NICE National Institute for Health and Care Excellence

NICE guideline

Unstable angina and NSTEMI: early management

Clinical guideline

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Contents

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This guideline partially replaces TA47 and TA80.

This guideline is the basis of QS68.

Introduction

This guideline updates and replaces recommendations for the early management of unstable angina and NSTEMI from NICE technology appraisal guidance 47 and 80.

Recommendation 1.3.6 has been replaced by recommendation 1.3.18 in MI – secondary prevention: Secondary prevention in primary and secondary care for patients following a myocardial infarction.

Recommendation 1.5.11 has been updated to take into account people with a learning disability.

See Changes after publication for details.

The term 'acute coronary syndromes' encompasses a range of conditions from unstable angina to ST-segment-elevation myocardial infarction (STEMI), arising from thrombus formation on an atheromatous plaque. This guideline addresses the early management of unstable angina and non-ST-segment-elevation myocardial infarction (NSTEMI) once a firm diagnosis has been made and before discharge from hospital. If untreated, the prognosis is poor and mortality high, particularly in people who have had myocardial damage. Appropriate triage, risk assessment and timely use of acute pharmacological or invasive interventions are critical for the prevention of future adverse cardiovascular events (myocardial infarction, stroke, repeat revascularisation or death). The guideline does not cover the management of STEMI or specific complications of unstable angina and NSTEMI such as cardiac arrest or acute heart failure. Assessment and classification of people presenting with undifferentiated chest pain are covered in 'Chest pain of recent onset' (NICE clinical guideline 95)[1].

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

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Unlicensed or off-label use is indicated by a footnote.

Throughout the guideline, the term 'angiography' refers to invasive angiography.

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Recommendations 1.3.4 to 1.3.8 update and replace recommendations for the early management of unstable angina and NSTEMI from 'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome', NICE technology appraisal guidance 80 (TA 80)

Recommendations 1.3.9 to 1.3.11 update and replace recommendations for the early management of unstable angina and NSTEMI from 'Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndrome', NICE technology appraisal guidance 47 (TA 47).

[1] More information on 'Chest pain of recent onset' (NICE clinical guideline 95) is available.

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Patient-centred care

This guideline offers best practice advice on the care of adults (18 years and older) with a diagnosis of unstable angina or non-ST-segment-elevation myocardial infarction (NSTEMI).

Treatment and care should take into account patients' needs and preferences. Patients with unstable angina or NSTEMI should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

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Key priorities for implementation

- As soon as the diagnosis of unstable angina or NSTEMI is made, and aspirin and antithrombin therapy have been offered, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, Global Registry of Acute Cardiac Events [GRACE]).
- Consider intravenous eptifibatide or tirofiban[2] as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.
- Offer coronary angiography (with follow-on PCI if indicated) within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%) if they have no contraindications to angiography (such as active bleeding or comorbidity). Perform angiography as soon as possible for patients who are clinically unstable or at high ischaemic risk.
- When the role of revascularisation or the revascularisation strategy is unclear, resolve this by discussion involving an interventional cardiologist, cardiac surgeon and other healthcare professionals relevant to the needs of the patient. Discuss the choice of revascularisation strategy with the patient.
- To detect and quantify inducible ischaemia, consider ischaemia testing before discharge for patients whose condition has been managed conservatively and who have not had coronary angiography.
- Before discharge offer patients advice and information about:
    - their diagnosis and arrangements for follow-up (in line with 'MI – secondary prevention', NICE clinical guideline 172)
    - cardiac rehabilitation (in line with 'MI – secondary prevention', NICE clinical guideline 172)
    - management of cardiovascular risk factors and drug therapy for secondary prevention (in line with 'MI – secondary prevention', NICE clinical guideline 172, and 'Lipid modification', NICE clinical guideline 67)
    - lifestyle changes (in line with 'MI – secondary prevention', NICE clinical guideline 172).

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[2] Eptifibatide and tirofiban are licensed for use with aspirin and unfractionated heparin. They do not have UK marketing authorisation for use with clopidogrel. This recommendation is therefore for an off-label use of these drugs. Informed consent should be obtained and documented before they are used in combination with clopidogrel.

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1 Guidance

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

1.1 Provision of information

1.1.1 Offer patients clear information about the risks and benefits of the treatments offered so that they can make informed choices about management strategies. Information should be appropriate to the patient's underlying risk of a future adverse cardiovascular event and any comorbidities.

1.2 Assessment of a patient's risk of future adverse cardiovascular events

1.2.1 As soon as the diagnosis of unstable angina or NSTEMI is made, and aspirin and antithrombin therapy have been offered, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, Global Registry of Acute Cardiac Events [GRACE]).

