National Guideline Centre

Draft for consultation

Chest pain of recent onset

Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin (update)

NICE guideline CG95

Appendices A – Q

1 June 2016

Draft for consultation

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians

The Royal College of Surgeons of England

Royal College of General Practitioners

Royal College of Nursing

NICE accredited

Disclaimer
Healthcare professionals are expected to take NICE guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and, where appropriate, their guardian or carer.

Funding
National Institute for Health and Care Excellence

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Appendix A: CG95 Surveillance review decision

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Recommendation for Guidance Executive

Clinical guideline
CG95: Chest pain of recent onset

Publication date
March 2010

Previous review dates
2 year review: 2012

Surveillance report for GE
December 2014

Surveillance recommendation
GE is asked to consider the proposal to update the following clinical questions in the guideline using the Standing Committee for Updates via the Clinical Guidelines Update Team:

Stable chest pain

- What is the incremental benefit and cost effectiveness of a clinical history, cardiovascular risk factors and a physical examination in evaluation of individuals with stable chest pain of suspected cardiac origin?
- What is the diagnostic utility of non-invasive and invasive tests for the evaluation of patients with stable chest pain of suspected cardiac origin?

Acute chest pain

- What is the utility and cost effectiveness of non-invasive tests in the evaluation of individuals with acute chest pain of suspected cardiac origin?
- What is the diagnostic utility of Multislice Computed Tomography (MSCT) coronary angiography in the diagnosis of patients with acute chest pain of suspected cardiac origin?
- What is the effectiveness and cost effectiveness of new, high-sensitivity troponin assay methods and other new cardiac biomarkers in low, medium, and high risk people with acute chest pain? (research recommendation)

It is proposed that the acute and stable sections are updated separately but in sequence by the same standing committee.

GE is asked to note that this 'yes to update' proposal will not be consulted on.

Key findings

			Potential impact on guidance	
			Yes	**No**
Evidence from previous surveillance review			✓	
Evidence identified from literature search			✓	
Feedback from Guideline Development Group			✓	
Anti-discrimination and equalities considerations			✓	
Feedback from Triage Panel meeting			✓	
No update	**CGUT update**	Standard update	Transfer to static list	Change review cycle
	✓			

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Surveillance review of CG95: Chest pain of recent onset

Recommendation for Guidance Executive

Background information

Guideline issue date: March 2010
2 year review: 2012
4 year review: 2014

NCC: National Clinical Guidelines Centre (formerly National Collaborating Centre for Acute and Chronic Conditions)

Outcome of four year surveillance review

1. A literature search for systematic reviews and RCTs was carried out between May 2012 (the end of the search period for the previous surveillance review) and June 2014 and relevant abstracts were assessed. Clinical feedback on the guideline was obtained from 7 members of the Guideline Development Group through a questionnaire, five of which felt that the guideline requires an update relating, in particular, to new higher sensitivity troponin assays, cardiac imaging and other biomarkers.

Outcome of two year surveillance review

2. A surveillance review was carried out in 2012 when it was recommended that the guideline needed an update, particularly in relation to computerised tomographic (CT) angiographies for the diagnosis of ACS in patients with acute chest pain; the use of highly sensitive troponins compared to the conventional cardiac troponins to diagnose ACS in patients with acute chest pain; and the use of updated Diamond-Forrester prediction model to better estimate the pre-test probability of coronary artery disease (CAD) in patients with stable chest pain without evidence for previous CAD. An update was not scheduled into the work programme following the two year surveillance review due to capacity.

