NHS
National Institute for Health and Clinical Excellence

Quick reference guide

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MI: secondary prevention

Secondary prevention in primary and secondary care for patients following a myocardial infarction

NICE clinical guideline 48 (replaces NICE inherited guideline A)
Developed by the National Collaborating Centre for Primary Care

About this booklet

This booklet summarises the recommendations NICE has made to the NHS in 'Secondary prevention in primary and secondary care for patients following a myocardial infarction' (NICE clinical guideline 48). It replaces the existing NICE guideline 'Prophylaxis for patients who have experienced a myocardial infarction' (NICE inherited guideline A, April 2001) for use in the NHS in England and Wales. The guideline also supports the implementation of the 'Coronary heart disease national service framework (NSF)'.

Who should read this booklet?

This quick reference guide is for healthcare professionals and other staff who care for people who have had a myocardial infarction (MI). It contains what you need to know to put the guideline's recommendations into practice.

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 and nurses), 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 on secondary prevention for post-MI patients?

The NICE website has the recommendations in full, summaries of the evidence they are based on, a summary of the guideline for patients and carers, and tools to support implementation (see page 13 for more details).

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This guidance is written in the following context

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. The guidance does not, however, 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.

Contents

Introduction

In the UK, about 838,000 men and 394,000 women have had an MI at some point in their lives. This is a total of 1.2 million people. MI is a complication of coronary heart disease (CHD), which is a preventable disease. Although the death rate from CHD has been falling since the early 1970s, when compared internationally, the UK death rate from CHD remains high, with more than 103,000 deaths per year. CHD death rates vary with age, gender, socioeconomic status, ethnicity and geographic location.

This guideline makes recommendations on a range of secondary prevention interventions, which reflect the best available evidence and developments in care, to improve outcomes for people after an MI.

Patient-centred care

Treatment and care should take into account patients' individual needs and preferences. Good communication, supported by evidence-based information, is essential to allow patients to reach informed decisions about their care. Carers and relatives should have the opportunity to be involved in discussions unless the patient thinks it inappropriate.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

- After an acute myocardial infarction (MI), confirmation of the diagnosis of acute MI and results of investigations, future management plans and advice on secondary prevention should be part of every discharge summary.
- Patients should be advised to undertake regular physical activity sufficient to increase exercise capacity.
- Patients should be advised to be physically active for 20–30 minutes a day to the point of slight breathlessness. Patients who are not achieving this should be advised to increase their activity in a gradual, step-by-step way, aiming to increase their exercise capacity. They should start at a level that is comfortable, and increase the duration and intensity of activity as they gain fitness.
- All patients who smoke should be advised to quit and be offered assistance from a smoking cessation service in line with 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health intervention guidance 1).
- Patients should be advised to eat a Mediterranean-style diet (more bread, fruit, vegetables and fish; less meat; and replace butter and cheese with products based on vegetable and plant oils).
- Cardiac rehabilitation should be equally accessible and relevant to all patients after an MI, particularly people from groups that are less likely to access this service. These include people from black and minority ethnic groups, older people, people from lower socioeconomic groups, women, people from rural communities and people with mental and physical health comorbidities.
- All patients who have had an acute MI should be offered treatment with a combination of the following drugs:
  - ACE (angiotensin-converting enzyme) inhibitor
  - aspirin
  - beta-blocker
  - statin.
- For patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment should be initiated within 3–14 days of the MI, preferably after ACE inhibitor therapy.
- Treatment with clopidogrel in combination with low-dose aspirin should be continued for 12 months after the most recent acute episode of non-ST-segment-elevation acute coronary syndrome. Thereafter, standard care, including treatment with low-dose aspirin alone, is recommended unless there are other indications to continue dual antiplatelet therapy.
- After an ST-segment-elevation MI, patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks. Thereafter, standard treatment including low-dose aspirin should be given, unless there are other indications to continue dual antiplatelet therapy.
- All patients should be offered a cardiological assessment to consider whether coronary revascularisation is appropriate. This should take into account comorbidity.

