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NICE guidance. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin

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► See Editorial, p 903

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Chest pain is a very common symptom; 20% to 40% of the general population will experience chest pain during their lives,¹ and in the UK, up to 1% of visits to a general practitioner are because of chest pain.² Approximately 700 000 visits (5%) to the emergency department in England and Wales and up to 25% of emergency hospital admissions are because of chest pain.³ There are many causes of chest pain, some of which are benign, while others are potentially life threatening. Importantly, in patients with chest pain caused by an acute coronary syndrome (ACS) or angina, there are effective treatments to improve symptoms and prolong life, emphasising the importance of making timely and accurate diagnoses in patients in whom chest pain may be of cardiac origin. This guideline⁴ addresses the assessment and diagnosis of patients with recent onset chest pain/discomfort that may be of cardiac origin. Unlike many other National Institute for Health and Clinical Excellence (NICE) clinical guidelines it does not make recommendations for the management of the condition once the diagnosis is made. The NICE unstable angina and NSTEMI clinical guideline⁵ was published at the same time as the chest pain guideline, and a NICE clinical guideline for the management of angina is currently being prepared.⁶

The guideline has two separate diagnostic pathways. The first is for patients with acute chest pain who may have an ACS and the second for those with intermittent stable chest pain who may have stable angina. The guideline deals with chest pain of suspected cardiac origin. Thus, for example, the guideline does not apply to patients with pain considered to be caused by recent trauma to the chest. However, many patients presenting with chest pain do not have such clearly apparent alternative explanations and need to have a cardiac cause considered.

The guideline has three main sections. The first addresses what information to provide to patients with chest pain, the second diagnosis in patients with a possible ACS and the third diagnosis in patients with possible stable angina. NICE guidelines also include up to 10 recommendations that the guideline development group agree will have most impact on current clinical practice (box 1).

PROVIDING INFORMATION FOR PATIENTS WITH CHEST PAIN

As with other NICE guidelines, the importance of offering a clear explanation of the possible causes and the uncertainties, while correcting any misunderstandings, is emphasised. Information should also be provided about further diagnostic testing so

patients can jointly agree decisions about their care with the clinician. The purpose and benefits of any test and any limitations of their diagnostic accuracy, what the test involves and any associated risks should be explained in everyday language.

PATIENTS PRESENTING WITH ACUTE CHEST PAIN Pre-hospital care

The adverse consequences of not making an early and accurate diagnosis of an ACS, in which early treatment saves lives, are substantial. The guideline has therefore generally adopted a cautious approach, with a cardiac cause for pain only being excluded when there is convincing evidence the pain is not cardiac. Clinical symptoms help inform if a patient may have an ACS, but the diagnostic performance of the history alone is not sufficient to rule out the diagnosis without further testing, unless an alternative diagnosis can be confidently made. Likewise, although there may be signs of complications of ACS (eg, pulmonary oedema) or signs to suggest an alternative diagnosis (eg, pneumothorax or pneumonia) there are no specific examination findings to confirm a diagnosis of ACS.

A resting 12-lead ECG is a key initial investigation in any patient with suspected ACS, and having determined that an ACS is a possible diagnosis in a patient with acute chest pain the guideline emphasises that this should be recorded as soon as possible, but not at the expense of delaying transfer to hospital. An abnormal ECG may inform further immediate management, such as when there is regional ST-segment elevation or presumed new left bundle branch block (LBBB) consistent with an acute ST-elevation myocardial infarction (STEMI). Increasingly, patients with acute STEMI are managed with primary percutaneous coronary intervention in heart attack centres, and the ECG informs not only the nature of immediate management, but also where this will take place.