1.2.2 Include in the formal risk assessment:

- a full clinical history (including age, previous myocardial infarction [MI] and previous percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG])
- a physical examination (including measurement of blood pressure and heart rate)
- resting 12-lead electrocardiography (ECG) (looking particularly for dynamic or unstable patterns that indicate myocardial ischaemia)
- blood tests (such as troponin I or T, creatinine, glucose and haemoglobin).

1.2.3 Record the results of the risk assessment in the patient's care record.

1.2.4 Use risk assessment to guide clinical management, and balance the benefit of a treatment against any risk of related adverse events in the light of this assessment.

1.2.5 Use predicted 6-month mortality to categorise the risk of future adverse cardiovascular events as follows:[3]

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Predicted 6-month mortality	Risk of future adverse cardiovascular events
1.5% or below	Lowest
> 1.5 to 3.0%	Low
> 3.0 to 6.0%	Intermediate
> 6.0 to 9.0%	High
over 9.0%	Highest

1.3 Antiplatelet therapy

Aspirin

1.3.1 Offer aspirin as soon as possible to all patients and continue indefinitely unless contraindicated by bleeding risk or aspirin hypersensitivity.

1.3.2 Offer patients a single loading dose of 300 mg aspirin as soon as possible unless there is clear evidence that they are allergic to it.

1.3.3 For patients with aspirin hypersensitivity, clopidogrel monotherapy should be considered as an alternative treatment. (This recommendation is from 'MI – secondary prevention', NICE clinical guideline 172.)

Clopidogrel[4]

Recommendations in this section update and replace recommendations for the early management of unstable angina and NSTEMI from 'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome', NICE technology appraisal guidance 80 (TA 80).

1.3.4 As soon as the risk of adverse cardiovascular events has been assessed, offer a loading dose of 300 mg clopidogrel in addition to aspirin to patients with a predicted 6-month mortality of more than 1.5% and no contraindications (for example, an excessive bleeding risk)[5].

1.3.5 Offer a 300-mg loading dose of clopidogrel to all patients with no contraindications who may undergo PCI within 24 hours of admission to hospital[5][6].

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1.3.6 Offer clopidogrel as a treatment option for up to 12 months to people who have had an NSTEMI, regardless of treatment[7]. (This recommendation is from MI – secondary prevention, NICE clinical guideline 172.)

1.3.7 Consider discontinuing clopidogrel treatment 5 days before CABG in patients who have a low risk of adverse cardiovascular events.

1.3.8 For patients at intermediate or higher risk of adverse cardiovascular events, discuss the continuation of clopidogrel before CABG with the cardiac surgeon and base the decision on the balance of ischaemic and bleeding risk.

Glycoprotein IIb/IIIa inhibitors

Recommendations in this section update and replace recommendations for the early management of unstable angina and NSTEMI from 'Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndrome', NICE technology appraisal guidance 47 (TA 47).

1.3.9 Consider intravenous eptifibatide or tirofiban[8] as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

1.3.10 Consider abciximab as an adjunct to PCI for patients at intermediate or higher risk of adverse cardiovascular events who are not already receiving a GPI.

1.3.11 Balance the potential reduction in a patient's ischaemic risk with any increased risk of bleeding, when determining whether a GPI should be offered.

1.4 Antithrombin therapy

1.4.1 Offer fondaparinux to patients who do not have a high bleeding risk, unless coronary angiography is planned within 24 hours of admission.

1.4.2 Offer unfractionated heparin as an alternative to fondaparinux to patients who are likely to undergo coronary angiography within 24 hours of admission.

1.4.3 Carefully consider the choice and dose of antithrombin in patients who have a high risk of bleeding associated with any of the following:

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- advancing age
- known bleeding complications
- renal impairment
- low body weight.

1.4.4 Consider unfractionated heparin, with dose adjustment guided by monitoring of clotting function, as an alternative to fondaparinux for patients with significant renal impairment (creatinine above 265 micromoles per litre).

1.4.5 Offer systemic unfractionated heparin (50–100 units/kg) in the cardiac catheter laboratory to patients receiving fondaparinux who are undergoing PCI[9].

1.4.6 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients who:

- are at intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3%), **and**
- are not already receiving a GPI or fondaparinux, **and**
- are scheduled to undergo angiography (with follow-on PCI if indicated) within 24 hours of admission.

1.4.7 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients undergoing PCI who:

- are at intermediate or higher risk of adverse cardiovascular events, **and**
- are not already receiving a GPI or fondaparinux.

1.5 Management strategies

Early invasive versus conservative management

1.5.1 Offer coronary angiography (with follow-on PCI if indicated) within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%) if they have no contraindications to angiography (such as active bleeding or

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comorbidity). Perform angiography as soon as possible for patients who are clinically unstable or at high ischaemic risk.

