

## Surveillance proposal consultation document

### 2019 surveillance of chest pain of recent onset: assessment and diagnosis (NICE CG95)

#### Surveillance proposal

We propose to not update the guideline on [chest pain of recent onset: assessment and diagnosis](#).

#### Reasons for the proposal to not update the guideline

Topic experts suggested key areas to focus on in this surveillance review, including the use of coronary computed tomography angiography-derived fractional flow reserve (CT-FFR) and high-sensitivity troponins. Focused searches for new evidence were undertaken in these areas as part of this surveillance. The new evidence that was identified was not considered to impact on the recommendations in this guideline.

We identified [ongoing research](#) on high-sensitivity troponins, the GRACE risk score, delay in help-seeking behaviour for acute coronary syndrome (ACS), coronary computed tomography angiography (CCTA) in suspected or confirmed ACS, and CT-FFR. The publication status of these studies and any potential impact on guideline recommendations upon publication will be monitored.

Topic experts in this surveillance review highlighted issues with the implementation of some recommendations from the 2016 update of the guideline on the use of CCTA in stable chest pain. The availability of suitable scanners and professionals were reported to pose difficulties with implementation of the recommendations. These issues were explored in this surveillance review (as detailed below in [implementation of the guideline](#)). No evidence was identified to suggest that CCTA should not be used as a diagnostic tool in stable chest pain and so we considered there to be no potential impact on recommendations in this area. However, we will ensure that the information on implementation issues gathered in this surveillance review is disseminated through appropriate channels within NICE.

We also considered external correspondence received, which requested the inclusion of further guidance on diagnosis of aortic dissection in this guideline. In order to inform our consideration of this point, we consulted with the topic experts already engaged with this surveillance and additional experts in emergency medicine. While the expert views we received on whether additional guidance should be included on diagnosis of aortic dissection

were mixed, more experts overall considered that this would not be appropriate within this guideline. This issue is described in more detail below in [other sources of information](#).

For further details and a summary of all evidence identified in surveillance, see [appendix A](#) below.

## Overview of 2019 surveillance methods

NICE's surveillance team checked whether recommendations in [chest pain of recent onset: assessment and diagnosis](#) (NICE guideline CG95) remain up to date.

The surveillance process consisted of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews.
- Consideration of evidence from previous surveillance.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the proposal with stakeholders (this document).

For further details about the process and the possible update decisions that are available, see [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual.

## Evidence considered in surveillance

### Search and selection strategy

We searched for new evidence related to specific parts of the guideline. These areas were suggested by topic experts as the key areas to focus on for this surveillance review.

Focused searches included:

#### **The diagnostic accuracy of high-sensitivity troponins in acute chest pain of suspected cardiac origin**

Studies were eligible if they determined the diagnostic accuracy of high-sensitivity cardiac troponins in the diagnosis of non-ST-segment elevation myocardial infarction

(NSTEMI)/unstable angina in adults with acute chest pain/discomfort of suspected cardiac origin.

Cross-sectional studies and cohort studies were eligible. Studies with unclear reference standard details were excluded.

We found 7 studies in a search for studies published between 10 May 2016 and 24 April 2019.

### **The clinical effectiveness of high-sensitivity troponins in people with acute chest pain of suspected cardiac origin**

Studies were eligible if they assessed the clinical effectiveness of high-sensitivity troponins in adults with acute chest pain of suspected cardiac origin (compared with standard cardiac troponins, any other high-sensitivity troponin assay, or no test) to identify/rapidly rule out NSTEMI/unstable angina and to improve patient outcomes.

Randomised controlled trials (RCTs) were eligible.

We found 4 studies in a search for studies published between 10 May 2016 and 24 April 2019.

### **The diagnostic accuracy of computed tomography angiography with fractional flow reserve in stable or acute chest pain of suspected cardiac origin.**

Studies were eligible if they determined the diagnostic accuracy of coronary computed tomography angiography with fractional flow reserve (CT-FFR) in adults with stable or acute chest pain of suspected cardiac origin. Cross-sectional studies and cohort studies were eligible. Studies with unclear reference standard details were excluded. Only studies reporting per-patient analyses were included (in line with the guideline).

We found 4 studies in a search for studies published between 21 May 2015 and 18 April 2019.

(NB: The difference in the start dates for the above searches reflects the difference in the start dates for the update searches for the acute chest pain and stable chest pain sections of the guideline).

We also included:

- 2 relevant studies from a total of 7 identified by topic experts
- 10 studies identified in previous surveillance in 2014
- 7 studies identified as ongoing at previous surveillance in 2014 that have subsequently published

From all sources, we considered 34 studies to be relevant to the guideline.

See appendix A below for details of all evidence considered, and references.

## Ongoing research

We checked for relevant ongoing research; of the ongoing studies identified, 6 studies were assessed as having the potential to change recommendations. Therefore, we plan to check the publication status regularly and evaluate the impact of the results on current recommendations as quickly as possible. These studies are:

- The LoDED study – safe & rapid chest pain management ([ISRCTN86184521](#))
- UK GRACE Risk Score Intervention Study ([ISRCTN29731761](#))
- Clinical and demographic characteristics associated with delay in help-seeking behaviour in patients with Acute Coronary Syndrome ([HS&DR 13/10/40](#))
- The RAPID-CTCA trial (Rapid Assessment of Potential Ischaemic Heart Disease with CTCA) The role of early CT Coronary Angiography in the evaluation, intervention and outcome of patients presenting to the Emergency Department with suspected or confirmed Acute Coronary Syndrome ([HTA 13/04/108](#))
- Fractional Flow Reserve Derived From Computed Tomography Coronary Angiography in the Assessment and Management of Stable Chest Pain (FORECAST) study ([NCT03187639](#))
- Evaluating Fractional Flow Reserve computed from Cardiac CT images ([ISRCTN11449939](#))

## Intelligence gathered during surveillance

### Views of topic experts

We considered the views of topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to the guideline.

We sent questionnaires to 12 topic experts and received 6 responses. Responding topic experts included consultant nurses, a general practitioner, and consultants in cardiology and cardiothoracic radiology.

The majority of topic experts did not think the guideline needed to be updated.

The topic expert feedback was used to inform the selection of the areas for focused searches.

Key points highlighted in topic expert feedback included:

- Issues relating to implementation of recommendations on the use of coronary computed tomography angiography (CCTA), specifically regarding availability of suitable scanners and professionals. This feedback was included, alongside other information identified on implementation, in the summary of evidence in this

surveillance review. These issues will be fed back to NICE's implementation team and will also be relayed by NICE internal processes to other key teams as appropriate.

- Coronary computed tomography angiography-derived fractional flow reserve (CT-FFR) should be considered as a diagnostic approach. A focused search was performed in this surveillance review to identify any new relevant evidence in this area.
- Uncertainty around the impact of high-sensitivity troponin assay use on patient outcomes. A focused search was performed in this surveillance review to identify any new relevant evidence in this area.
- Need for further guidance on management of incidental findings from computed tomography (CT) scanning (e.g. lung lesions), which can be associated with anxiety in patients, and increased costs and resource use. No evidence was identified on this topic in this surveillance review.
- Need for the guideline to reinforce the importance of reducing lifelong radiation dose from scanning (no further details provided). No evidence was identified on this topic in this surveillance review.
- Need for further guidance on avoidance of over-investigation in patients with frailty or many comorbidities. No evidence was identified on this topic in this surveillance review.
- European Society of Cardiology (ESC) guidelines i) still use pre-test probability in assessment of stable chest pain, and ii) do not recommend any specific test to diagnose chest pain (no further details provided). No evidence was identified on this topic in this surveillance review.

## Implementation of the guideline

Topic expert feedback in this surveillance review emphasised difficulties in implementation of the recommendations from the 2016 guideline update on the use of CCTA in stable chest pain.

The resource impact report produced in development of this guideline noted that the availability of suitable scanners and trained professionals may affect speed of implementation and that this resource impact should be considered locally.

A [statement from the British Society of Cardiovascular Imaging](#), which provided details on challenges in provision of CCTA, was identified in this surveillance review. Hospital Episode Statistics data for 2017/18 were also analysed to explore the delivery of CCTA for people with chest pain in hospital trusts in England (copyright © 2019, the Health and Social Care Information Centre. Re-used with the permission of the Health and Social Care Information Centre. All rights reserved). Both sources of information confirmed the geographical variation in delivery of CCTA. There is no evidence from this surveillance to suggest that CCTA should no longer be recommended as a diagnostic tool.

An adoption support resource for HeartFlow FFRCT for estimating fractional flow reserve from CCTA (NICE MTG32) has been described in the summary of evidence for this surveillance. The adoption of HeartFlow analysis for estimation of fractional flow reserve from CCTA is being supported as part of the [Accelerated Access Collaborative](#).

The use of high-sensitivity troponin tests for early rule out of myocardial infarction, which is also within the scope of this guideline, is another technology being supported by the Accelerated Access Collaborative.

## Other sources of information

We considered all other correspondence received since the guideline was published.

External correspondence was received requesting that additional guidance on diagnosis of aortic dissection be considered as part of any potential update of this guideline. Topic experts were consulted on this issue, including topic experts engaged with this surveillance review and additional experts in emergency medicine.

Nine responses were received. Of these, 3 agreed with further inclusion of aortic dissection in this guideline, 5 considered that this was not appropriate for this guideline, and 1 response was unclear.

The topic experts who considered that additional guidance on diagnosis of aortic dissection should be included in the guideline commented on the potential lethality of the condition, the need for guidance on diagnosis and immediate treatment (including follow-up of inconclusive rises in high-sensitivity troponins, and medical management of type B dissection), variation in investigation pathways and imaging availability between settings, and value of addressing clinical questions, such as the role of bedside transthoracic echocardiography for non-invasive screening, relevance of bilateral blood pressures in aortic dissection prediction, and diagnostic relevance of chest X-ray.

The topic experts who did not consider that additional guidance on diagnosis of aortic dissection should be included in this guideline noted that there was sufficient content on chest pain of suspected cardiac origin for a guideline on this area alone, that aortic dissection is a very rare differential diagnosis, and that it has a different pathology, with differences in clinical urgency and presentation, and has a different diagnostic pathway to chest pain of suspected cardiac origin once aortic syndrome was suspected. It was also commented that there are several existing non-NICE guidelines and educational resources for acute aortic syndrome, and that, if further guidance on this condition was added to this guideline, then other potential causes of chest pain may also need to be considered for inclusion.