3. New evidence that may impact on recommendations was identified relating to the following areas within the guideline:

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
Q: What is the incremental benefit and cost effectiveness of a clinical history, in evaluation of individuals with stable chest pain of suspected cardiac origin? **Q: What is the incremental benefit and cost-effectiveness of assessment of cardiovascular risk factors in evaluation of individuals with stable chest pain of suspected cardiac origin?** **Q: What is the incremental benefit and cost-effectiveness of a physical examination in evaluation of individuals with stable chest pain of suspected cardiac origin?**		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence identified from 2-year surveillance review One study1 was identified which found that an updated version of the Diamond–Forrester model, including age, sex, symptoms, coronary calcium scores, and cardiovascular risk factors, allowed for a more accurate estimation of the pre-test probability of CAD in stable chest pain without evidence for previous CAD. The authors concluded that this could lead to decreased referral for cardiac coronary angiography (CCA), a higher yield of angiography, and increased use of non-invasive testing for risk stratification. Evidence identified from 4-year surveillance review A systematic review2 assessing the diagnostic accuracy of clinical prediction models, reported that the six models identified showed good diagnostic accuracy for determining short-term outcomes in a pre-hospital population with suspected ACS. A meta-analysis3 aimed to determine the diagnostic value of single symptoms and signs for coronary heart disease (CHD) in patients with chest pain. In total, 172 studies were included covering 42 signs and symptoms. The findings indicated that the most accurate predictors for a diagnosis of stable CHD were history of CHD, known acute MI, typical angina, history of diabetes mellitus, exertional pain, history of angina pectoris, and male sex. These are consistent with the factors listed in the guideline.	Clinical feedback at the 2-year surveillance review suggested that there is additional evidence for the validity of using Diamond and Forrester to assess pre-test likelihood of CAD in contemporary practice. Feedback at the 4-year surveillance review indicated that there is evidence that the Diamond-Forrester risk prediction model over-estimates disease probability in patients with suspected angina. Feedback was also provided at both review points indicating that parameters to assess the pre-test likelihood of coronary disease in patients with stable chest pain have changed. Further information was sought from the GDG regarding these changes and the following reference was provided: Genders TS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, et al. A clinical prediction rule for the diagnosis of coronary artery	At the 2-year surveillance review, it was considered that the evidence relating to the use of an updated Diamond-Forrester prediction model in patients with stable chest pain could potentially have an impact on the current guideline. Although no further evidence was found relating to an updated Diamond-Forrester prediction model at the 4-year review, feedback from the GDG indicated that the Diamond-Forrester model may over estimate disease probability in suspected angina. Evidence from the 4-year surveillance review showed that 6 unspecified clinical prediction models demonstrated good diagnostic accuracy for determining short-term outcomes in a pre-hospital population with suspected ACS. Furthermore, clinical feedback indicated that the parameters to assess the pre-test likelihood of coronary disease in patients with stable chest pain have changed. Further evidence was provided which supported the view that the Diamond-Forrester model overestimates the probability of CAD, particularly in women. The evidence also suggested than an updated and extended version of the model improved its performance, supporting the evidence found at the 2-year surveillance review. The diagnostic pathway presented in the guideline

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
	disease: validation, updating, and extension. Eur Heart J2011;32:1316-30. An assessment of the abstract indicated that the Diamond-Forrester model overestimates the probability of CAD, particularly in women. A subsequent update and extension of the model in relation to the predictive value of age, sex, and type of chest pain improved its performance.	for people who present with stable chest pain, states that the application of the Diamond Forrester algorithm, as modified by consideration of additional risk factors, may permit a diagnosis of angina if the probability estimate is sufficiently high. The new evidence relating to an updated version of this model may therefore impact on this statement.
Clinical area: Investigations and diagnosis of patients with stable chest pain suspected to be stable angina - recommendations – 1.3.3.16, 1.3.4.4, 1.3.4.5, 1.3.4.6, 1.3.4.7, 1.3.4.8, 1.3.6.1		
Q: What is the diagnostic utility of non-invasive and invasive tests for the evaluation of patients with stable chest pain of suspected cardiac origin?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence identified from 2-year surveillance review</u> Through a focused search, 29 studies4-32 were identified related to non-invasive and invasive tests for patients with stable chest pain. The evidence showed that various non-invasive techniques including stress echocardiography, PET, myocardial perfusion imaging, CT coronary calcium score, coronary computed tomography, single-photon emission computed tomography (SPECT) and cardiovascular magnetic resonance, were effective in diagnosing CAD when compared to coronary angiography. Other studies found that exercise stress testing, real-time three-dimensional echocardiography and coronary artery calcium were not effective in the diagnosis of CAD when compared to angiography. <u>Evidence identified from 4-year surveillance review</u> **Computed coronary tomographic angiography** A systematic review and meta-analysis33 was identified which compared CCTA versus invasive coronary angiography in the diagnosis of CHD. For	Clinical feedback indicated that there is new evidence about diagnostic assessment in patients with suspected stable angina, including the comparative effectiveness of different imaging modalities. It was suggested that novel imaging techniques are now more widely available, particularly CT coronary angiography and MR perfusion imaging for diagnosis of chest pain. CT coronary angiography is also able to pick up other issues with lungs and mediastinum which might be missed in the old paradigm.	At the 2-year review it was considered that there was no new evidence which would invalidate the current guideline recommendations regarding assessment of patients with stable chest pain. **Computed coronary tomographic angiography** There was new evidence identified at the 4-year review which suggested that CCTA is an effective first line imaging test for the diagnosis of CAD, although it was not clear from all the abstracts what the level of CAD risk was in the study populations. There was also evidence relating to the diagnostic effectiveness of lower radiation CCTA. The new evidence for CCTA together with clinical feedback may potentially impact on the current guideline recommendations relating to the use of