Lifestyle

Intervention	Recommended advice for patients
Improving diet	Advise patients not to take supplements containing beta-carotene. Do not advise patients to take antioxidant supplements (vitamin E and/or C) or folic acid to reduce cardiovascular risk. Advise patients to consume at least 7 g of omega 3 fatty acids per week from two to four portions of oily fish. Consider providing at least 1 g daily of omega-3-acid ethyl esters treatment licensed for secondary prevention post MI for up to 4 years for patients who have had an MI within 3 months and are not achieving 7 g of omega 3 fatty acids per week. Do not routinely initiate omega-3-acid ethyl esters supplements for patients who have had an MI more than 3 months earlier. Encourage patients to eat a Mediterranean-style diet.
Delivering dietary advice	Give consistent healthy eating advice that is tailored to the patient's needs and that can be extended to the whole family. Offer patients an individual consultation to discuss diet, including their current eating habits, and advice on improving their diet.
Controlling alcohol consumption	Advise patients to keep weekly alcohol consumption within safe limits (no more than 21 units of alcohol per week for men or 14 units per week for women) and to avoid binge drinking.
Improving physical activity levels	Encourage patients to undertake sufficient regular physical activity to increase exercise capacity. They should aim to be physically active for 20–30 minutes a day to the point of slight breathlessness. For patients not achieving this, advise them to increase their activity in a step-by-step way, aiming to increase their exercise capacity. They should start at a level that is comfortable, and increase the duration and intensity of activity as they gain fitness. Discuss current and past activity levels and preferences with patients. The benefit of exercise may be enhanced by tailored advice from a suitably qualified professional.
Smoking cessation	Advise smokers to quit and offer assistance from a smoking cessation service. Offer smokers who have expressed a desire to quit support, advice and referral to an intensive support service. If a patient is unable or unwilling to accept a referral, offer pharmacotherapy. Refer to NICE technology appraisal guidance 39 and NICE public health intervention guidance 1.
Controlling weight	Offer overweight and obese patients advice and support to achieve and maintain a healthy weight. Refer to NICE clinical guideline 43.

Cardiac rehabilitation after an acute MI

General	• Give all patients who have had an acute MI advice about cardiac rehabilitation programmes, and offer a programme with an exercise component. • Programmes should provide a range of options. Encourage patients to attend all options appropriate to their needs. Do not exclude patients from the programme if they choose not to attend certain components. • If a patient has cardiac or other clinical conditions that may worsen during exercise, treat these if possible before the patient is offered the exercise component of cardiac rehabilitation. For some patients, the exercise component may be adapted by an appropriately qualified healthcare professional. • Patients with LV dysfunction who are stable can safely be offered the exercise component.
Engaging patients	• Cardiac rehabilitation should be equally accessible and relevant to all patients after an MI, particularly people from groups that are less likely to access this service. Consider patients' wider health and social needs. This may be a particular issue for patients in more deprived circumstances, and rehabilitation services should assess the likely scale of these needs when planning how their services meet the needs of the local population. • Programmes should be culturally sensitive. Consider employing bilingual peer educators or cardiac rehabilitation assistants who reflect the diversity of the local population. • Programmes should include an exercise component designed to meet the needs of older patients or patients with significant comorbidity. Address any transport problems. • Ask patients whether they would prefer single-sex or mixed classes. • Establish patients' health beliefs and levels of health literacy before offering appropriate lifestyle advice. • Healthcare professionals, including senior medical staff involved in providing care for patients after an MI, should actively promote cardiac rehabilitation. • Promote cardiac rehabilitation, using telephone calls, direct contact from a healthcare professional or motivational letters.
Health education and information	• Comprehensive cardiac rehabilitation programmes should include health education and stress management components. • A home based programme validated for patients who have had an MI (such as 'The Edinburgh heart manual'; see www.cardiacrehabilitation.org.uk/heart_manual/heartmanual.htm) may be used to provide comprehensive cardiac rehabilitation. • Most patients who have had an MI can return to work. Consider the physical and psychological status of the patient, the nature of the work and the work environment. • Be up to date with the latest Driver and Vehicle Licensing Agency guidelines. Refer to www.dvla.gov.uk. • After an MI without complications, patients can usually travel by air within 2–3 weeks. Patients who have had a complicated MI may need expert advice. • Patients who hold a pilot's licence should seek advice from the Civil Aviation Authority. • Most patients can return to normal daily activities. Consider the patient's physical and psychological status and the type of activity planned. • Tables of metabolic equivalents (METS) of different activities can be used to estimate the physical demand of a particular activity and to compare different activities. Refer to www.cdc.gov/nccdphp/dnpa/physical/measuring/met.htm. Advise patients how to use a perceived exertion scale to help monitor physiological demand. After a complicated MI, patients may need expert advice. • Advice on competitive sport may need expert assessment of function and risk, and depends on the sport and level of competitiveness.