Therefore, while views received from topic experts were mixed, the majority view was that inclusion of further guidance on aortic dissection would not be appropriate within this guideline. Furthermore, we note that several existing recommendations in this guideline specifically refer to aortic dissection (e.g. as an alternative, non-cardiac potential cause of chest pain). These specific recommendations are described more detail in [Appendix A](#).

Therefore, we do not consider there to be potential impact on recommendations in the guideline.

One topic expert in this surveillance review raised an issue with the current title of the guideline not being specific enough in terms of the population covered, i.e. chest pain suspected to be cardiac in origin. The topic expert noted that aortic dissection is an important cause of acute chest pain. It was commented that the title of the guideline should better reflect the intended content. We considered the most suitable approach to address this point, including the revision of the title to make it more specific and/or inclusion of additional explanatory text on the guidance overview page. We plan to amend the title of the guideline to reflect the content more clearly. A potential revision of the guideline title is: 'Recent-onset chest pain of suspected cardiac origin: assessment and diagnosis.'

## Views of stakeholders

Stakeholders are consulted on all surveillance reviews except if the whole guideline will be updated and replaced. Because this surveillance proposal is to not update the guideline, we are consulting with stakeholders.

See [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual for more details on our consultation processes.

## Equalities

No equalities issues were identified during the surveillance process.

## Editorial amendments

We received topic expert feedback in this surveillance review that the current title of the guideline is not specific enough in terms of the population covered, i.e. chest pain suspected to be cardiac in origin. We considered the most suitable approach to address this point, including the revision of the title to make it more specific and/or inclusion of additional explanatory text on the guidance overview page.

We plan to amend the title of the guideline to reflect the content more clearly. A potential revision of the guideline title is: 'Recent-onset chest pain of suspected cardiac origin: assessment and diagnosis.'

## Overall surveillance proposal

After considering all evidence and other intelligence and the impact on current recommendations, we propose that no update is necessary.

# Appendix A: Summary of evidence from surveillance

## 2019 surveillance of chest pain of recent onset: assessment and diagnosis (2010) NICE guideline CG95

### Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review was considered alongside the evidence to reach a view on the need to update each section of the guideline.

### 1.1 Providing information for people with chest pain

#### Recommendations in this section of the guideline

- 1.1.1.1 Discuss any concerns people (and where appropriate their family or carer/advocate) may have, including anxiety when the cause of the chest pain is unknown. Correct any misinformation. [2010].
- 1.1.1.2 Offer people a clear explanation of the possible causes of their symptoms and the uncertainties. [2010]
- 1.1.1.3 Clearly explain the options to people at every stage of investigation. Make joint decisions with them and take account of their preferences:
  - Encourage people to ask questions
  - Provide repeated opportunities for discussion
  - Explain test results and the need for any further investigations. [2010]
- 1.1.1.4 Provide information about any proposed investigations using everyday, jargon-free language. Include:
  - their purpose, benefits and any limitations of their diagnostic accuracy
  - duration
  - level of discomfort and invasiveness
  - risk of adverse events. [2010]
- 1.1.1.5 Offer information about the risks of diagnostic testing, including any radiation exposure. [2010]
- 1.1.1.6 Address any physical or learning difficulties, sight or hearing problems and difficulties with speaking or reading English, which may affect people's understanding of the information offered. [2010]
- 1.1.1.7 Offer information after diagnosis as recommended in the relevant disease management guidelines[\*]. [2010]



- 1.1.1.8 Explain if the chest pain is non-cardiac and refer people for further investigation if appropriate. [2010]
- 1.1.1.9 Provide individual advice to people about seeking medical help if they have further chest pain. [2010]

\* For example, the NICE guidelines on unstable angina and NSTEMI: early management (CG94), stable angina: management (CG126), generalised anxiety disorder and panic disorder in adults (CG113) and gastro-oesophageal reflux disease and dyspepsia in adults (CG184).

## Surveillance proposal

These recommendations should not be updated.

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### 1.1 Providing information for people with chest pain

#### 2014 surveillance summary

One randomised controlled trial (RCT) (n=204) (1) showed that a decision aid increased patient knowledge and reduced patient preference for admission to the observation unit and cardiac stress testing with no major cardiac events.

#### 2019 surveillance summary

No relevant evidence was identified.

#### Intelligence gathering

No intelligence was identified.

#### Impact statement

Recommendation 1.1.1.3 states that joint decisions should be made with patients, clearly explaining options and taking account of their preferences. The identified RCT is consistent with this recommendation in that, while a decision aid is not specifically mentioned, such an aid would be useful in informing discussions with patients. A [NICE guideline on shared decision making](#) is currently in development. No additional evidence or intelligence was identified through the 2019 surveillance with potential impact on recommendations.

New evidence is unlikely to change guideline recommendations.

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## 1.2 People presenting with acute chest pain

### Recommendations in this section of the guideline

This section of the guideline covers the assessment and diagnosis of people with recent acute chest pain or discomfort, suspected to be caused by an acute coronary syndrome (ACS). The

term ACS covers a range of conditions including unstable angina, ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI).

The guideline addresses assessment and diagnosis irrespective of setting, because people present in different ways. Please note that the NICE guideline on unstable angina and NSTEMI (CG94) covers the early management of these conditions once a firm diagnosis has been made and before discharge from hospital.

## 1.2.1 Initial assessment and referral to hospital

- 1.2.1.1 Check immediately whether people currently have chest pain. If they are pain free, check when their last episode of pain was, particularly if they have had pain in the last 12 hours. [2010].
- 1.2.1.2 Determine whether the chest pain may be cardiac and therefore whether this guideline is relevant, by considering:
  - the history of the chest pain
  - the presence of cardiovascular risk factors
  - history of ischaemic heart disease and any previous treatment
  - previous investigations for chest pain. [2010]
- 1.2.1.3 Initially assess people for any of the following symptoms, which may indicate an ACS:
  - pain in the chest and/or other areas (for example, the arms, back or jaw) lasting longer than 15 minutes
  - chest pain associated with nausea and vomiting, marked sweating, breathlessness, or particularly a combination of these
  - chest pain associated with haemodynamic instability
  - new onset chest pain, or abrupt deterioration in previously stable angina, with recurrent chest pain occurring frequently and with little or no exertion, and with episodes often lasting longer than 15 minutes. [2010]
- 1.2.1.4 Do not use people's response to glyceryl trinitrate (GTN) to make a diagnosis. [2010]
- 1.2.1.5 Do not assess symptoms of an ACS differently in men and women. Not all people with an ACS present with central chest pain as the predominant feature. [2010]
- 1.2.1.6 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. [2010]
- 1.2.1.7 Refer people to hospital as an emergency if an ACS is suspected (see recommendation 1.2.1.3) and:
  - they currently have chest pain or
  - they are currently pain free, but had chest pain in the last 12 hours, and a resting 12-lead ECG is abnormal or not available. [2010]
- 1.2.1.8 If an ACS is suspected (see recommendation 1.2.1.3) and there are no reasons for emergency referral, refer people for urgent same-day assessment if:

- they had chest pain in the last 12 hours, but are now pain free with a normal resting 12-lead ECG or
  - the last episode of pain was 12–72 hours ago. [2010]
- 1.2.1.9 Refer people for assessment in hospital if an ACS is suspected (see recommendation 1.2.1.3) and:
- the pain has resolved and
  - there are signs of complications such as pulmonary oedema.
- Use clinical judgement to decide whether referral should be as an emergency or urgent same-day assessment. [2010]
- 1.2.1.10 If a recent ACS is suspected in people whose last episode of chest pain was more than 72 hours ago and who have no complications such as pulmonary oedema:
- carry out a detailed clinical assessment (see recommendations 1.2.4.2 and 1.2.4.3)
  - confirm the diagnosis by resting 12-lead ECG and blood troponin level
  - take into account the length of time since the suspected ACS when interpreting the troponin level.
- Use clinical judgement to decide whether referral is necessary and how urgent this should be. [2010]
- 1.2.1.11 Refer people to hospital as an emergency if they have a recent (confirmed or suspected) ACS and develop further chest pain. [2010]
- 1.2.1.12 When an ACS is suspected, start management immediately in the order appropriate to the circumstances (see section 1.2.3) and take a resting 12-lead ECG (see section 1.2.2). Take the ECG as soon as possible, but do not delay transfer to hospital. [2010]
- 1.2.1.13 If an ACS is not suspected, consider other causes of the chest pain, some of which may be life-threatening (see recommendations 1.2.6.5, 1.2.6.7 and 1.2.6.8). [2010]

## 1.2.2 Resting 12-lead ECG

- 1.2.2.1 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. [2010].
- 1.2.2.2 Follow local protocols for people with a resting 12-lead ECG showing regional ST-segment elevation or presumed new left bundle branch block (LBBB) consistent with an acute STEMI until a firm diagnosis is made. Continue to monitor (see recommendation 1.2.3.4). [2010]
- 1.2.2.3 Follow the NICE guideline on unstable angina and NSTEMI: early management (CG94) for people with a resting 12-lead ECG showing regional ST-segment depression or deep T wave inversion suggestive of a NSTEMI or unstable angina until a firm diagnosis is made. Continue to monitor (see recommendation 1.2.3.4). [2010]

- 1.2.2.4 Even in the absence of ST-segment changes, have an increased suspicion of an ACS if there are other changes in the resting 12-lead ECG, specifically Q waves and T wave changes. Consider following the NICE guideline on unstable angina and NSTEMI: early management (CG94) if these conditions are likely. Continue to monitor (see recommendation 1.2.3.4). [2010]
- 1.2.2.5 Do not exclude an ACS when people have a normal resting 12-lead ECG. [2010]
- 1.2.2.6 If a diagnosis of ACS is in doubt, consider:
- taking serial resting 12-lead ECGs
  - reviewing previous resting 12-lead ECGs
  - recording additional ECG leads.
- Use clinical judgement to decide how often this should be done. Note that the results may not be conclusive. [2010]
- 1.2.2.7 Obtain a review of resting 12-lead ECGs by a healthcare professional qualified to interpret them as well as taking into account automated interpretation. [2010]
- 1.2.2.8 If clinical assessment (as described in recommendation 1.2.1.10) and a resting 12-lead ECG make a diagnosis of ACS less likely, consider other acute conditions. First consider those that are life-threatening such as pulmonary embolism, aortic dissection or pneumonia. Continue to monitor (see recommendation 1.2.3.4). [2010]

### 1.2.3 Immediate management of a suspected acute coronary syndrome

Management of ACS should start as soon as it is suspected, but should not delay transfer to hospital. The recommendations in this section should be carried out in the order appropriate to the circumstances.