The guideline addresses the issue of which patients should have emergency referral to hospital and which need same-day hospital assessment, but can be referred urgently. An immediate resting ECG may be helpful in a patient who is completely pain-free but who has had chest pain within the last 12 hours: patients with a normal ECG may be referred to hospital urgently (rather than as an emergency) providing there are no complications warranting emergency transfer. In practical terms, GPs having access to an immediate ECG recording at their surgery will facilitate more efficient use of ambulance services: patients with a normal resting ECG can be referred

Box 1 Key priorities for implementation**Presentation with acute chest pain**

- Take a resting 12-lead ECG as soon as possible. When people are referred, send the results to hospital before they arrive if possible. Recording and sending the ECG should not delay transfer to hospital. (1.2.2.1)
- Do not exclude an acute coronary syndrome (ACS) when people have a normal resting 12-lead ECG. (1.2.2.5)
- Do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
 - people with oxygen saturation (SpO₂) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO₂ of 94–98%
 - people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO₂ of 88–92% until blood gas analysis is available. (1.2.3.3)
- Do not assess symptoms of an ACS differently in ethnic groups. There are no major differences in symptoms of an ACS among different ethnic groups. (1.2.1.6)

Presentation with stable chest pain

- Diagnose stable angina based on one of the following:
 - clinical assessment alone or
 - clinical assessment plus diagnostic testing (that is, anatomical testing for obstructive coronary artery disease (CAD) and/or functional testing for myocardial ischaemia). (1.3.1.1)
- If people have features of typical angina based on clinical assessment and their estimated likelihood of CAD is greater than 90% (see table 1), further diagnostic investigation is unnecessary. Manage as angina. (1.3.3.5)

Table 1 Percentage of people estimated to have coronary artery disease (CAD) according to typicality of symptoms, age, sex and risk factors

Age (years)	Non-anginal chest pain				Atypical angina				Typical angina			
	Men		Women		Men		Women		Men		Women	
	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
35	3	35	1	19	8	59	2	39	30	88	10	78
45	9	47	2	22	21	70	5	43	51	92	20	79
55	23	59	4	25	45	79	10	47	80	95	38	82
65	49	69	9	29	71	86	20	51	93	97	56	84

For men older than 70 with atypical or typical symptoms, assume an estimate >90%.

For women older than 70, assume an estimate of 61–90% *except* women at high risk *and* with typical symptoms where a risk of > 90% should be assumed.

Values are percentage of people at each mid-decade age with significant CAD.¹⁰

High = high risk = diabetes, smoking and hyperlipidaemia (total cholesterol > 6.47 mmol/l). Low = low risk = none of these three.

The shaded area represents people with symptoms of non-anginal chest pain, who would not be investigated for stable angina routinely.

Note: These results are likely to overestimate CAD in primary care populations.

If there are resting ECG ST-T changes or Q waves, the likelihood of CAD is higher in each cell of the table.

- Unless clinical suspicion is raised based on other aspects of the history and risk factors, exclude a diagnosis of stable angina if the pain is non-anginal (see recommendation 1.3.3.1). Other features that make a diagnosis of stable angina unlikely are when the chest pain is:
 - continuous or very prolonged and/or
 - unrelated to activity and/or
 - brought on by breathing in and/or
 - associated with symptoms such as dizziness, palpitations, tingling or difficulty swallowing.

Consider causes of chest pain other than angina (such as gastrointestinal or musculoskeletal pain). (1.3.3.6)

- In people without confirmed CAD, in whom stable angina cannot be diagnosed or excluded based on clinical assessment alone, estimate the likelihood of CAD (see table 1). Take the clinical assessment and the resting 12-lead ECG into account when making the estimate.

Arrange further diagnostic testing as follows:

- If the estimated likelihood of CAD is 61–90%, offer invasive coronary angiography as the first-line diagnostic investigation if appropriate (see recommendations 1.3.4.4 and 1.3.4.5).
- If the estimated likelihood of CAD is 30–60%, offer functional imaging as the first-line diagnostic investigation (see recommendation 1.3.4.6).
- If the estimated likelihood of CAD is 10–29%, offer CT calcium scoring as the first-line diagnostic investigation (see recommendation 1.3.4.7). (1.3.3.16)

- Do not use exercise ECG to diagnose or exclude stable angina for people without known CAD. (1.3.6.5)

The numbers in parentheses refer to those in the NICE clinical guideline; Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin.