Psychological and social support	• Offer stress management in the context of comprehensive cardiac rehabilitation. • Do not routinely offer complex psychological interventions such as cognitive behavioural therapy. • Involve partners or carers in the cardiac rehabilitation programme if the patient wishes. • Refer to NICE clinical guidelines 22 and 23 for patients with clinical anxiety or depression.
Sexual activity	• Discuss sexual activity within the context of cardiac rehabilitation and aftercare. • Reassure patients that after recovery, sexual activity presents no greater risk of triggering a subsequent MI than if they had never had an MI. • Patients who have made an uncomplicated recovery after their MI can resume sexual activity when they feel comfortable to do so, usually after about 4 weeks. • When treating erectile dysfunction, consider a PDE5 inhibitor for patients who have had an MI more than 6 months ago and who are now stable. Avoid PDE5 inhibitors in patients treated with nitrates and/or nicorandil because this can lead to dangerously low blood pressure.

Drug therapy – after an MI in the last 12 months

Offer all patients who have had an acute MI treatment with a combination of the following drugs:
- ACE inhibitor
- aspirin
- beta-blocker
- statin.

ACE inhibitors

- Offer ACE inhibitors early after presentation and titrate upwards to the maximum tolerated or target dose.
- Do not routinely prescribe ARBs unless the patient is intolerant or allergic to an ACE inhibitor.
- Continue ACE inhibitors indefinitely in patients with preserved LV function or LVSD, whether or not they have heart failure symptoms.
- Early after an acute MI, do not routinely use the combination of ACE inhibitor/ARB for patients with heart failure and/or LVSD.

Assessment/monitoring
- Assess LV function in all patients who have had an MI.
- Measure renal function, serum electrolytes and BP before starting an ACE inhibitor or ARB and again within 1 or 2 weeks.
- Monitor patients as the dose is titrated and more frequently for patients at increased risk of deterioration in renal function.
- Monitor patients with chronic heart failure in line with NICE clinical guideline 5.

Antiplatelet therapy

- Offer aspirin and continue indefinitely.
- Do not offer clopidogrel alone as first-line therapy but consider it for patients with aspirin hypersensitivity.
- If the patient has not been treated with a combination of aspirin and clopidogrel during the acute phase of an MI, do not routinely initiate this combination.
- The combination of aspirin and clopidogrel is not recommended for any longer than 12 months after the acute phase of MI, unless there are other indications to continue dual antiplatelet therapy. The combination is usually recommended for a shorter duration after a STEMI.
- Clopidogrel in combination with low-dose aspirin is recommended in the management of non-ST-segment-elevation acute coronary syndrome in people who are at moderate to high risk of MI or death. It is recommended that this combination is continued for 12 months after the most recent acute episode. Thereafter standard care, including low-dose aspirin alone, is recommended[1]. For patients after a STEMI treated with the combination of aspirin and clopidogrel during the first 24 hours, this combination should be continued for at least 4 weeks. Thereafter standard treatment including low-dose aspirin should be given unless there are other indications to continue dual antiplatelet therapy.
- For patients with a history of dyspepsia, consider a PPI and low-dose aspirin. Refer to NICE clinical guideline 17.
- For patients with a history of aspirin-induced ulcer bleeding whose ulcers have healed and who are *H. pylori* negative, consider a full-dose PPI and low-dose aspirin. Refer to NICE clinical guideline 17.

Assessment/monitoring
- The risk of MI or death in patients presenting with non-ST-segment-elevation acute coronary syndrome can be determined by clinical signs and symptoms, plus one or both of the following:
  - clinical investigations indicating ongoing myocardial ischaemia
  - raised blood levels of markers of cardiac cell damage, such as troponin.[1]

Beta-blockers

- Offer a beta-blocker as soon as the patient is clinically stable and titrate upwards to the maximum tolerated dose. Continue treatment indefinitely.
- For patients with LVSD being offered treatment, a beta-blocker licensed for use in heart failure may be preferred.

Potassium channel activators

- Nicorandil is not recommended to reduce cardiovascular risk.

[1] This recommendation is from 'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome' (NICE technology appraisal guidance 80). It has been incorporated into this guideline in line with NICE procedures for developing clinical guidelines.

Vitamin K antagonists

- High-intensity warfarin (INR >3) should not be considered as an alternative to aspirin in first-line treatment.
- For patients unable to take aspirin or clopidogrel, consider moderate-intensity warfarin (INR 2–3) for up to 4 years and possibly longer.
- For patients unable to take clopidogrel and at low risk of bleeding, consider treatment with aspirin and moderate-intensity warfarin (INR 2–3) combined.
- The combination of warfarin and clopidogrel is not routinely recommended.
- Continue warfarin for patients already being treated for another indication. Consider adding aspirin for patients being treated with moderate-intensity warfarin (INR 2–3) who are at low risk of bleeding.