- 1.2.3.1 Offer pain relief as soon as possible. This may be achieved with GTN (sublingual or buccal), but offer intravenous opioids such as morphine, particularly if an acute myocardial infarction (MI) is suspected. [2010].
- 1.2.3.2 Offer people a single loading dose of 300 mg aspirin as soon as possible unless there is clear evidence that they are allergic to it.
- If aspirin is given before arrival at hospital, send a written record that it has been given with the person
- Only offer other antiplatelet agents in hospital. Follow appropriate guidance (the NICE guideline on unstable angina and NSTEMI: early management or local protocols for STEMI). [2010]
- 1.2.3.3 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 (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94–98%
  - people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88–92% until blood gas analysis is available. [2010]

- 1.2.3.4 Monitor people with acute chest pain, using clinical judgement to decide how often this should be done, until a firm diagnosis is made. This should include:
- exacerbations of pain and/or other symptoms
  - pulse and blood pressure
  - heart rhythm
  - oxygen saturation by pulse oximetry
  - repeated resting 12-lead ECGs and
  - checking pain relief is effective. [2010]
- 1.2.3.5 Manage other therapeutic interventions using appropriate guidance (the NICE guideline on unstable angina and NSTEMI: early management or local protocols for STEMI). [2010]

## **1.2.4 Assessment in hospital for people with a suspected acute coronary syndrome**

- 1.2.4.1 Take a resting 12-lead ECG and a blood sample for high-sensitivity troponin I or T measurement (see section 1.2.5) on arrival in hospital. [2010, amended 2016].
- 1.2.4.2 Carry out a physical examination to determine:
- haemodynamic status
  - signs of complications, for example, pulmonary oedema, cardiogenic shock and
  - signs of non-coronary causes of acute chest pain, such as aortic dissection. [2010]
- 1.2.4.3 Take a detailed clinical history unless a STEMI is confirmed from the resting 12-lead ECG (that is, regional ST-segment elevation or presumed new LBBB). Record:
- the characteristics of the pain
  - other associated symptoms
  - any history of cardiovascular disease
  - any cardiovascular risk factors and
  - details of previous investigations or treatments for similar symptoms of chest pain. [2010]

## **1.2.5 Use of biochemical markers for diagnosis of an acute coronary syndrome**

- 1.2.5.1 Do not use high-sensitivity troponin tests for people in whom ACS is not suspected. [new 2016].
- 1.2.5.2 For people at high or moderate risk of MI (as indicated by a validated tool), perform high-sensitivity troponin tests as recommended in the NICE diagnostics guidance on myocardial infarction (DG15). [new 2016]
- 1.2.5.3 For people at low risk of MI (as indicated by a validated tool):

- perform a second high-sensitivity troponin test as recommended in the NICE diagnostics guidance on myocardial infarction (DG15) if the first troponin test at presentation is positive.
  - consider performing a single high-sensitivity troponin test only at presentation to rule out NSTEMI if the first troponin test is below the lower limit of detection (negative). [new 2016]
- 1.2.5.4 Ensure that patients understand that a detectable troponin on the first high-sensitivity test does not necessarily indicate that they have had an MI. [new 2016]
- 1.2.5.5 Do not use biochemical markers such as natriuretic peptides and high-sensitivity C-reactive protein to diagnose an ACS. [2010]
- 1.2.5.6 Do not use biochemical markers of myocardial ischaemia (such as ischaemia-modified albumin) as opposed to markers of necrosis when assessing people with acute chest pain. [2010]
- 1.2.5.7 When interpreting high-sensitivity troponin measurements, take into account:
- the clinical presentation
  - the time from onset of symptoms
  - the resting 12-lead ECG findings
  - the pre-test probability of NSTEMI
  - the length of time since the suspected ACS
  - the probability of chronically elevated troponin levels in some people
  - that 99th percentile thresholds for troponin I and T may differ between sexes. [2010, amended 2016]

## 1.2.6 Making a diagnosis

- 1.2.6.1 When diagnosing MI, use the universal definition of myocardial infarction<sup>[\*\*]</sup>. This is the detection of rise and/or fall of cardiac biomarkers values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile of the upper reference limit and at least one of the following:
- symptoms of ischaemia
  - new or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB)
  - development of pathological Q waves in the ECG
  - imaging evidence of new loss of viable myocardium or new regional wall motion abnormality<sup>[†]</sup>
  - identification of an intracoronary thrombus by angiography. [2010, amended 2016]
- 1.2.6.2 When a raised troponin level is detected in people with a suspected ACS, reassess to exclude other causes for raised troponin (for example, myocarditis, aortic dissection or pulmonary embolism) before confirming the diagnosis of ACS. [2010]

- 1.2.6.3 When a raised troponin level is detected in people with a suspected ACS, follow the appropriate guidance (the NICE guideline on unstable angina and NSTEMI: early management or local protocols for STEMI) until a firm diagnosis is made. Continue to monitor (see recommendation 1.2.3.4). [2010]
- 1.2.6.4 When a diagnosis of ACS is confirmed, follow the appropriate guidance (the NICE guideline on unstable angina and NSTEMI: early management or local protocols for STEMI). [2010]
- 1.2.6.5 Reassess people with chest pain without raised troponin levels and no acute resting 12-lead ECG changes to determine whether their chest pain is likely to be cardiac.  
If myocardial ischaemia is suspected, follow the recommendations on stable chest pain in this guideline (see section 1.3). Use clinical judgement to decide on the timing of any further diagnostic investigations. [2010, amended 2016]
- 1.2.6.6 Do not routinely offer non-invasive imaging or exercise ECG in the initial assessment of acute cardiac chest pain. [new 2016]
- 1.2.6.7 Only consider early chest computed tomography (CT) to rule out other diagnoses such as pulmonary embolism or aortic dissection, not to diagnose ACS. [2010]
- 1.2.6.8 Consider a chest X-ray to help exclude complications of ACS such as pulmonary oedema, or other diagnoses such as pneumothorax or pneumonia. [2010]
- 1.2.6.9 If an ACS has been excluded at any point in the care pathway, but people have risk factors for cardiovascular disease, follow the appropriate guidance, for example, the NICE guidelines on cardiovascular disease and hypertension in adults. [2010]

\*\* Thygesen K, Alpert JS, Jaffe AS *et al.* (2012) Third universal definition of myocardial infarction. *Circulation* 126: 2020–5. The definition also includes post-mortem diagnosis in the diagnostic classification.

† The Guideline Development Group did not review the evidence for the use of imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in the diagnosis of MI, but recognised that it was included as a criterion in the universal definition of MI. The Guideline Development Group recognised that it could be used, but would not be done routinely when there were symptoms of ischaemia and ECG changes.

## Surveillance proposal

These recommendations should not be updated.

## 1.2.1 Initial assessment and referral to hospital

### 2014 surveillance summary

A systematic review and meta-analysis (2) reported that telemedicine systems (including early telemetry of ECG data) reduced the risk of in-hospital mortality due to acute myocardial infarction (AMI).

An RCT (n=7083) (3) found that electronic risk alerts to primary care physicians for chest pain patients did not alter risk-appropriate management of high and low risk patients.

An RCT secondary data analysis (4) and a meta-analysis (5) reported that patients with ACS were more likely to experience chest pain and arm pain, and pain radiation to the right arm/shoulder, palpitation, and visceral pain.

### 2019 surveillance summary

No relevant evidence was identified.

### Intelligence gathering

Recommendation 1.2.1.13 advises that, if an ACS is not suspected, other causes of chest pain be considered, some of which may be life-threatening.

External correspondence was received in the 2019 surveillance review requesting that NICE consider the inclusion of more detailed guidance on the diagnosis of aortic dissection (or acute aortic syndrome). This external correspondence highlighted the issue of delayed or incorrect diagnosis for people with aortic dissection, contributing to the high mortality rate for this condition. Due to the timeline of the receipt of this

correspondence, it was not possible to perform focused searches for evidence in this area as part of this surveillance review. However, we consulted with the topic experts engaged with this surveillance review and sought additional views from experts in emergency medicine in order to inform our consideration of this issue. Of 9 responses received from experts, 5 considered that it would not be appropriate to include further guidance on aortic dissection in this guideline (for reasons including that aortic dissection has different pathology and presentation, noting that existing non-NICE guidelines are available). It was also stated that further inclusion of aortic dissection may necessitate inclusion of other potential causes of chest pain. Three topic experts considered that further guidance on aortic dissection would be beneficial and one response was unclear. Therefore, the majority view of experts consulted was that further guidance on diagnosis of aortic dissection would not be appropriate within this guideline.

### Impact statement

Four studies relevant to this section of the guideline were identified in the 2014 surveillance review.

A systematic review and meta-analysis was identified showing that telemedicine systems (including early telemetry of ECG data) could reduce the risk of in-hospital mortality due to AMI. This evidence of the importance of timeliness of ECG delivery has relevance to recommendations 1.2.1.12 and 1.2.2.1 that state that a resting ECG should be taken as soon as possible and that (when people are referred), results should be sent to hospital before they arrive if possible. This



evidence is consistent with this and is unlikely to impact on current recommendations.

An RCT (n=7,083) found that electronic risk alerts to primary care physicians for chest pain patients did not change patient management. As there was no benefit of the intervention, and this guideline does not cover electronic risk alerts, this evidence is unlikely to impact on current recommendations.

An RCT secondary data analysis and a meta-analysis describing symptoms associated with ACS were also considered to be consistent with current recommendations describing the

assessment of symptoms that may indicate ACS.

No additional evidence was identified in the 2019 surveillance review. While intelligence was considered relating to the inclusion of further guidance on diagnosis of aortic dissection within this guideline, the majority view of experts was that this would not be appropriate. Therefore, the evidence and intelligence identified are not considered to have potential impact on recommendations in this area.

New evidence is unlikely to change guideline recommendations.

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## 1.2.2 Resting 12-lead ECG

### 2014 surveillance summary

One systematic review (6) reported that there was insufficient evidence for the use of ECG-based signal analysis technologies compared with standard 12-lead ECG in detection of ischaemia or infarction in ACS patients.