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
the diagnosis of obstructive stenosis, compared to invasive coronary angiography as the reference standard, CCTA had high sensitivity and specificity, and at a pre-test probability of CHD of 50% or less, resulted in a lower cost per patient. However, at a pre-test probability of CHD of 70% or higher, invasive coronary angiography provided a lower cost per patient. For the diagnosis of functionally relevant stenosis, using intracoronary pressure measurement as the reference standard, CCTA had a higher sensitivity but lower specificity than invasive coronary angiography and both types of coronary angiography resulted in substantially higher cost per patient. As such, the review recommended that neither type of angiography should be used in the diagnosis of functionally relevant stenosis. The results of a meta-analysis34 (n=2567) indicated that patients undergoing CCTA as the first imaging test for the detection of CAD were more likely to undergo percutaneous or surgical revascularisation, and there was a reduction in the time to diagnosis and costs of care compared to non-CCTA patients. A meta-analysis35 (n=3300) was identified which compared image quality, diagnostic accuracy, and radiation dose of prospectively triggered CCTA with retrospectively gated CTA in patients with suspected or known CAD. The results indicated that the image quality and diagnostic accuracy of both types of CTA were similarly high, but with lower radiation doses provided by prospectively triggered coronary CTA. The findings of a systematic review and meta-analysis36 indicated that prospective ECG gating CCTA had high positive and negative predictive values (94% and 99% respectively) for the diagnosis of significant coronary stenosis. The authors concluded that the use of CCTA with prospective ECG gating allows for a reduced radiation exposure without a sacrifice in diagnostic efficacy in a population with high disease prevalence.	Radiation exposure from CT imaging is now lower with the newer scanners, so exposure will be less. It was reported that the value of zero calcium score for excluding CAD has been questioned. Furthermore, the advice to do a calcium score prior to CT angiography is now increasingly ignored because low radiation CT angiography is now available. One GDG member identified that the US guideline recommends exercise ECG as first diagnostic test for many patients, and neither the European nor the US guidelines recommend invasive coronary angiography for patients with high probability of disease. One GDG member suggested that the right test to use in lower risk groups is individualised and does not fit into a risk profile. As such, most health care professionals will determine the right diagnostic approach on a patient by patient basis. There is also a concern that the time needed to organise tests, such as	CCTA for the diagnosis of CAD in patients with stable chest pain, particularly the level of CAD risk at which to undertake CCTA. Currently the guideline only recommends 64-slice (or above) CT coronary angiography in people who have an estimated likelihood of CAD of 10–29% and have a calcium score of 1-400. For people with an estimated likelihood of CAD of 10–29% and a calcium score over 400, invasive coronary angiography is recommended. Non-invasive functional imaging is recommended for people who have an estimated likelihood of CAD of 30–60%, or for people who have an estimated likelihood of 61–90% and for whom coronary revascularisation is not being considered or invasive coronary angiography is not clinically appropriate. Invasive coronary angiography is recommended for people who have an estimated likelihood of 61–90% and for whom coronary revascularisation is being considered and invasive coronary angiography is clinically appropriate. **Functional stress testing** The GDG found that the diagnostic performance for diagnosing CAD did not support the use of one functional imaging test in preference to another and they concluded that the tests were generally comparable and any could be used. The new evidence from the 4 year surveillance review relating to functional imaging generally supports this conclusion and is therefore consistent with the guideline recommendation which states: When offering non-invasive functional imaging for myocardial ischaemia use:

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
A pilot RCT37 (n=180) found that CCTA was associated with increased revascularisation, lower costs and lower effective radiation dose compared with myocardial perfusion single-photon emission (MPS) CT in patients presenting with stable chest pain and suspected CAD. CTA and MPS resulted in comparable improvements in angina-specific health status. A systematic review38 was identified which compared 64-slice CCTA and coronary angiography (CA). Ten studies, including 1188 patients with angina with suspected or known CAD, were included in the review. At a patient level, 64-slice CCTA had positive predictive values ranging from 86-97% and negative predictive values of 76.9-100%. The authors concluded that the findings supported the use of 64-slice CCTA as a non-invasive alternative to CA for standalone diagnosis of significant stenosis in patients with angina. The results of a systematic review and meta-analysis39 (n=3,539) indicated that "triple rule-out" computed tomography (TRO CT) had high sensitivity and specificity for diagnosing CAD, although with greater radiation exposure and contrast exposure compared to non-TRO CT. A systematic review40 was identified which assessed the clinical effectiveness and cost-effectiveness of new-generation computed tomography (NGCCT) for diagnosing CAD in patients who are difficult to image using 64-slice computed tomography (e.g. obese patients, patients with high or irregular heartbeats and patients who have high levels of coronary calcium or a previous stent or bypass graft). The results indicated that NGCCT had good diagnostic accuracy for diagnosing CAD in difficult-to-image patients. An NGCCT only strategy was most cost-effective in patients with suspected CAD, whereas invasive coronary angiography after a positive NGCCT was the most cost-effective strategy in patients with known CAD.	nuclear scans and CT angiography is longer and may leave some high risk patients waiting for too long.	• 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.

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
Functional stress testing A meta-analysis41 (n=761) reported that stress perfusion cardiac MRI had a high sensitivity and specificity (89.1% and 84.9% respectively) for diagnosing flow-limiting obstructive CAD. The results of two RCTs42,43 suggested that stress real-time myocardial contrast echocardiography (RTMCE) increased the detection of CAD compared to conventional stress echocardiography. The results of a meta-analysis44 (n=13304) suggested that compared to exercise tolerance testing, stress imaging with MPI and stress echocardiography were the most accurate at stratifying cardiac risk in patients over 65 years of age with known or suspected CAD. A systematic review45 was identified which found that referral bias reduced the sensitivity and increased the specificity of exercise echocardiography and MPI for CAD. The authors concluded that further research was needed to assess the ability of these and other tests to rule-in rather than rule-out CAD. The results of a meta-analysis46 (n=11,862) found that Positron emission tomography (PET) had higher mean sensitivity than SPECT (92.6% v 88.3%) for diagnosing >50% stenosis in patients with known or suspected CAD. A second systematic review and meta-analysis47 indicated that rubidium (Rb)-82 PET provided more accurate diagnosis of obstructive CAD in comparison to SPECT. However, the review was limited by heterogeneity among study populations and referral bias in some studies. Finally, the results of a meta-analysis48 indicated that SPECT demonstrated moderate accuracy in diagnosing functional stenotic CAD, with a sensitivity and specificity of 77% and 77% respectively. The results of a meta-analysis49 suggested that cardiac magnetic		

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
resonance (CMR) had higher sensitivity for the detection of obstructive CAD than SPECT. A systematic review and meta-analysis50 was identified which aimed to assess the diagnostic accuracy of CMR imaging assessing myocardial viability in patients with chronic left ventricular (LV) dysfunction due to CAD. The review included 24 studies including 698 patients, evaluating myocardial viability using three techniques. Of the techniques assessed, Contrast delayed enhancement CMR had the highest sensitivity (95%) for predicting improved segmental LV contractile function after revascularisation, and low-dose dobutamine had the highest specificity (91%). The authors concluded that integrating the two methods would increase accuracy in evaluating patients with chronic LV dysfunction. An RCT51 was identified which assessed the effect of provider-directed imaging stress testing in lower-risk chest pain patients presenting to the emergency department. Patients were randomised to receive a CMR stress test (n=60) or a provider-selected stress test (n=60) (e.g. stress echo, CMR, cardiac catheterisation, nuclear, and coronary CT). The results of the study indicated that the median cost was higher for those receiving the CMR mandated test, with no differences in other outcomes between the two groups. A systematic review and meta-analysis52 examining the diagnostic accuracy of magnetocardiography (MCG) reported that MCG had a sensitivity of 83% and a specificity of 77% for the diagnosis of CAD. However, the authors reported that there was significant heterogeneity present in all meta-analyses. A systematic review and meta-analysis53 was identified which assessed the efficacy of Tissue Doppler imaging (TDI) in the diagnosis of CAD. The results showed that among CAD patients, TDI was associated with a decrease in the maximum systolic velocity at rest, and a decrease in		

