modifying drug therapy.

Lifestyle	Recommended advice for people with FH
Smoking	• Smoking greatly increases the risk of coronary heart disease in people with FH, therefore: – discourage people who do not smoke (especially children) from starting – advise people who smoke to stop. • Offer people who want to stop smoking support, advice and referral to an intensive support service[1]. • If a person is unwilling or unable to accept a referral, offer pharmacotherapy[2].
Diet	• Offer individualised nutritional advice. Advice should be given by a healthcare professional with specific expertise in nutrition. • Advise people to consume a diet in which: – total fat intake is 30% or less of total energy intake – saturated fats are 10% or less of total energy intake – intake of dietary cholesterol is less than 300 mg a day – saturated fats are replaced by increasing the intake of monounsaturated and polyunsaturated fats. • Advise people to eat: – at least five portions of fruit and vegetables a day – at least two portions of fish a week (one of which should be oily). • Advise pregnant women to limit their oily fish to two portions a week. • Advise people that if they wish to consume food products containing stanols and sterols then these need to be taken consistently to be effective. • Do not routinely recommend people to take omega-3 fatty acid supplements[3]. • For further advice, refer people to www.eatwell.gov.uk/healthydiet and www.5aday.nhs.uk
Physical activity	• Advise people to take at least 30 minutes of physical activity a day, of at least moderate intensity, at least 5 days a week[4]. • Encourage people who are unable to perform moderate-intensity physical activity at least 5 days a week because of comorbidity, disability, medical conditions or personal circumstances to exercise at their maximum safe capacity. • Recommend activity that can be incorporated into everyday life, such as brisk walking, using stairs and cycling[4]. • Advise people that bouts of physical activity of 10 minutes or more accumulated throughout the day are as effective as longer sessions[4].
Weight management	• Offer people who are overweight or obese appropriate advice and support to achieve and maintain a healthy weight[5].
Alcohol consumption	• Advise adult men to limit their alcohol intake to no more than 3–4 units of alcohol a day. • Advise adult women to limit their alcohol intake to no more than 2–3 units of alcohol a day. • Advise people to avoid binge drinking. • For further advice, refer people to www.eatwell.gov.uk/healthydiet

[1] See 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health intervention guidance 1).
[2] See 'Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation' (NICE technology appraisal guidance 39), and 'Varenicline for smoking cessation' (NICE technology appraisal guidance 123).
[3] For people with FH who have already had a myocardial infarction (MI), refer to 'MI: secondary prevention. Secondary prevention in primary and secondary care for patients following a myocardial infarction' (NICE clinical guideline 48).
[4] See 'At least five a week: evidence on the impact of physical activity and its relationship to health. A report from the Chief Medical Officer' (2004; available from www.dh.gov.uk).
[5] See 'Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children' (NICE clinical guideline 43).

Specialist treatment

LDL apheresis

- Consider offering LDL apheresis for the treatment of adults and children/young people with clinical homozygous FH. Assess the patient's response to lipid-modifying drug therapy and the presence of coronary heart disease to determine when to start treatment.
- In exceptional instances (such as when there is progressive, symptomatic coronary heart disease, despite maximal tolerated lipid-modifying drug therapy and optimal medical and surgical therapy), consider offering LDL apheresis for the treatment of people with heterozygous FH. This treatment should take place in a specialist centre on a case-by-case basis and data recorded in an appropriate registry.
- Recommend arterio-venous fistulae as the preferred method of access.
- Discuss the possible benefits and complications of the procedure with patients.
- Discontinue warfarin approximately 4 days before LDL-apheresis treatment. Substitute warfarin with low molecular weight heparin.
- On the morning of the day of LDL-apheresis treatment, review all blood pressure-lowering drug therapy being taken. Consider for discontinuation.
- Continue anti-platelet therapy.
- Do not use angiotensin-converting enzyme (ACE) inhibitors. Substitute ACE inhibitors with angiotensin-receptor blocking agents.
- Routinely monitor iron status during treatment.
- If required, initiate iron supplementation.

Liver transplantation

- Consider offering liver transplantation as an option to people with homozygous FH after treatment with lipid-modifying drug therapy and LDL apheresis.
- When deciding whether to refer a person for liver transplantation, discuss the benefits and potential harms of undertaking or declining transplantation with the patient and/or their relatives in an appropriate specialist setting. Make this decision in partnership with the patient and/or their relative.

Review

- Carry out a structured review, at least once a year, for all people with FH.
- Consider a baseline electrocardiogram (ECG) for adults with FH.
- The annual review should include all of the following.
  - Ask if the person has had any symptoms of coronary heart disease.
  - Ask whether the person smokes.
  - Take a fasting lipid profile to monitor LDL-C concentration.
  - Discuss whether they are taking their medication correctly.
  - Enquire about any possible side effects of treatment the patient may be experiencing.
  - Discuss any changes that may be required to lifestyle or lipid-modifying drug therapy to achieve recommended LDL-C concentrations.
  - Record the progress of cascade testing among relatives. This should include at least first- and second-, and when possible, third-degree relatives. If there are still relatives who have not been tested, discuss further action.
  - Update family history – note any changes in the coronary heart disease status of relatives. This should include at least first- and second-, and when possible, third-degree relatives.

Implementation tools

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG071).

- Slides highlighting key messages for local discussion.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- Costing tools:
  - costing report to estimate the national savings and costs associated with implementation
  - costing template to estimate the local costs and savings involved.
- Audit support for monitoring local practice.

Further information

Ordering information

You can download the following documents from www.nice.org.uk/CG071

- A quick reference guide (this document) – a summary of the recommendations for healthcare professionals.
- The NICE guideline – all the recommendations.
- 'Understanding NICE guidance' – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1640 (quick reference guide)
- N1641 ('Understanding NICE guidance').

Related NICE guidance

For information about NICE guidance that has been issued or is in development, see the website (www.nice.org.uk).

- Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 67 (2008). Available from: www.nice.org.uk/CG067
- MI: secondary prevention. Secondary prevention in primary and secondary care for patients following a myocardial infarction. NICE clinical guideline 48 (2007). Available from: www.nice.org.uk/CG048
- Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guideline 43 (2006). Available from: www.nice.org.uk/CG043
- Long-acting reversible contraception. NICE clinical guideline 30 (2005). Available from: www.nice.org.uk/CG030

- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. NICE technology appraisal guidance 132 (2007). Available from: www.nice.org.uk/TA132
- Varenicline for smoking cessation. NICE technology appraisal guidance 123 (2007). Available from: www.nice.org.uk/TA123
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006). Available from: www.nice.org.uk/TA094
- Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation. NICE technology appraisal guidance 39 (2002). Available from: www.nice.org.uk/TA039
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006). Available from: www.nice.org.uk/PHI001

Updating the guideline

This guideline will be updated as needed, and information about the progress of any update will be posted on the NICE website (www.nice.org.uk/CG071).

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