An RCT (n=354) (7) showed that an ECG technician improved in-hospital first medical contact-to-ECG time versus control.

### 2019 surveillance summary

No relevant evidence was identified.

### Intelligence gathering

Recommendation 1.2.2.8 states that if clinical assessment and a resting 12-lead ECG make diagnosis of ACS less likely, other acute conditions should be

considered, including those that are life-threatening, specifically citing aortic dissection as an example.

External correspondence was received in the 2019 surveillance review requesting that NICE consider the inclusion of more detailed guidance on the diagnosis of aortic dissection (or acute aortic syndrome) and differentiation from ACS within this guideline. Due to the timeline of the receipt of this correspondence, it was not possible to perform focused searches for evidence in this area as part of this surveillance review. However, we consulted with the topic experts engaged with this surveillance review and sought additional views from experts in emergency medicine in order to inform our consideration of this issue. Of 9 responses received from experts, 5 considered that it would not be appropriate to include further guidance on aortic dissection in this guideline (for reasons including that aortic dissection has different pathology

and presentation, noting that existing non-NICE guidelines are available). It was also stated that further inclusion of aortic dissection may necessitate inclusion of other potential causes of chest pain. Three topic experts considered that further guidance on aortic dissection would be beneficial and one response was unclear. Therefore, the majority view of experts consulted was that further guidance on diagnosis of aortic dissection would not be appropriate within this guideline.

### Impact statement

A systematic review identified in previous surveillance found insufficient evidence for ECG-based signal analysis technologies versus standard 12-lead ECG in ACS patients. An RCT showed improvement in in-hospital first medical contact-to-ECG time from input of an ECG technician. Since the identified evidence is not

sufficient to disagree with standard 12-lead ECG delivery and since recommendations state that a resting 12-lead ECG should be taken as soon as possible and do not specify which health professional should perform the procedure, this evidence is unlikely to impact on current recommendations.

No additional evidence was identified in the 2019 surveillance review. While intelligence was considered relating to the inclusion of further guidance on diagnosis of aortic dissection within this guideline, the majority view was that this would not be appropriate. Therefore, the evidence and intelligence identified are not considered to have potential impact on recommendations.

New evidence is unlikely to change guideline recommendations.

## 1.2.3 Immediate management of a suspected acute coronary syndrome

### 2014 surveillance summary

#### Pain management

One RCT (n=1,763) (8) showed that combined anxiolytics and analgesics gave no difference in pain compared with analgesics alone in the pre-hospital treatment of patients with suspected ACS.

### 2019 surveillance summary

#### Oxygen administration

In a registry based RCT (9), patients with suspected MI and an oxygen saturation of  $\geq 90\%$  (n=6,629) were randomised to supplemental oxygen (6 litres per minute via an open face mask for 6 to 12 hours) or ambient air. There were no significant differences between groups in either i) death from any cause within 1-year post-randomisation (p=0.80) or, ii) rehospitalisation with MI within 1 year (p=0.33).

A subsequent trial publication (10) reported that there were no significant differences (p>0.05) between supplemental oxygen and ambient air groups in all-cause death or hospitalisation for heart failure at 1 year and longer-term follow-up (median 2.1 years). There was also no significant difference (p>0.05) between groups in cardiovascular death at a median of 2.1 years follow-up.

### Intelligence gathering

#### Antiplatelet agents

One topic expert suggested that recommendations on type, combination and duration of single/dual antiplatelet therapy for ACS be covered in this surveillance. However, since management once the cause of chest pain is known is outside the scope of this guideline, this was not considered further in this surveillance. Antiplatelet therapy for people with unstable angina and NSTEMI is covered in the NICE guideline on [unstable angina and NSTEMI: early management](#) (CG94).

### Impact statement

#### Pain management

An RCT identified in previous surveillance compared anxiolytics and analgesics with analgesics alone in the pre-hospital treatment of patients with suspected ACS and resulted in no between-group difference in pain. This evidence is consistent with the current recommendation to offer pain relief as soon as possible. No additional evidence or intelligence was identified in the 2019 surveillance with potential impact on recommendations on pain relief.

#### Antiplatelet agents

One topic expert commented that antiplatelet therapy for management of ACS be considered in this surveillance. Recommendation 1.2.3.2 states that people with suspected ACS should be offered a single loading dose of aspirin and only be offered other antiplatelet agents in hospital, following appropriate guidance (citing the NICE guideline on [unstable angina and NSTEMI: early management](#) [CG94]). As management once the cause of chest pain is known is outside the scope of this guideline, this feedback is not

considered to have potential impact on recommendations relating to the use of antiplatelet agents in people with acute chest pain of suspected cardiac origin.

### Oxygen administration

Two trial reports were identified in this 2019 surveillance, both of which gave inconclusive results of the effects of oxygen on hospitalisation or death compared with ambient air. The evidence

and intelligence identified in this surveillance review does not have potential impact on the current recommendation not to administer oxygen and monitor oxygen saturation using pulse oximetry.

New evidence is unlikely to change guideline recommendations.

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## 1.2.4 Assessment in hospital for people with a suspected acute coronary syndrome

### 2014 surveillance summary

In previous surveillance, no studies relevant to this section of the guideline were identified.

### 2019 surveillance summary

No evidence was identified.

### Intelligence gathering

Recommendation 1.2.4.2 states that a physical examination should be carried out to determine factors including signs of non-coronary causes of acute chest pain, such as aortic dissection.

External correspondence was received in the 2019 surveillance review requesting that NICE consider the inclusion of more detailed guidance on the diagnosis of aortic dissection (or acute aortic syndrome) and differentiation from ACS within this guideline. Due to the timeline of the receipt of this correspondence, it was not possible to perform focused

searches for evidence in this area as part of this surveillance review. However, we consulted with the topic experts engaged with this surveillance review and sought additional views from experts in emergency medicine in order to inform our consideration of this issue. Of 9 responses received from experts, 5 considered that it would not be appropriate to include further guidance on aortic dissection in this guideline (for reasons including that aortic dissection has different pathology and presentation, noting that existing non-NICE guidelines are available). It was also stated that further inclusion of aortic dissection may necessitate inclusion of other potential causes of chest pain. Three topic experts considered that further guidance on aortic dissection would be beneficial and one response was unclear. Therefore, the majority view of experts consulted was that further guidance on diagnosis of aortic dissection would not be appropriate within this guideline.

### Impact statement

No evidence was identified with potential impact on recommendations in this section of the guideline. While intelligence was considered relating to the inclusion of

further guidance on diagnosis of aortic dissection within this guideline, the majority view was that this would not be appropriate. Therefore, the evidence and intelligence identified are not considered

to have potential impact on recommendations.

New evidence is unlikely to change guideline recommendations.

## 1.2.5 Use of biochemical markers for diagnosis of an acute coronary syndrome

### 2014 surveillance summary

The 2014 surveillance review included one RCT (11) and one systematic review (12) on the effectiveness of the use of point-of-care testing.

The use of high-sensitivity troponins was covered in the 2016 guideline update. It is stated in the update that the review questions on high-sensitivity troponins seek to address whether high-sensitivity troponin assays could be used differently in people presenting with acute chest pain based on their risk of ACS. The eligible population was to be considered by low risk, medium risk, and high risk strata (as defined by the included studies).

Diagnostic accuracy of high-sensitivity troponins was also considered for different risk levels (with prevalence mapped to risks reported in TIMI for papers not reporting validated risk tool scores, e.g. TIMI or GRACE).

### 2019 surveillance summary

#### Use of high-sensitivity troponins

The use of high-sensitivity troponins was suggested in topic expert feedback as a priority area for consideration in this surveillance review. Focused searches for diagnostic accuracy and clinical evidence were undertaken in this review.

#### Diagnostic evidence

In this surveillance review, studies with insufficient population or unclear reference standard details were excluded. Studies were excluded if they included mixed AMI populations/patients with STEMI and the results were not reported separately for the STEMI and NSTEMI/unstable angina populations (in line with details in the guideline protocol). This guideline excluded non-OECD countries (as described in the guideline protocol). However, this limit has not been applied in this surveillance, due to limited available details in the included abstracts. It has also been assumed in this surveillance that study populations are adults, where this is not reported in abstracts.

The 7 included studies are tabulated below.

**Table 1. Diagnostic accuracy of high-sensitivity troponins in people with acute chest pain**

Study and population	Test(s)	Reference standard	Key methods	Key results
<p>Badertscher, 2018 (13) Patients with acute chest discomfort presenting to emergency department (ED) (n=3828 patients eligible for analysis)</p>	<p>hs-cTnI (hs-cTnT also measured but no data reported in abstract)</p>	<p>Final diagnosis adjudicated by 2 independent cardiologists</p>	<p>Design: Prospective stratification of patients into 3 groups based on ACS probability assessed by treating ED clinician using visual analog scale (10%, 11% to 79% and 80%) by review of all available information at 90 minutes.</p>	<p>1,189 patients had low (10%) ACS probability. Incidence of NSTEMI increased from 1.3% to 12.2% to 54.8% in low, intermediate, and high ACS probability respectively. hs-cTnI Area Under Curve (AUC) 0.96 (95% confidence interval (CI) 0.94 to 0.97); 0.87 (95% CI 0.85 to 0.89); 0.89 (95% CI 0.87 to 0.92%) across strata (assumed low to intermediate to high)</p>
<p>Body, 2016 (14) TRAPID-AMI study Patients with suspected cardiac chest pain (within 6 hours of peak symptoms). Subgroup of patients (n=471) had initial hs-cTnT below limit of detection [LOD] and no ischaemia on ECG</p>	<p>hs-cTnT (blood taken on arrival, LOD 5 ng/l)</p>	<p>Adjudicated using sensitivity troponin I</p>	<p>Design: Prospective multicentre diagnostic cohort study at 12 sites (9 countries). All patients received serial troponin sampling across 4 to 14 hours Outcome: prevalent AMI. Data reported for subgroup of patients (n=471) with</p>	<p>0.4% (n=2) probability of AMI. Sensitivity 99.1% (95% CI 96.7% to 99.9%), Negative predictive value (NPV) 99.6% (95% CI 98.5% to 100%)</p>