1.5.2 Offer conservative management without early coronary angiography to patients with a low risk of adverse cardiovascular events (predicted 6-month mortality 3.0% or less).

1.5.3 Offer coronary angiography (with follow-on PCI if indicated) to patients initially assessed to be at low risk of adverse cardiovascular events (predicted 6-month mortality 3.0% or less) if ischaemia is subsequently experienced or is demonstrated by ischaemia testing.

Percutaneous coronary intervention versus coronary artery bypass grafting

1.5.4 When advising patients about the choice of revascularisation strategy (PCI or CABG), take account of coronary angiographic findings, comorbidities, and the benefits and risks of each intervention.

1.5.5 When the role of revascularisation or the revascularisation strategy is unclear, resolve this by discussion involving an interventional cardiologist, cardiac surgeon and other healthcare professionals relevant to the needs of the patient. Discuss the choice of revascularisation strategy with the patient.

Testing for ischaemia

1.5.6 To detect and quantify inducible ischaemia, consider ischaemia testing before discharge for patients whose condition has been managed conservatively and who have not had coronary angiography.

Assessing left ventricular function

1.5.7 Assessment of left ventricular function is recommended in all patients who have had an MI. (This recommendation is from 'MI – secondary prevention', NICE clinical guideline 172.)

1.5.8 Consider assessing left ventricular function in all patients with unstable angina.

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1.5.9 Record measures of left ventricular function in the patient's care record and in correspondence with the primary healthcare team and the patient.

Rehabilitation and discharge planning

1.5.10 Before discharge offer patients advice and information about:

- their diagnosis and arrangements for follow-up (in line with 'MI – secondary prevention', NICE clinical guideline 172)
- cardiac rehabilitation (in line with 'MI – secondary prevention', NICE clinical guideline 172)
- management of cardiovascular risk factors and drug therapy for secondary prevention (in line with 'MI – secondary prevention', NICE clinical guideline 172, and 'Lipid modification', NICE clinical guideline 67)
- lifestyle changes (in line with 'MI – secondary prevention', NICE clinical guideline 172).

1.5.11 Make cardiac rehabilitation equally accessible and relevant to all people 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, people with a learning disability and people with mental and physical health conditions. (This recommendation is from MI – secondary prevention, NICE clinical guideline 172.)

1.5.12 All patients who smoke should be advised to quit and be offered support and advice, and referral to an intensive support service (for example, the NHS Stop Smoking Services) in line with 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health guidance 1). (This recommendation is adapted from 'MI – secondary prevention', NICE clinical guideline 172.)

[3] Categories of risk are derived from the Myocardial Ischaemia National Audit Process (MINAP) database. More details are in the full guideline.

[4] In this guideline, clopidogrel refers to clopidogrel hydrogen sulphate.

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[5] In line with 'Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention' (NICE technology appraisal guidance 182), prasugrel in combination with aspirin is an option for patients undergoing PCI who have diabetes or have had stent thrombosis with clopidogrel treatment.

[6] There is emerging evidence about the use of a 600-mg loading dose of clopidogrel for patients undergoing PCI within 24 hours of admission. Clopidogrel does not have UK marketing authorisation for use at doses above 300 mg. The GDG was not able to formally review all the evidence for a 600-mg loading dose and was therefore not able to recommend this at the time of publication (March 2010).

[7] This recommendation updates and replaces recommendation 1.3 in Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome (NICE technology appraisal guidance 80).

[8] Eptifibatide and tirofiban are licensed for use with aspirin and unfractionated heparin. They do not have UK marketing authorisation for use with clopidogrel. This recommendation is therefore for an off-label use of these drugs. Informed consent should be obtained and documented before they are used in combination with clopidogrel.

[9] Unfractionated heparin is not licensed for use during angiography and PCI. Such use is an off-label use. Informed consent should be obtained and documented before it is used during angiography and PCI.

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2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available (see 'How this guidance was produced').

How this guideline was developed

NICE commissioned the National Clinical Guideline Centre for Acute and Chronic Conditions to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is available.

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3 Implementation

NICE has developed tools to help organisations implement this guidance.

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4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Testing for ischaemia

4.1.1 What is the role of ischaemia testing in people after an acute coronary syndrome and what is the comparative efficacy and cost effectiveness of the different non-invasive tests (for example, stress ECG, echocardiography, radionuclide scanning and magnetic resonance imaging)?

Why this is important

An increasing number of non-invasive tests are now available for the investigation of suspected myocardial ischaemia. These tests need different equipment, different clinical expertise, come at different costs and may differ in their ability to detect and quantify myocardial ischaemia. Their place in the routine investigation of patients admitted with unstable angina and NSTEMI (particularly those who have not undergone angiography), as opposed to their selective use, is not clear. Management of unstable angina and NSTEMI would be enhanced if the relative place of these investigations was better understood and an assessment of their cost effectiveness made.