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urgently, reserving emergency calls for those who (i) still have chest pain or (ii) are pain-free but who have had chest pain was within the last 12 hours and have an abnormal resting ECG, or (iii) have suspected complications such as acute pulmonary oedema.

Patients may also present who are now pain-free having had chest pain more than 12 hours ago but within 72 hours. In such cases, same-day urgent (rather than emergency) hospital assessment is recommended, unless there are reasons for greater urgency. If the last episode of pain was more than 72 hours earlier, the guideline recommends confirming the diagnosis with a 12-lead ECG and blood troponin level and using clinical judgment to determine the need for hospital referral and how urgently this is required. In many cases this will be done in hospital, but if the tests are done in primary care, GPs should generally have an early discussion with their local cardiologist about further management if a recent ACS is confirmed. In all patients with recent suspected ACS, a further episode of chest pain should prompt an emergency referral and patients should be provided with appropriate information about this.

Other ECG abnormalities, apart from ST elevation, in patients with suspected ACS may also prompt early specific management and the guideline recommends following the NICE unstable angina and NSTEMI guideline if the resting 12-lead ECG shows regional ST-segment depression or deep T wave inversion suggestive of a NSTEMI or unstable angina, pending a firm diagnosis. Abnormalities such as Q waves and T wave changes (even in the absence of ST-segment changes) increase the suspicion of an ACS; following the NICE unstable angina and NSTEMI guideline should also be considered in these instances. However, the chest pain guideline also emphasises that a normal resting 12-lead ECG does not exclude an ACS and further hospital assessment is still required. In some cases serial resting 12-lead ECGs, reviewing previous ECGs and recording additional ECG leads may be informative, and while automated ECG interpretation may be helpful, resting 12-lead ECGs should always be reviewed by somebody qualified to interpret them.

Immediate management of suspected ACS should start as soon as it is suspected, but should not delay transfer to hospital. The guideline recommends ensuring adequate pain relief. This may be achieved with glyceryl trinitrate (sublingual or buccal), and/or an intravenous opioid where appropriate. All patients irrespective of whether they are already taking aspirin, should receive a loading dose of aspirin 300 mg unless there are clear reasons not to do so (eg, allergy). If this is given before arrival at hospital, a written record should be sent with the patient. However, other antiplatelet agents are recommended only in hospital following other appropriate guidance, including the NICE unstable and NSTEMI guideline or local protocols for STEMI.

A major change for many healthcare providers is the recommendation in the guideline not to offer oxygen to all patients, but to check oxygen saturation using pulse oximetry and to only offer supplemental oxygen if there is hypoxia, with a lower target recommended in those suspected of being at risk of hypercapnic respiratory failure.⁷ This is consistent with other recent oxygen therapy guidance⁸ for the use of supplemental oxygen in emergency situations, which has already been adopted by the UK ambulance service. There is still an appropriate emphasis on the correction of hypoxia whenever it is detected. ACS is an unstable clinical condition and the guideline emphasises the importance of continued assessment with ongoing monitoring of clinical and haemodynamic status, and repeated ECG recordings, using clinical judgment to decide how frequently these are needed. For example, recurrent chest pain should prompt a repeat assessment and ECG.