Study and population	Test(s)	Reference standard	Key methods	Key results
			initial hs-cTnT below LOD and no ischaemia on ECG	
Ljung, 2019 (15) NSTEMI cohort presenting ≤ 2 hours from symptom onset identified from SWEDEHEART registry (n=911)	hs-cTnT (< 5 ng/l at presentation) combined with non-ischaemic ECG	Diagnosis of NSTEMI verified from hospital medical records (no further details)	Design: Multicentre study (5 sites in Sweden) Outcome: Diagnosis of NSTEMI	Patients presenting > 1 to ≤ 2 hours from symptom onset: sensitivity for MI with combined hs-cTnT and ECG = 99.4% (95% CI 98.4% to 99.8%)
Tajsic, 2018 (16) Consecutive patients admitted to ED with suspected ACS (n=311)	High-sensitivity cardiac troponin I (penultimate generation)	Type 1 infarction: Angiographically confirmed Type 2 infarction: Not reported	Design: Prospective cohort study Outcome: Detection of type 1 and type 2 non-ST-segment elevation acute coronary syndrome (NSTEMI)	17.6% (n=55) final diagnosis of NSTEMI: 9.6% (n=31) type 1 infarction, 8.0% (n=25) type 2 infarction. Data reported for very early presenters (≤ 2 hours symptom onset time): Type 1 NSTEMI: NPV = 96.7% (95% CI 87.5% to 99.4%), Type 2 NSTEMI: NPV = 98.3% (95% CI 89.8% to 99.9%)

Study and population	Test(s)	Reference standard	Key methods	Key results
<p>Twerenbold, 2018a (17)</p> <p>Unselected patients with suspected NSTEMI presenting to ED (patients with serial hs-cTnT readings, n=4,368; patients with serial hs-cTnI readings n=3,500)</p>	<p>hs-cTnT and hs-cTnI measured at presentation and after 1 hour (ESC 0/1-hour algorithm)</p>	<p>Final diagnosis centrally adjudicated by 2 independent cardiologists</p>	<p>Design: Prospective multicentre study (in 6 countries)</p> <p>Outcome: Diagnosis of NSTEMI</p>	<p>Prevalence of NSTEMI = 17%.</p> <p>hs-cTnT: NPV = 99.8%, positive predictive value (PPV) = 74.5%, 57% assigned to rule out and 18% to rule in.</p> <p>hs-cTnI: NPV = 99.7%, PPV = 62.3%, 44% assigned to rule out and 23% to rule in.</p>
<p>Twerenbold, 2018b (18)</p> <p>Unselected patients with suspected NSTEMI presenting to ED (with or without renal dysfunction [RD], defined as estimated glomerular filtration rate &lt; 60 ml/min/1.73<sup>2</sup>) (n total =3,254, n with RD = 487)</p>	<p>hs-cTnT (ESC 0/1-hour algorithm)</p>	<p>Final diagnosis centrally adjudicated by 2 independent cardiologists (based on all available information including cardiac imaging)</p>	<p>Design: Prospective multicentre diagnostic study. Safety quantified as sensitivity in rule out zone, accuracy as the specificity in rule in zone, efficacy as proportion of overall cohort allocated to either rule out or rule in based on 0- and 1-hour assay.</p> <p>Outcome: Diagnosis of AMI (population had</p>	<p>Prevalence of NSTEMI higher in patients with RD compared with normal renal function (31% vs. 13%, p&lt;0.001).</p> <p>hs-cTnT with RD</p> <p>Sensitivity of rule out = 100% (95% CI 97.6 to 100%)</p> <p>Specificity of rule in = 88.7% (95% CI 84.8% to 91.9%)</p> <p>Overall efficacy = 51%</p> <p>hs-cTnT without RD</p> <p>Sensitivity of rule out = 99.2% (95% CI 97.6% to 99.8%, p=0.559)</p> <p>Specificity of rule in = 96.5% (95% CI 95.7% to 97.2%)</p> <p>Overall efficacy = 81%, p&lt;0.0001)</p>
	<p>hs-cTnI (ESC 0/1-hour algorithm)</p>			<p>hs-cTnI with RD</p> <p>Sensitivity of rule out = 98.6% (95% CI 95.0% to 99.8%)</p> <p>Specificity of rule in = 84.4% (95% CI 79.9 to 88.3%)</p> <p>Overall efficacy = 54%</p>



Study and population	Test(s)	Reference standard	Key methods	Key results
			suspected NSTEMI)	<p>hs-cTnI without RD</p> <p>Sensitivity of rule out = 98.5% (95% CI 96.5 to 99.5%, p=1.0)</p> <p>Specificity of rule in = 91.7% (95% CI 90.5% to 92.9%, p&lt;0.001)</p> <p>Overall efficacy = 76%, p&lt;0.001)</p>
Wildi, 2016 (19) Consecutive patients (n=2,727) presenting to ED with suspected AMI without persistent ST-segment elevation	ESC rapid 0-hour / 3-hour rule out protocol	Final diagnosis of AMI adjudicated by 2 independent cardiologists	<p>Design: Prospective international multicentre study.</p> <p>Outcome: Detection of AMI (study population was without persistent ST-segment elevation)</p>	<p>AMI was diagnosed in 473 patients (17.3%).</p> <p>Using the 4 high-sensitivity troponin assays, 0-hour rule out protocol correctly ruled out 99.8% (95% CI 98.7% to 100%), 99.6% (95% CI 98.5% to 99.9%), 100% (95% CI 97.9% to 100%) and 100% (95% CI 98.0% to 100%) of late-presenting (&gt; 6 hours from onset of chest pain) patients.</p> <p>Using the 4 high-sensitivity troponin assays, 3-hour rule out protocol correctly ruled out 99.9% (95% CI 99.1% to 100%), 99.5% (95% CI 98.3% to 99.9%), 100% (95% CI 98.1% to 100%) and 100% (95% CI 98.2% to 100%) of early-presenting (&lt; 6 hours from onset of chest pain) patients.</p>

### Clinical evidence

Four RCTs were included from the focused search for RCT evidence reporting clinical outcome data for the use of high-

sensitivity troponins in people with acute chest pain of suspected cardiac origin.

A stepped-wedge, cluster-randomised RCT was performed by Shah *et al.* (2018) (20) in 10 secondary or tertiary care hospitals in

Scotland. The RCT assessed the impact on efficacy outcomes of early versus late introduction of a high-sensitivity cardiac troponin I (hs-cTnI) assay with a sex-specific 99<sup>th</sup> centile diagnostic threshold. Consecutive patients admitted to EDs with suspected ACS were included (n=48,282, mean 61 years [SD=17], 47% female). In a validation phase of 6-12 months, hs-cTnI results were concealed from clinicians and care was guided by a contemporary cardiac troponin I assay (cTnI). Hospitals were randomised to early (n=5 hospitals, hs-cTnI assay introduced immediately after validation phase) or late (n=5 hospitals, hs-cTnI assay deferred for 6 months) implementation of the hs-cTnI assay. Patients were defined as being reclassified by the hs-cTnI assay if they had an increased hs-cTnI concentration and cTnI concentrations below the diagnostic threshold. Of the 10,360 patients who were not identified by the cTnI assay, the hs-cTnI assay reclassified 1771 (17%). The adjusted odds ratio for subsequent myocardial infarction (MI) or cardiovascular death within 1 year for the implementation versus the validation phase was 1.10 (95% CI 0.75 to 1.61, p=0.620). This study showed that, while the hs-cTnI assay reclassified patients with myocardial injury or infarction, this was not associated with lower incidence at 1-year of MI or cardiovascular death.

Patients (n=1,937, median age 61 years [IQR 48 to 74], 46.3% female) with chest pain without ST-segment elevation presenting to 5 EDs were randomised in a multicentre RCT (Chew, 2016) (21) to high-sensitivity troponin T reporting (hs-TnT-report) or standard reporting (std-report). There was no difference in use of angiography between hs-TnT-reporting

(11.9%) versus standard reporting (10.9%, p=0.479). No overall difference in 12-month mortality or new/recurrent ACS was found between groups (hazard ratio 0.83, 95% CI 0.57 to 1.22, p=0.362).

An Australian trial-based cost-effectiveness analysis (Kaambwa, 2017) (22) was undertaken in 1,937 patients presenting with undifferentiated chest pain who were randomised to hs-TnT or c-TnT. The study concluded that hs-TnT resulted in reduced adverse clinical effects with a higher incremental cost-effectiveness ratio.

A single-site USA RCT (Dadkhah, 2017) (23) tested the use of an accelerated diagnostic protocol based on sensitive cardiac troponin I (cTnI) 2 hours after admission with subsequent stress testing. Sixty-four consecutive patients with atypical chest pain and non-diagnostic ECG were randomised to this accelerated 2 hours protocol (29 patients) or the site's pre-existing 4-hour protocol (31 patients). Measurements of troponin I were made at 0- and 2-hours post-presentation with a further measurement for patients in the 4-hour protocol group. Patients having normal serial biomarker readings underwent stress testing and possible earlier discharge with a negative stress test. Patients with a positive biomarker test were admitted. Fifty-three patients had a normal stress test and were therefore discharged. No patient with a normal stress test experienced a major cardiac event or adverse cardiac outcome at 6 months follow-up.

## Intelligence gathering

One topic expert commented that evidence suggests that the use of high-

sensitivity troponins may not affect patient outcomes, highlighting a study (Shah, 2018) that has been included in the 2019 surveillance summary. The use of high-sensitivity troponin tests is also covered by NICE guidance [myocardial infarction \(acute\): Early rule-out using high-sensitivity troponin tests](#) (DG15). The adoption of high-sensitivity troponin testing is being supported by the [Accelerated Access Collaborative](#).

## Impact statement

The 2014 surveillance review included one RCT and one systematic review that demonstrated uncertainty in the effectiveness of the use of point-of-care testing. The focused searches in the 2019 surveillance review were specific to the use of high-sensitivity troponins. As this guideline does not currently include recommendations on the use of point-of-care testing, and the evidence identified in previous surveillance was limited to only 2 studies, further evidence would be required to have potential impact on recommendations under this heading.

A total of 7 studies on the diagnostic accuracy of high-sensitivity troponins were included in the 2019 surveillance review. The [full version of the guideline](#) (page 37) emphasised the importance of high sensitivity in the context of acute chest pain of suspected cardiac origin, reflecting the potentially serious consequences of a missed diagnosis (false negative) in patients who may then experience a major cardiac event. The included studies

confirm the high sensitivity, high NPV and high AUC of high-sensitivity troponins.