Calcium channel blockers

- Do not routinely use calcium channel blockers for secondary prevention.
- If beta-blockers are contraindicated or need to be discontinued, consider diltiazem or verapamil for secondary prevention in patients without pulmonary congestion or LVSD.[2]
- For patients who are stable, calcium channel blockers may be used to treat hypertension and/or angina. For patients with heart failure, use amlodipine and avoid verapamil, diltiazem and short-acting dihydropyridine agents in line with NICE clinical guideline 5.

Aldosterone antagonists

- For patients with symptoms and/or signs of heart failure and LVSD, initiate treatment with an aldosterone antagonist licensed for post-MI treatment within 3–14 days of the MI, preferably after ACE inhibitor therapy.
- For patients with clinical heart failure and LVSD already being treated with an aldosterone antagonist for a concomitant condition, continue with the aldosterone antagonist or an alternative, licensed for early post-MI treatment.

Assessment/monitoring

- Monitor renal function and serum potassium before and during treatment. If hyperkalaemia is a problem, halve the dose or stop the treatment.

Statins and other lipid lowering agents

- Statin treatment is recommended for adults with clinical evidence of CVD and should be offered as soon as possible. Refer to NICE technology appraisal guidance 94.[3]
- Discuss the risks and benefits of treatment with the patient, taking into account comorbidities and life expectancy.
- Start therapy with a drug with a low acquisition cost (taking into account required daily dose and product price per dose).
- For patients intolerant of statins, other lipid lowering agents should be considered.
- Reduce or stop the dose of statins if there are issues surrounding the metabolic pathway, food and/or drug interactions and/or concomitant illness.
- Discontinue the statin and seek specialist advice if patients develop peripheral neuropathy that may be attributable to the statin treatment.

Assessment/monitoring

- Measure baseline liver enzymes before initiation.
- Do not routinely exclude patients who have raised liver enzymes from treatment.
- Routine monitoring of creatine kinase in asymptomatic patients is not recommended, but should be measured in patients who develop muscle symptoms.

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[2] At the time of publication (May 2007) diltiazem and verapamil did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

[3] The clinical guideline 'Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease' is in development and is expected to be published in January 2008.

Drug therapy – after a proven MI in the past (more than 12 months ago)

ACE inhibitors

- For patients without heart failure and with preserved LV function, offer an ACE inhibitor and titrate upwards to the maximum tolerated effective dose.
- For patients with LVSD (asymptomatic), offer ACE inhibitor treatment and titrate upwards to the effective clinical dose for patients with heart failure and LVSD.
- For patients with heart failure and LVSD, ACE inhibitor and ARB treatment should be in line with NICE clinical guideline 5.
- Continue indefinitely in patients with preserved LV function or LVSD, whether or not they have symptoms of heart failure.
- For patients with LVSD (asymptomatic) who are intolerant or allergic to an ACE inhibitor, substitute an ARB.

Assessment/monitoring

- Assess LV function in all patients who have had an MI.
- Measure renal function, serum electrolytes and BP before starting an ACE inhibitor or ARB and again within 1 or 2 weeks.
- Monitor patients as the dose is titrated and more frequently if patients are at increased risk of deterioration in renal function.
- Monitor patients with chronic heart failure in line with NICE clinical guideline 5.

Antiplatelet therapy

- Offer aspirin and continue indefinitely.
- Do not offer clopidogrel alone as first-line therapy, but consider it for patients with aspirin hypersensitivity.
- The combination of aspirin and clopidogrel is not recommended for routine use for any longer than 12 months after the acute phase of MI, unless there are other indications to continue dual antiplatelet therapy. The combination is usually recommended for a shorter duration after a STEMI.
- For patients with a history of dyspepsia, consider treatment with a PPI and low-dose aspirin. Refer to NICE clinical guideline 17.
- For patients with a history of aspirin-induced ulcer bleeding whose ulcers have healed and who are *H. pylori* negative, consider a full-dose PPI and low-dose aspirin. Refer to NICE clinical guideline 17.

Beta-blockers

- Offer all patients with LVSD treatment with a beta-blocker whether or not they have symptoms.
- Manage patients with heart failure plus LVSD in line with NICE clinical guideline 5.
- Do not routinely offer treatment with a beta-blocker for patients with preserved LV function who are asymptomatic, unless they are at increased risk of further cardiovascular events, or there are other compelling indications for beta-blocker treatment.