In-hospital care

Once patients arrive in hospital a detailed clinical history and physical examination is required, with a repeat resting 12-lead ECG, unless a STEMI has already been confirmed on the ECG. Troponin is the preferred biomarker for making a diagnosis of acute myocardial infarction (MI) and blood samples should be taken on arrival in hospital and again 10–12 hours after the onset of symptoms. Measuring troponin on arrival at hospital in *all* patients with a recent episode of cardiac-sounding chest pain will also represent a change to current practice for many hospital departments who perform a single, delayed troponin assay as the definitive component of a 'rule-out' pathway in patients thought to be at low risk upon initial presentation. The criteria for universal definition of MI should be used to make a diagnosis of acute MI—that is, detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th centile of a reference population together with evidence of myocardial ischaemia.⁹ If the diagnostic criteria are met, appropriate intervention should be started. The guideline emphasises the importance of not interpreting troponin results in isolation, but doing so in the context of the clinical history and ECG changes. Troponin release may occur in other conditions, including pulmonary embolus, myocarditis and aortic dissection, and while an early chest x-ray or CT scan is not recommended to make a diagnosis of ACS, these investigations may be indicated to rule out other conditions such as pneumothorax, pulmonary embolism or aortic dissection.

A particular strength of the guideline is that simply excluding an acute MI is not sufficient. Patients who do not have raised troponin levels and acute ECG changes should be reassessed. Other causes should be considered and managed appropriately, and those in whom the pain may have been due to myocardial ischaemia, but without an ACS, require further investigation following the recommendations for patients with stable chest pain in the relevant part of this guidance. Guidance for the further investigation of patients who have had an acute MI excluded should be of benefit to emergency healthcare providers for whom, until now, there has been little specific guidance on who should have further testing and which investigations are appropriate. Clinical judgment should be used to determine the timeliness with which these should be carried out.

Patients with cardiovascular risk factors should have these managed appropriately.

PATIENTS PRESENTING WITH STABLE CHEST PAIN

In patients with stable chest pain the guideline makes recommendations for diagnosing angina not for screening for CAD. This is an important distinction. The question being addressed is whether the pain of which the patient complains is due to angina, and the guideline makes detailed recommendations for diagnosing angina due to CAD. It recognises that there are other causes of angina, such as severe aortic stenosis and hypertrophic cardiomyopathy, and emphasises that these should be considered although does not make detailed recommendations for their investigative pathways.

In some cases, the diagnostic probability that the pain is or is not angina is such that additional diagnostic testing is of little incremental value and in these patients the guideline recommends that the clinical history alone is sufficient to make or exclude the diagnosis. The cut-off of diagnostic probability chosen is driven in part by the prognostic consequences of an incorrect diagnosis: for patients with suspected stable angina a >90% likelihood of CAD for diagnostic rule-in, and a <10% likelihood of CAD for diagnostic rule-out, has been chosen. The

Table 2 Sensitivity and specificity of non-invasive testing for coronary artery disease

	Sensitivity	Specificity	Meta-analysis
Exercise testing	68%	77%	Gianrossi <i>et al</i> , 1989 ¹²
Myocardial perfusion scintigraphy with SPECT	88%	73%	Heijenbrok-Kal <i>et al</i> , 2007 ¹³
Dobutamine stress echocardiography	81%	84%	Heijenbrok-Kal <i>et al</i> , 2007 ¹³
First pass contrast enhanced magnetic resonance (MR) perfusion	91%	81%	Nandalur <i>et al</i> , 2007 ¹⁴
MR imaging for stress induced wall motion abnormalities	83%	86%	Nandalur <i>et al</i> , 2007 ¹⁴
64-slice CT coronary angiography	99%	89%	Mowatt <i>et al</i> , 2008 ¹⁵

guideline accepts that in setting these arbitrary thresholds, occasional false positive and false negative diagnoses are an inevitable consequence of the recommendations, but aims to guide and support clinical judgment. When there is diagnostic uncertainty in patients with typical or atypical angina pain (diagnostic probability 10–90%), further diagnostic testing is needed. However, the guideline emphasises that in patients who clearly have non-anginal pain, angina is excluded by clinical assessment and further diagnostic testing is not indicated.