The recommendations in this guideline differ based on whether patients are at low, medium or high risk of MI (as indicated by a validated tool). The reporting of risk level in the abstracts included in this surveillance review was limited. However, the diagnostic accuracy evidence identified in this surveillance review confirms the good diagnostic performance of high-sensitivity troponins.

Additionally, 4 RCTs were included in the 2019 surveillance. Some evidence identified in this surveillance suggested that the use of high-sensitivity troponins may not result in reductions in subsequent mortality or cardiac events. However, other included RCTs reported that high-sensitivity troponins were associated with reduced adverse clinical effects, a higher cost-effectiveness ratio, and could identify a low risk population for discharge from the ED. While the diagnostic accuracy studies do not have any potential impact on recommendations, the RCTs included in this surveillance agree with the topic expert feedback that there may be uncertainty in clinical outcomes from the use of high-sensitivity troponins in people with acute chest pain of suspected cardiac origin. Since the identified RCT evidence was mixed, considering this uncertainty, we do not anticipate any impact on the current recommendations.

New evidence is unlikely to change guideline recommendations.

## 1.2.6 Making a diagnosis

### 2014 surveillance summary

#### Non-invasive testing in acute chest pain

This area was included in the 2016 guideline update and so evidence identified in the 2014 surveillance review was available for consideration in the update.

### 2019 surveillance summary

No relevant evidence was identified.

#### Intelligence gathering

Recommendation 1.2.6.2 advises that, when a raised troponin level is observed in people with suspected ACS, that other causes for raised troponins be considered, specifically citing aortic dissection as an example.

Recommendation 1.2.6.7 states that early chest CT only be considered to rule out other diagnoses, again specifically citing aortic dissection as an example.

External correspondence was received in the 2019 surveillance review requesting that NICE consider the inclusion of more detailed guidance on the diagnosis of aortic dissection (or acute aortic syndrome) and differentiation from ACS within this guideline. Due to the timeline of the receipt of this correspondence, it was not possible to perform focused searches for evidence in this area as part of this surveillance review. However, we consulted with the topic experts engaged with this surveillance review and sought additional views from experts in

emergency medicine in order to inform our consideration of this issue. Of 9 responses received from experts, 5 considered that it would not be appropriate to include further guidance on diagnosis of aortic dissection in this guideline (for reasons including that aortic dissection has different pathology and presentation, noting that existing non-NICE guidelines are available). It was also stated that further inclusion of aortic dissection may necessitate inclusion of other potential causes of chest pain. Three topic experts considered that further guidance on aortic dissection would be beneficial and one response was unclear. Therefore, the majority view of experts consulted was that further guidance on diagnosis of aortic dissection would not be appropriate within this guideline.

#### Impact statement

The evidence identified in the 2014 surveillance review on non-invasive imaging in acute chest pain was available for the 2016 partial update of this guideline. No additional evidence was identified in the 2019 surveillance review. While intelligence was considered relating to the inclusion of further guidance on diagnosis of aortic dissection within this guideline, the majority view of experts was that this would not be appropriate. Therefore, the evidence and intelligence identified are not considered to have potential impact on recommendations under this heading.

New evidence is unlikely to change guideline recommendations.

## 1.3 People presenting with stable chest pain

### Recommendations in this section of the guideline

This section of the guideline addresses the assessment and diagnosis of intermittent stable chest pain in people with suspected stable angina.

- 1.3.1.1 Exclude a diagnosis of stable angina if clinical assessment indicates non-anginal chest pain (see recommendation 1.3.3.1) and there are no other aspects of the history or risk factors raising clinical suspicion. [new 2016].
- 1.3.1.2 If clinical assessment indicates typical or atypical angina (see recommendation 1.3.3.1), offer diagnostic testing (see sections 1.3.4, 1.3.5 and 1.3.6). [new 2016]

### 1.3.2 Clinical assessment

- 1.3.2.1 Take a detailed clinical history documenting:
  - the age and sex of the person
  - the characteristics of the pain, including its location, radiation, severity, duration and frequency, and factors that provoke and relieve the pain
  - any associated symptoms, such as breathlessness
  - any history of angina, MI, coronary revascularisation or other cardiovascular disease and
  - any cardiovascular risk factors. [2010]
- 1.3.2.2 Carry out a physical examination to:
  - identify risk factors for cardiovascular disease
  - identify signs of other cardiovascular disease
  - identify non-coronary causes of angina (for example, severe aortic stenosis, cardiomyopathy) and
  - exclude other causes of chest pain. [2010]

### 1.3.3 Making a diagnosis based on clinical assessment

- 1.3.3.1 Assess the typicality of chest pain as follows:
  - Presence of three of the features below is defined as typical angina.
  - Presence of two of the three features below is defined as atypical angina.
  - Presence of one or none of the features below is defined as non-anginal chest pain.

Anginal pain is:

  - constricting discomfort in the front of the chest, or in the neck, shoulders, jaw or arms
  - precipitated by physical exertion
  - relieved by rest or GTN within about 5 minutes. [2010, amended 2016]

- 1.3.3.2 Do not define typical and atypical features of anginal chest pain and non-anginal chest pain differently in men and women. [2010]
- 1.3.3.3 Do not define typical and atypical features of anginal chest pain and non-anginal chest pain differently in ethnic groups. [2010]
- 1.3.3.4 Take the following factors, which make a diagnosis of stable angina more likely, into account when estimating people's likelihood of angina:
- age
  - whether the person is male
  - cardiovascular risk factors including:
    - a history of smoking
    - diabetes
    - hypertension
    - dyslipidaemia
    - family history of premature CAD
  - other cardiovascular disease
  - history of established CAD, for example, previous MI, coronary revascularisation [2010]
- 1.3.3.5 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). Features which 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). [2010]
- 1.3.3.6 Consider investigating other causes of angina, such as hypertrophic cardiomyopathy, in people with typical angina-like chest pain and a low likelihood of CAD. [2010, amended 2016]
- 1.3.3.7 Arrange blood tests to identify conditions which exacerbate angina, such as anaemia, for all people being investigated for stable angina. [2010]
- 1.3.3.8 Only consider chest X-ray if other diagnoses, such as a lung tumour, are suspected. [2010]
- 1.3.3.9 If a diagnosis of stable angina has been excluded at any point in the care pathway, but people have risk factors for cardiovascular disease, follow the appropriate guidance, for example, the NICE guideline on cardiovascular disease and the NICE guideline on hypertension in adults. [2010]

- 1.3.3.10 For people in whom stable angina cannot be excluded on the basis of the clinical assessment alone, take a resting 12-lead ECG as soon as possible after presentation. [2010, amended 2016]
- 1.3.3.11 Do not rule out a diagnosis of stable angina on the basis of a normal resting 12-lead ECG. [2010]
- 1.3.3.12 Do not offer diagnostic testing to people with non-anginal chest pain on clinical assessment (see recommendation 1.3.3.1) unless there are resting ECG ST-T changes or Q waves. [new 2016]
- 1.3.3.13 A number of changes on a resting 12-lead ECG are consistent with CAD and may indicate ischaemia or previous infarction. These include:
- pathological Q waves in particular
  - LBBB
  - ST-segment and T wave abnormalities (for example, flattening or inversion)
- Note that the results may not be conclusive
- Consider any resting 12-lead ECG changes together with people's clinical history and risk factors. [2010]
- 1.3.3.14 For people with confirmed CAD (for example, previous MI, revascularisation, previous angiography) in whom stable angina cannot be excluded based on clinical assessment alone, see recommendation 1.3.4.4 about functional testing. [2010, amended 2016]
- 1.3.3.15 Consider aspirin only if the person's chest pain is likely to be stable angina, until a diagnosis is made. Do not offer additional aspirin if there is clear evidence that people are already taking aspirin regularly or are allergic to it. [2010]
- 1.3.3.16 Follow local protocols for stable angina[††] while waiting for the results of investigations if symptoms are typical of stable angina. [2010]

### **1.3.4 Diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone**

The Guideline Development Group emphasised that the recommendations in this guideline are to make a diagnosis of chest pain, not to screen for CAD. Most people diagnosed with non-anginal chest pain after clinical assessment need no further diagnostic testing. However in a very small number of people, there are remaining concerns that the pain could be ischaemic.

- 1.3.4.1 Include the typicality of anginal pain features (see recommendation 1.3.3.1) in all requests for diagnostic investigations and in the person's notes. [2010, amended 2016].
- 1.3.4.2 Use clinical judgement and take into account people's preferences and comorbidities when considering diagnostic testing. [2010]
- 1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:

- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical angina or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves. [new 2016]

1.3.4.4 For people with confirmed CAD (for example, previous MI, revascularisation, previous angiography), offer non-invasive functional testing when there is uncertainty about whether chest pain is caused by myocardial ischaemia. See section 1.3.6 for further guidance on non-invasive functional testing. An exercise ECG may be used instead of functional imaging. [2010]

### 1.3.5 Additional diagnostic investigations

1.3.5.1 Offer non-invasive functional imaging (see section 1.3.6) for myocardial ischaemia if 64-slice (or above) CT coronary angiography has shown CAD of uncertain functional significance or is non-diagnostic. [2016]

1.3.5.2 Offer invasive coronary angiography as a third-line investigation when the results of non-invasive functional imaging are inconclusive. [2016]

### 1.3.6 Use of non-invasive functional testing for myocardial ischaemia

1.3.6.1 When offering non-invasive functional imaging for myocardial ischaemia use:

- myocardial perfusion scintigraphy with single photon emission computed tomography (MPS with SPECT) or
- stress echocardiography or
- first-pass contrast-enhanced magnetic resonance (MR) perfusion or
- MR imaging for stress-induced wall motion abnormalities.

Take account of locally available technology and expertise, the person and their preferences, and any contraindications (for example, disabilities, frailty, limited ability to exercise) when deciding on the imaging method. [This recommendation updates and replaces recommendation 1.1 of the NICE technology appraisal guidance on myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction]. [2016]

1.3.6.2 Use adenosine, dipyridamole or dobutamine as stress agents for MPS with SPECT and adenosine or dipyridamole for first-pass contrast-enhanced MR perfusion. [2010]

1.3.6.3 Use exercise or dobutamine for stress echocardiography or MR imaging for stress-induced wall motion abnormalities. [2010]

1.3.6.4 Do not use MR coronary angiography for diagnosing stable angina. [2010]

1.3.6.5 Do not use exercise ECG to diagnose or exclude stable angina for people without known CAD. [2010]



### 1.3.7 Making a diagnosis following investigations

#### **Box 1 Definition of significant coronary artery disease**

Significant coronary artery disease (CAD) found during CT coronary angiography is  $\geq 70\%$  diameter stenosis of at least one major epicardial artery segment or  $\geq 50\%$  diameter stenosis in the left main coronary artery:

#### **Factors intensifying ischaemia**

Such factors allow less severe lesions (for example,  $\geq 50\%$ ) to produce angina:

- reduced oxygen delivery: anaemia, coronary spasm
- increased oxygen demand: tachycardia, left ventricular hypertrophy
- large mass of ischaemic myocardium: proximally located lesions
- longer lesion length.