4.2 Risk assessment

4.2.1 What is the clinical and cost effectiveness of the systematic use of risk scoring systems (in addition to clinical assessment) for ischaemic outcomes and bleeding complications in the management of unstable angina and NSTEMI (at all levels of risk) compared with clinical assessment alone?

Why this is important

Most risk scoring systems currently predict the likelihood of mortality or ischaemic cardiovascular events at various times after a patient's admission to hospital with an acute coronary syndrome. A number of interventions (such as drugs and revascularisation procedures) have been shown to reduce these adverse outcomes. This effect tends to be greatest in patients at highest risk. However, as a broad generalisation patients who are at highest ischaemic risk are also those who

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are at higher risk of bleeding complications associated with the use of multiple antiplatelet and antithrombin agents. There are fewer scoring systems that predict bleeding risk, but we know that bleeding complications are associated with a significantly worse outcome. Using a combination of scoring systems assessing ischaemic and bleeding risk when evaluating data from randomised trials and registries may help to determine where the net clinical benefit (reduction in ischaemic risk minus any increase in bleeding risk) lies.

4.2.2 For patients with unstable angina and NSTEMI (at differing levels of risk), how do clinical outcome data (adverse cardiovascular events and bleeding complications) collected in cardiac registries compare with data derived from randomised clinical trials (RCTs).

Why this is important

Patients recruited to participate in clinical trials are often highly selected; trials tend not to include patients who are very elderly, are at high risk, or have significant comorbidity. On the other hand, good registry data include information on all patients, but are observational and not randomised. Often there is uncertainty about how the outcome data from RCTs can be applied to the much larger unselected population of patients admitted to UK hospitals with unstable angina or NSTEMI. A greater understanding of the differences between RCT and registry populations, and their levels of ischaemic and bleeding risk would help inform future management. Collection of well-validated registry data is essential if conclusions from RCTs are to be applied appropriately to all patients with unstable angina and NSTEMI, not just to patients who are comparable to trial populations.

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5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction' contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guideline Centre for Acute and Chronic Conditions, and is available from our website.

5.2 Information for the public

NICE has produced 'information for the public' explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this information in their own materials about unstable angina and NSTEMI.

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6 Related NICE guidance

Published

- Chest pain of recent onset. NICE clinical guideline 95 (2010).
- Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention. NICE technology appraisal guidance 182 (2009).
- Transmyocardial laser revascularisation for refractory angina pectoris. NICE interventional procedure guidance 301 (2009).
- Percutaneous laser revascularisation for refractory angina pectoris. NICE interventional procedure guidance 302 (2009).
- Lipid modification. NICE clinical guideline 67 (2008).
- Drug-eluting stents for the treatment of coronary artery disease. NICE technology appraisal guidance 152 (2008).
- Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities. NICE public health guidance 10 (2008).
- MI: secondary prevention. NICE clinical guideline 48 (2007). [Replaced by NICE clinical guideline 172]
- Hypertension. NICE clinical guideline 34 (2006). [Replaced by NICE clinical guideline 127]
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006).
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health guidance 1 (2006).
- Off-pump coronary artery bypass (OPCAB). NICE interventional procedure guidance 35 (2004). [Replaced by NICE interventional procedure guidance 377]
- Guidance on the use of coronary artery stents. NICE technology appraisal guidance 71 (2003).
- Stable angina. NICE clinical guideline 126 (2011)

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7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

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Appendix A: The Guideline Development Group and NICE project team

Guideline Development Group

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Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr Robert Walker (Chair)
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Mr Robin Beal
Consultant in Accident and Emergency Medicine, Isle of Wight

Ms Ailsa Donnelly
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Appendix C: The algorithm

There is a care pathway for the management of unstable angina and NSTEMI on pages 33 and 34 of the full guideline.

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Changes after publication

November 2013: Recommendation 1.3.6 has been replaced by recommendation 1.3.18 in MI – secondary prevention: Secondary prevention in primary and secondary care for patients following a myocardial infarction to reflect that TA80 was updated within CG172. Recommendation 1.5.11 has been updated to take into account people with a learning disability. Cross-references to CG48 have been updated to CG172.

August 2013: minor maintenance.

January 2012: minor maintenance.

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About this guideline

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

The guideline was developed by the National Collaborating Centre for Acute and Chronic Conditions. 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.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual.

This guideline updates and replaces recommendations for the early management of unstable angina and NSTEMI from NICE technology appraisal guidance 47 and 80.

We have produced information for the public explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also available.

Changes after publication

November 2013: NICE clinical guideline 48 has been replaced by NICE clinical guideline 172, links amended to go to new guidance.

Your responsibility

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

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