The guideline has adopted the Diamond and Forrester criteria to stratify patients with chest pain into those with typical angina, atypical angina and non-anginal pain, with a further recommendation emphasising features that make a diagnosis of angina unlikely. There is further stratification with not only typicality of symptoms, age and gender, but also risk factors (smoking, diabetes and hyperlipidaemia) and the presence ECG changes, being incorporated to estimate the likelihood of CAD.¹⁰ These estimates are presented in a table (box 1, table 1) and are incorporated into the recommendations for which further diagnostic tests to use.

The guideline recommends two types of testing: (i) anatomical testing which diagnoses coronary artery luminal narrowing and/or (ii) non-invasive functional testing which diagnoses myocardial ischaemia. Clinical and cost-effectiveness data have informed which testing strategy is recommended dependent on the estimated likelihood of CAD from clinical assessment. The conventional measures of efficacy of a particular test are sensitivity and specificity, which have usually been set against a 'gold standard' of angiographically demonstrated CAD. This posed some problems in that the degree of luminal obstruction required to diagnose CAD is variably defined between studies, that CAD alone may not be sufficient to diagnose angina as the cause of the chest pain, and that the need for CAD to make the diagnosis may bias its value in the diagnostic work up and

overestimate its diagnostic value in everyday practice. Notwithstanding this, the guideline has used published evidence for clinical and cost-effectiveness from which to generate the recommendations. In a minority of patients, both types of test may be needed, although there is a paucity of clinical data on the incremental value of diagnostic tests. It is also important to note that prognostic assessment is outside the scope of the guideline—for example, patients in whom a diagnosis of angina is made from clinical assessment alone (who do not need further diagnostic testing), may nevertheless need tests to guide prognosis. Prognostic testing is being addressed in the NICE angina guideline⁶ currently being developed.

Following clinical assessment, the guideline recommends invasive coronary angiography as the most cost-effective first test¹¹ if the likelihood of CAD is 61–90%, providing coronary revascularisation is being considered and the test is clinically appropriate and acceptable to the patient. Non-invasive functional imaging, with either myocardial perfusion scintigraphy with SPECT, stress echocardiography, first pass contrast enhanced magnetic resonance (MR) perfusion or MR imaging for stress induced wall motion abnormalities, is recommended as the most cost-effective first test if the likelihood of CAD is 30–60%. The choice of non-invasive functional imaging test will be determined by local availability and expertise, relevant contraindications and patient preferences. When the likelihood of CAD is 10–29% CT scanning is recommended, explicitly with 64-slice or above. Many patients with a low likelihood of CAD will not need further testing as the chest pain from the initial clinical assessment will be clearly non-anginal. CT scanning is only recommended in those with suspected cardiac chest pain and a low likelihood of CAD when they have atypical or typical angina symptoms. CT scanning has a higher sensitivity for the diagnosis of CAD (table 2) than exercise testing and non-invasive functional imaging (which is often used in current clinical practice) and is cost-effective,^{15 16} and is recommended as the preferred test in this group in whom CAD is generally being ruled out. Radiation exposure with contemporary scanners is low¹⁷ (*see page 922*) but to minimise it further, a calcium score should be undertaken initially, with no further testing if this is zero on the grounds that significant CAD has been ruled out with a high degree of accuracy; sensitivity up to 99%.¹⁸ If the calcium score is 1–400 the recommendation is to proceed to CT coronary angiography. However, if the calcium score is >400, proceeding straight to invasive coronary angiography is proposed because CT coronary angiography is unlikely to be informative in the presence of such a high calcium score. Table 3 summarises the diagnostic strategy in patients with suspected

Table 3 Diagnostic strategy in patients with suspected cardiac chest pain. Indicative analysis of patients with previously undiagnosed chest pain attending rapid access chest pain clinics, with data for Newcastle (Dr P C Adams, personal communication,) and a multicentre study (Skehri *et al*¹⁹, and Professor A Timmis, personal communication) are presented