#### **Factors reducing ischaemia which may render severe lesions ( $\geq 70\%$ ) asymptomatic:**

- Well-developed collateral supply.
- Small mass of ischaemic myocardium: distally located lesions, old infarction in the territory of coronary supply. [2016]

1.3.7.1 Confirm a diagnosis of stable angina and follow local guidelines for angina[††] when:

- significant CAD (see box 1) is found during invasive or 64-slice (or above) CT coronary angiography or
- reversible myocardial ischaemia is found during non-invasive functional imaging. [2016]

1.3.7.2 Investigate other causes of chest pain when:

- significant CAD (see box 1) is not found during invasive coronary angiography or 64-slice (or above) CT coronary angiography or

- reversible myocardial ischaemia is not found during non-invasive functional imaging. [2016]

1.3.7.3 Consider investigating other causes of angina, such as hypertrophic cardiomyopathy or syndrome X, in people with typical angina-like chest pain if investigation excludes flow-limiting disease in the epicardial coronary arteries. [2010]

†† Stable angina: management (2011) NICE guideline CG126.

## Surveillance proposal

These recommendations should not be updated.

### 1.3.3 Making a diagnosis based on clinical assessment

#### 2014 surveillance summary

The use of clinical prediction models/tools in patients with stable chest pain was reviewed in the 2016 update. Evidence identified in the 2014 surveillance review was available for consideration in the update.

#### 2019 surveillance summary

A substudy (Adamson, 2018a) (24) of the SCOT-HEART trial in 943 adults with suspected stable angina found that increased high-sensitivity troponin levels were associated with obstructive coronary artery disease (CAD) and that high-sensitivity troponin I improved the discrimination and calibration of the CAD Consortium risk model in identifying obstructive CAD.

The PROMISE (PROspective Multicentre Imaging Study for Evaluation of chest pain) minimal-risk tool was externally validated in SCOT-HEART study patients (n=1,764) with suspected stable angina due to CAD

(Adamson, 2018b) (25). PROMISE aims to identify patients with suspected stable angina who are at very low risk of CAD and clinical events. PROMISE was compared with the CAD Consortium (CADC) risk score in this external validation. It was reported that the PROMISE minimal-risk tool showed better prognostic discrimination than the CADC model (p<0.001).

#### Intelligence gathering

One topic expert noted that the European Society of Cardiology (ESC) guidelines still use pre-test probability in assessment of patients with stable chest pain (no further details provided).

#### Impact statement

One identified study suggested that the use of high-sensitivity troponin could improve the performance of the CAD Consortium risk model in people with stable chest pain of suspected cardiac origin. The guideline does not include recommendations on the use of high-sensitivity troponins in stable chest pain. An additional study suggested that the PROMISE risk tool may have better

prognostic discrimination than the CAD Consortium risk tool. However, since i) the committee did not decide to provide recommendations on the use of risk tools in stable chest pain in the updated guideline and, ii) the evidence from surveillance was based on a single study in each case, further evidence would be required to have potential impact on current recommendations.

This surveillance review noted that the [2013 ESC guideline on the management of stable coronary artery disease](#) refers to the use of pre-test probability (defined in the ESC guideline as the likelihood that a patient will have CAD) in decision making. The NICE guideline on chest pain of recent onset: assessment and diagnosis (CG95) update committee considered (page 2010

of the full guideline) a table of probability data based on the Diamond-Forrester model as published in the [2013 ESC guideline on the management of stable coronary artery disease](#). The update committee decided not to include this probability table in the guideline and concluded that diagnostic testing should be offered for all patients assessed as having typical or atypical angina. Therefore, since the issue of pre-test probability was considered in the 2016 update, this intelligence on the 2013 ESC guideline was not considered to have potential impact on the guideline.

New evidence is unlikely to change guideline recommendations.

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### 1.3.4 Diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone

#### 2014 surveillance summary

Non-invasive and invasive imaging for stable chest pain were reviewed in the 2016 guideline update. Evidence identified in the 2014 surveillance review was available for consideration in the update.

#### 2019 surveillance summary

##### CT coronary angiography (CCTA)

Four reports from the SCOT-HEART trial were included in the 2019 surveillance review. Post-hoc analyses (26) of the SCOT-HEART trial (4,146 patients

randomised to standard care or standard care plus CCTA) were performed to determine the impact of CCTA-assisted diagnosis on use of invasive coronary angiography, preventative therapies, and clinical outcomes. It was reported that invasive angiography was less likely to demonstrate normal coronary arteries ( $p < 0.001$ ) and more likely to demonstrate obstructive CAD in patients allocated to CCTA. Following CCTA, significantly more preventative therapies were initiated ( $p < 0.001$ ). Fatal and non-fatal MI were significantly reduced following initiation of preventative therapies in patients in the CCTA group compared with standard care ( $p = 0.02$ ). The authors concluded that CCTA informs appropriate use of invasive angiography and leads to changes in preventative therapies that subsequently reduce MI.

A report (27) from the SCOT-HEART trial of 4,146 patients with suspected angina due to coronary heart disease randomised to standard care alone or standard care plus CCTA showed that, compared with standard care alone, CCTA resulted in less marked improvements in symptoms ( $p < 0.05$ ) and quality of life ( $p < 0.0001$ ) attributed to the detection of moderate non-obstructive CAD.

A post-hoc analysis (28) of the SCOT-HEART study ( $n = 3,770$  eligible patients) reported the diagnostic and prognostic benefits of CCTA using the 2016 NICE guidance for assessment of suspected stable angina. Patients were classed as NICE guideline-defined possible angina and non-angina. CCTA increased diagnostic certainty more in patients with possible angina ( $p < 0.001$ ) versus patients with non-anginal symptoms ( $p = 0.002$ ). In patients with possible angina, CCTA did not reduce use of invasive angiography ( $p = 0.481$ ) but significantly reduced use of normal coronary angiography ( $p < 0.001$ ). In patients with non-anginal symptoms, the use of invasive angiography increased ( $p = 0.014$ ) and did not reduce use of normal coronary angiography ( $p = 0.622$ ). Fatal or non-fatal MI was reduced at 3.2 years of follow-up in patients with possible angina ( $p = 0.045$ ) but not in patients with non-anginal symptoms ( $p = 0.379$ ). This study concluded that NICE-guided patient selection yielded benefits from CCTA in diagnostic certainty, invasive coronary angiography use and reduced MI but that patients with non-anginal chest pain did not show benefits from CCTA, with increased use of invasive testing.

The SCOT-HEART multicentre RCT ( $n = 4,146$  patients randomised) allocated

patients with stable chest pain to standard care plus CCTA (coronary CT angiography) ( $n = 2,073$  patients) or standard care alone ( $n = 2,073$  patients). At five-year follow-up (29), the rate of death from coronary heart disease or non-fatal MI was lower in the CCTA group compared with standard care (hazard ratio 0.59, 95% CI 0.41 to 0.84,  $p = 0.004$ ). Overall rates of invasive coronary angiography and coronary revascularisation were similar between groups at 5 years. More preventative and more anti-anginal therapies (no further details in abstract) were commenced in CCTA group patients.

### **CT coronary angiography with fractional flow reserve**

CT coronary angiography with fractional flow reserve (CT-FFR) was suggested in topic expert feedback as a priority area for consideration in this surveillance review. A focused search was undertaken in the 2019 surveillance review to identify evidence on the diagnostic accuracy of CT coronary angiography with fractional flow reserve in people with chest pain of suspected cardiac origin. Studies with insufficient population or unclear reference standard details were excluded. In line with the guideline, studies with populations described as having suspected CAD were also considered eligible. It is noted in the guideline protocol that only studies that provided per-patient analysis were included (with studies reporting only per vessel or per segment analysis only being excluded). In line with this, only studies reporting per-patient data were included in this surveillance review (with studies summarised from their abstracts in surveillance). Four studies were included.

**Table 2. Diagnostic accuracy of CT-FFR in stable chest pain of suspected cardiac origin**

Study and population	Test(s)	Reference standard	Key methods	Key results
Norgaard, 2017 (30) Patients referred for CCTA, including all patients with new onset chest pain with no known CAD and with intermediate coronary lesions referred for CT-FFR (CT-FFR results in 185 patients)	CT-FFR	FFR $\leq$ 0.80 or instantaneous wave-free ratio (iFR) $\leq$ 0.90	Design: Review of complete diagnostic work-up over 12-month period. Invasive angiography performed after CT-FFR, and FFR and iFR measured. Outcome: Assumed detection of ischaemia.	CT-FFR correctly classified 73% (27/37) of patients
Pontone, 2018 (31) Symptomatic patients with suspected CAD (n=147 patients)	CT-FFR	Invasive coronary angiography (ICA) + invasive FFR	Design: Consecutive patients scheduled for ICA + invasive FFR assessed by CCTA, CT-FFR and stress-CTP. Outcome: Detection of functionally significant coronary artery lesions	CCTA+CT-FFR Patient-based sensitivity, specificity, NPV, PPV, accuracy = 90%, 85%, 92%, 83%, 87% Both CT-FFR and stress-CTP significantly improved specificity and PPV vs. CCTA. Patient-based AUC = 0.94 (p<0.001 vs. CCTA)
	CCTA			CCTA Patient-based sensitivity, specificity, NPV, PPV, accuracy = 95%, 54%, 94%, 63%, 73% Patient-based AUC = 0.90

Study and population	Test(s)	Reference standard	Key methods	Key results
	CCTA + static stress-computed tomography perfusion (stress-CTP)			CCTA+stress-CTP Patient-based sensitivity, specificity, NPV, PPV, accuracy = 98%, 87%, 99%, 86%, 92% Patient-based AUC = 0.93 (p<0.001 vs. CCTA)
Rother, 2018 (32) Patients with suspected CAD (91 vessels in 71 patients)	CT-based FFR (novel prototype for on-site determination on a standard personal computer)	Invasive coronary angiography with FFR measurement	Design: Diagnostic accuracy study Outcome: Sensitivity, specificity, PPV, NPV and accuracy for detection of haemodynamically significant lesions. Threshold FFR ≤ 0.80 indicated haemodynamically relevant stenosis	Sensitivity = 91% (95% CI 70-99%) Specificity = 96% (95% CI 88-99%) PPV = 86% (95% CI 65-97%) NPV = 97% (95% CI 90-100%) Accuracy = 93%
Shi, 2017 (33) Patients with suspected CAD (N=29 patients)	CT-FFR	Invasive FFR	Design: Patients assessed by CCTA and then clinically indicated invasive coronary angiography Outcome: Ischaemia defined as FFR or CT-FFR ≤ 0.80	CT-FFR Accuracy, sensitivity and specificity (per-patient) = 79.3%, 93.7%, 61.5%
	CCTA			CCTA Accuracy, sensitivity and specificity (per-patient) = 62.1%, 87.5%, 30.7%

An additional study was suggested by a topic expert in this surveillance review. The PLATFORM study (34) included patients with stable new onset chest pain and assessed clinical, economic and quality of life outcomes at 1 year from using coronary computed tomographic angiography plus estimation of fractional

flow reserve (CT-FFR) (analysed n=177) compared with usual testing (n=287). In patients with planned invasive coronary angiography, care guided by CT-FFR was reported to be associated with similar clinical outcomes and quality of life and reduced costs compared with usual care.