Potassium channel activators

- Nicorandil is not recommended to reduce cardiovascular risk.

Vitamin K antagonists

- High-intensity warfarin (INR >3) should not be considered as an alternative to aspirin in first-line treatment.
- The combination of warfarin and clopidogrel is not routinely recommended.
- Continue warfarin for patients already being treated for another indication.

Calcium channel blockers

- Calcium channel blockers should not routinely be used for secondary prevention.
- For patients who are stable, calcium channel blockers may be used to treat hypertension and/or angina. For patients with heart failure, use amlodipine and avoid verapamil, diltiazem and short-acting dihydropyridine agents in line with NICE clinical guideline 5.

Aldosterone antagonists

- For patients with heart failure due to LVSD, aldosterone antagonist treatment should be in line with NICE clinical guideline 5.

Assessment/monitoring

- Monitor renal function and serum potassium before and during treatment. If hyperkalaemia is a problem, halve the dose or stop the treatment.

Statins and other lipid lowering agents

- Statin treatment is recommended for adults with clinical evidence of CVD and should be offered as soon as possible. Refer to NICE technology appraisal guidance 94.[4]
- Discuss the risks and benefits of treatment with the patient, taking into account comorbidities and life expectancy.
- Start therapy with a drug with a low acquisition cost (taking into account required daily dose and product price per dose).
- For patients intolerant of statins, consider other lipid lowering agents.
- Reduce or stop the dose of statins if there are issues surrounding the metabolic pathway, food and/or drug interactions and/or concomitant illness.
- Discontinue the statin and seek specialist advice if patients develop peripheral neuropathy that may be attributable to the statin treatment.

Assessment/monitoring

- Measure baseline liver enzymes before initiation.
- Do not routinely exclude patients who have raised liver enzymes from treatment.
- Routine monitoring of creatine kinase in asymptomatic patients is not recommended, but should be measured in patients who develop muscle symptoms.

[4] The clinical guideline 'Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease' is in development and is expected to be published in January 2008.

Coronary revascularisation

- Offer all patients a cardiological assessment to consider whether coronary revascularisation is appropriate, taking into account comorbidities.

Patients with hypertension

- Treat hypertension to the target recommended in NICE clinical guideline 34, to the currently recommended target of 140/90 mmHg or lower. For patients with relevant comorbidities, for example diabetes or renal disease, treatment should be to a lower target.

Patients with LVSD

- Consider an implantable cardioverter defibrillator. Refer to NICE technology appraisal guidance 95.

Communication of diagnosis and advice

- After an acute MI, every discharge summary should include a confirmation of the diagnosis of acute MI and results of investigations, future management plans and advice on secondary prevention.
- A copy of the discharge summary should be offered to the patient.

Implementation

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG048).

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

Further information

Ordering information

You can download the following documents from www.nice.org.uk/CG048

- 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 summaries of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone the NHS Response Line on 0870 1555 455 and quote:

- N1251 (quick reference guide)
- N1252 ('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).

- Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guideline 43 (2006).
- Hypertension: management of hypertension in adults in primary care. NICE clinical guideline 34 (2006).
- Depression: management of depression in primary and secondary care. NICE clinical guideline 23 (2007).
- Anxiety: management of anxiety (panic disorder, with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community care. NICE clinical guideline 22 (2007).
- Dyspepsia: management of dyspepsia in adults in primary care. NICE clinical guideline 17 (2004).
- Diagnosis and management of type 1 diabetes in children, young people and adults. NICE clinical guideline 15 (2004).
- Management of chronic heart failure in adults in primary and secondary care. NICE clinical guideline 5 (2003).
- Type 2 diabetes – management of blood pressure and blood lipids (guideline H) (2002).
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006).
- Implantable cardioverter defibrillators for arrhythmias. NICE technology appraisal guidance 95 (2006).
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006).
- Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events. NICE technology appraisal guidance 90 (2005).
- Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome. NICE technology appraisal guidance 80 (2004).
- Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. NICE technology appraisal guidance 73 (2003).
- The use of nicotine replacement therapy (NRT) and bupropion for smoking cessation. NICE technology appraisal guidance 39 (2002).

NICE is developing the following guidance (details available from www.nice.org.uk).

- Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline (publication expected January 2008).
- Type 2 diabetes – management of blood pressure and blood lipids. NICE clinical guideline (updated publication expected February 2008).
- Familial hypercholesterolaemia: identification and management. NICE clinical guideline (publication expected August 2008).

Updating the guideline

The 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/CG048).

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