Likelihood of CAD	Proportion of patients within likelihood categories		Investigative strategy
	Newcastle (n = 4522)	Multicentre study (n = 8762)	
<10% and or non-anginal cp	29.3%	28.9%	Trust your clinical judgment No further testing for CAD
10-29%	11%	16.9%	Rule-out test needed CT calcium ± angiography
30-60%	16.8%	18.0%	Uncertainty Non-invasive functional imaging
61-90%	15.4%	15.3%	Rule-in test needed Invasive coronary angiography
>90% with typical angina	9.1%	6.2%	Trust your clinical judgment No further diagnostic testing
Aged >70	20.2%	13.5%	

In allocating patients to groups based on pretest likelihood of disease either current smoking or diabetes (or both) defined high risk without consideration of either hypercholesterolaemia or hypertension. Thus, "high risk" is almost certainly underestimated within these data ensuring that the data presented are skewed towards the lower likelihood estimates.

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cardiac chest pain and no prior history of CAD, and includes indicative estimates of the proportion of patients in each likelihood category (P C Adams, personal communication), (A Timmis, personal communication).¹⁹

Exercise testing is not recommended in the investigative pathway for patients with no prior history of established CAD representing a significant change to current practice. This is based on the evidence of poorer diagnostic accuracy of exercise testing compared to the other tests (table 2), supported by the cost-effectiveness within the accepted threshold of other diagnostic strategies in those being investigated.¹⁶ When the likelihood of CAD is 30–50%, a model developed specifically for the guideline indicated that first-line functional testing, rather than first line anatomical testing with invasive coronary angiography, was the least cost testing strategy.¹⁶ The guideline group were concerned about the proportion of patients with a likelihood of 50–60% who may have intermediate lesions of uncertain functional significance on coronary angiography and functional imaging looking for evidence of myocardial ischaemia as the substrate for causing angina, is recommended when the likelihood of CAD is 30–60%.

Non-invasive functional imaging is recommended if invasive coronary angiography is the first-line test, but is not acceptable to the patient or is not clinically appropriate, or if CT or invasive coronary angiography shows anatomical disease of uncertain functional significance. Similarly, invasive coronary angiography is recommended as a second-line test if the results of functional imaging tests are inconclusive.

In patients with established CAD, but in whom after clinical assessment it is uncertain if the chest pain is caused by myocardial ischaemia, non-invasive functional testing is recommended. This may be functional imaging, although in these patients exercise testing may also be used.

The guideline has recognised the importance of taking into account exposure to radiation during diagnostic testing, which is particularly relevant for isotope perfusion imaging and angiographic procedures.²⁰ It therefore emphasises that most patients with non-anginal chest pain after clinical assessment require no further diagnostic testing for angina unless there is real clinical concern that the pain could still be ischaemic.

The guideline includes recommendations for managing patients until a firm diagnosis is reached. If chest pain is likely to be angina, aspirin is recommended and if symptoms are typical of angina, guidelines for managing stable angina should be followed.

CONCLUSIONS

This NICE guideline summarises how a diagnosis of ACS or stable angina is reached in patients presenting with chest pain which is suspected to be of cardiac origin. The clinical history alone is not sufficient to make or exclude a diagnosis in suspected ACS, and the guideline emphasises the importance of the resting 12-lead ECG and measurement of blood troponins. In patients with suspected stable angina, it recommends substantial changes to diagnostic testing compared to current practice. A careful history and initial clinical assessment will avoid unnecessary or inappropriate testing and, in those requiring diagnostic testing, invasive or CT coronary angiography, or functional imaging, is recommended dependent on the likelihood of CAD. Exercise testing is not used for diagnostic purposes in those with no history of established CAD. Many of these patients will be seen in rapid access chest pain clinics and

these clinics will need to have in place procedures to estimate the likelihood of CAD before arranging further diagnostic testing. Clinicians should review their current pathways and, in particular, review their approach and access to diagnostic testing for patients with stable chest pain, and establish systems to monitor implementation of the guideline.

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