## Intelligence gathering

### CT coronary angiography

#### General issues

A topic expert noted that CT scanning yields incidental findings that can pose issues in terms of appropriate management, increased costs and resource use and potential for increased patient anxiety.

Topic expert feedback flagged that the issue of reducing lifelong radiation dose exposure should be reinforced in the guideline.

It was also raised in topic expert feedback that CCTA alone may lead to higher rates of revascularisation in coronary disease without reduction in event rates. This expert flagged that CT-FFR may improve this, highlighting the PLATFORM trial (Douglas, 2016), which has been included in the summary of evidence.

One topic expert commented on the costs used for CCTA and invasive imaging in the guideline.

A topic expert suggested that the cost-effectiveness of CT should be considered in this surveillance. Evidence from the SCOT-HEART study was provided in support of this comment and included in the summary of evidence.

#### Implementation issues

Issues relating to the implementation of recommendations on CCTA from the 2016 guideline update have been expressed by several topic experts in this surveillance review.

As part of the 2016 update of this guideline, a NICE [resource impact report](#) was produced. The recommendations on

CCTA were identified as having the greatest resource impact and the report noted that availability of suitable scanners and trained professionals may affect the speed of implementation, stating that this resource impact should be considered locally.

One topic expert in this surveillance review commented that the considerable increase in CCTA scanning required is posing difficulties in implementation across the country, due to limitations in availability of qualified specialists (radiologists or cardiologists) and suitable scanners. This comment was supported by an additional topic expert who stated that CT angiography for patients with chest pain does not appear to be implemented. A further topic expert raised availability of CCTA for all patients attending a rapid access chest pain clinic as an issue for consideration. It was noted that some hospitals still offer an exercise test as a first investigation in a rapid access chest pain clinic (potentially due to lack of access to CCTA). A further topic expert confirmed that the stable chest pain diagnostic pathway has had variable adoption across the country as a result of resource limitations. Topic expert feedback also commented on the use of coronary CT in a higher risk population than previously researched and use of CT-FFR with limited evidence of benefit in clinical cohorts. The FORECAST study was flagged, with the comment that the guideline should be updated once evidence has been published from this work. Additional expert feedback was supportive of the use of CCTA as an effective, low risk, and rapid method but also confirmed the lack of scanner access and variation in uptake by clinicians.

One topic expert referred to the British Society for Cardiovascular Imaging [statement](#) on the resource implications of CCTA recommendations in this guideline. This document presents data on location of cardiac capable scanners, number of professionals accredited in cardiovascular CT (and where these are located), and delivery of CCTA according to centre and population.

In order to inform this surveillance review, Hospital Episode Statistics data for 2017/18 were analysed to explore the delivery of CCTA for people with chest pain in hospital trusts in England.

The data in the British Society for Cardiovascular Imaging [statement](#) and the Hospital Episode Statistics data analysis conducted for this surveillance review (copyright © 2019, the Health and Social Care Information Centre. Re-used with the permission of the Health and Social Care Information Centre. All rights reserved) support the topic expert feedback indicating the geographical variation in CCTA availability and delivery in the United Kingdom.

A positive example of implementation of CCTA in detection of CAD relating to this guideline was identified on the NICE [shared learning database](#) (published January 2012, pre-dating the 2016 update of this guideline).

### **CT-FFR**

One topic expert expressed the view that the use of CT-FFR should be covered in the guideline (no further details provided).

A [NICE adoption support resource](#) was developed to support the implementation of recommendations from NICE [medical technologies guidance](#) on the use of

HeartFlow FFRCT for estimation of fractional flow reserve from CCTA (MTG32). The resource noted that FFR was not considered as part of the update of the guideline on chest pain (CG95) and that the successful adoption of this technology is dependent on the availability of adequate CCTA resources. The adoption of CT-FFR is a technology that is being supported by the [Accelerated Access Collaborative](#).

### **General**

A comment was raised relating to concern about over-investigation in patients with frailty/many comorbidities.

One topic expert noted that the ESC guidelines do not recommend any particular test to diagnose chest pain (no further details provided).

### **Impact statement**

Four publications reporting outcomes on the use of CT coronary angiography (CCTA) from the SCOT-HEART study were included in the 2019 surveillance review. The use of CCTA was associated with initiation of preventative therapies and reductions in MI in patients with possible angina (but less marked improvements in symptoms and quality of life). The included evidence on CCTA is considered to agree with existing recommendations on the use of CCTA and does not have potential impact on current recommendations. Much of the topic expert feedback received in this surveillance review focused on the perceived difficulties associated with the implementation of the recommendations on CCTA in this guideline. The positive example of implementation of CCTA in detection of CAD relating to this guideline on the NICE



[shared learning database](#) (published January 2012, pre-dating the 2016 update of this guideline) showed that CCTA performed better than exercise tolerance testing in exclusion of CAD, need for second-line investigations and reduced costs. However, it is acknowledged that this example is from a single case, whereas we have identified intelligence on national variation in resources available for implementation of CCTA in this surveillance review.

The topic expert feedback indicates geographical variation in the availability of suitable scanners and qualified radiologists and cardiologists. This observation is supported by the [statement](#) identified in this surveillance from the British Society of Cardiovascular Imaging and the analysis of Hospital Episodes Statistics data that provides additional detail on the variation in delivery of CCTA (copyright © 2019, the Health and Social Care Information Centre. Re-used with the permission of the Health and Social Care Information Centre. All rights reserved). This information on implementation issues will be fed back to NICE's implementation team and will also be relayed by NICE internal processes to other key stakeholders as appropriate.

Topic expert feedback commented on identification of incidental findings on CCTA, radiation exposure from CCTA, and over-investigation in patients with frailty or many comorbidities. However, no evidence was identified in this surveillance on these areas.

Topic expert feedback noted that the ESC guidelines do not recommend any particular test to diagnose chest pain (with no further details provided). This surveillance review identified the [2013](#)

[ESC guideline on the management of stable coronary artery disease](#). Since diagnostic testing in stable chest pain was considered in the subsequent 2016 update of NICE guideline on chest pain of recent onset: assessment and diagnosis (CG95), this information is not considered to have potential impact on recommendations in this guideline.

Topic expert feedback in this surveillance review indicated that the use of CT-FFR should be considered in the guideline. A focused search for evidence of the diagnostic accuracy of CT-FFR in people with chest pain of suspected cardiac origin identified 4 eligible studies. An additional trial (PLATFORM) suggested by a topic expert was also included in the summary of evidence. The diagnostic accuracy evidence demonstrates that CT-FFR shows promising diagnostic performance. Indeed, CT-FFR shows better diagnostic performance than CCTA in studies where these are directly compared. The PLATFORM study showed similar outcomes and quality of life for CT-FFR compared with usual testing but reduced costs. While the evidence for CT-FFR identified in this surveillance is promising, this is based on a relatively small number of studies. It is also noted that implementation of CT-FFR may be subject to the implementation issues already identified for CCTA as part of this surveillance review. CT-FFR adoption is being supported via the Accelerated Access Collaborative. Further evidence from large studies comparing CT-FFR with CCTA is needed before determining impact on current recommendations. Through surveillance we have become aware of a large, UK-based ongoing RCT comparing patients with new onset pain

assigned to CT-FFR or standard care (FORECAST). This area will be considered again at the next surveillance review of the guideline.

New evidence is unlikely to change guideline recommendations.

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## Research recommendations

### 1 Cost-effectiveness of multislice CT coronary angiography for ruling out obstructive CAD in people with troponin-negative acute coronary syndromes

Is multislice CT coronary angiography a cost-effective first-line test for ruling out obstructive CAD in people with suspected troponin-negative acute coronary syndromes?

#### Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

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### 2 Refining the use of telephone advice in people with chest pain

In what circumstances should telephone advice be given to people calling with chest pain? Is the appropriateness influenced by age, sex or symptoms?

#### Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### **3 Establishing a national registry for people who are undergoing initial assessment for stable angina**

Can a national registry of people presenting with suspected angina be established to allow cohort analysis of treatments, investigations and outcomes in this group? Such a registry would provide a vital resource for a range of important research projects, including:

- development and validation of a new score for assessing the pre-test probability of disease, addressing outstanding uncertainties in the estimation of the pre-test probability of CAD based on simple measures made at initial assessment (history, examination, routine bloods, resting 12-lead ECG)
- assessment of the extent to which new circulating biomarkers add additional information to measures made at initial assessment
- provision of a framework for trial recruitment without significant work-up bias allowing evaluation of the diagnostic and prognostic test performance of CT-based, MR, echocardiography and radionuclide technologies.

#### **Summary of findings**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

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### **4 Information about presenting and explaining tests**

All people presenting with chest pain will need to decide whether to accept the diagnostic and care pathways offered. How should information about the diagnostic pathway and the likely outcomes, risks and benefits, with and without treatment, be most effectively presented to particular groups of people, defined by age, ethnicity and sex?

#### **Summary of findings**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

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