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
maximum early diastolic velocity and maximum late diastolic velocity post stress. The authors concluded that TDI may have a role in the evaluation of CAD.		
Clinical area: Investigations and diagnosis of patients with acute chest pain - recommendations 1.2.6.6, 1.2.6.7		
Q: What is the utility and cost effectiveness of non-invasive tests in the evaluation of individuals with acute chest pain of suspected cardiac origin?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence identified from 2-year surveillance review</u> Through a focused search two studies were identified relating to stress testing in patients with acute chest pain. One study54 found that the addition of stress echocardiography to electrocardiography (ECG) was more effective than the individual tests alone in assessing patients with acute chest pain. The results of another study55 suggested that routine cardiac provocative cardiac testing added little to the diagnostic evaluation of low-risk young adult patients with acute coronary syndromes (ACS) compared to cardiac biomarkers. <u>Evidence identified from 4-year surveillance review</u> An RCT56 (n=1508) found that stress myocardial perfusion imaging (SMPI) added to a standard triage strategy (including clinical evaluation, serial ECGs, and cardiac markers) more effectively identified patients with ACS, with reduced hospital admission rates for participants who underwent SMPI compared to those who received just clinical assessment. The findings of an RCT57, including 105 intermediate-risk participants without a definite diagnosis of ACS following ECG and troponin testing, indicated that stress cardiac magnetic resonance (CMR) imaging in an observation unit reduced coronary artery revascularisation, hospital readmissions, and recurrent cardiac testing compared to usual care provided by cardiologists and internists. The results of a systematic review and meta-analysis58 (n=634) indicated that CMR had a higher sensitivity but lower specificity than low-dose	Clinical feedback indicated that the guideline needs to be updated. One of the reasons supporting this was that cardiac imaging has moved on over the last 4 years although no further details were provided.	The evidence identified at the 2-year surveillance review found limited evidence for stress testing in the assessment of patients presenting with acute chest pain in the emergency department. The evidence was considered to be in keeping with the current recommendations relating to the evaluation of individuals with acute chest pain, which include resting 12-lead ECG and troponin testing, as well as carrying out a physical examination and taking a detailed clinical history. The new evidence identified at the 4-year review suggests that non-invasive cardiac imaging, including stress myocardial perfusion imaging and stress cardiac magnetic resonance imaging, may be an alternative method for excluding other diagnoses in people with symptoms of ACS but with an uncertain diagnosis following ECG and troponin testing. Currently the guideline recommends a chest X-ray to help exclude complications of ACS, and early chest computed tomography (CT) should only be considered to rule out other diagnoses. The new evidence relating to non-invasive cardiac imaging may potentially impact on these recommendations.

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
dobutamine CMR for the assessment of myocardial stunning after acute myocardial infarction.		
Clinical area: Investigations and diagnosis of patients with acute chest pain - recommendation 1.2.6.7		
Q: What is the diagnostic utility of Multislice Computed Tomography (MSCT) coronary angiography in the diagnosis of patients with acute chest pain of suspected cardiac origin?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence identified from 2-year surveillance review</u> Through a high-level search, one systematic review59 was identified which determined that 64-section coronary computed tomography angiography (CCTA) was best for identifying patients with symptoms of ACS who can safely be discharged home rather than diagnosing patients who have positive symptoms. An additional focused literature search identified 13 studies60-72 relating to computerised angiographies in patients with acute chest pain. Overall, the studies showed that various forms of computerised angiography were diagnostically effective in detecting coronary artery disease (CAD) in patients presenting with acute chest pain in emergency departments. Two of the studies also showed that computed tomography was cost effective. <u>Evidence identified from 4-year surveillance review</u> An RCT73 comparing early CCTA and standard emergency department evaluation in patients with acute chest pain found that CCTA reduced hospital length of stay and admission rates, and lessened the increased cumulative radiation dose in women with suspected ACS compared to men. The results also indicated that there were no differences in major adverse cardiac events between CCTA and standard care, or between men and women. The results of a systematic review and meta-analysis74 indicated that CCTA led to an increase in referral rates for invasive coronary angiography and coronary revascularisation compared to usual care triage of acute chest pain in the emergency department. An RCT75 also found that CCTA	Clinical feedback indicated that there is evolving evidence for the use of CT coronary angiography in patients with acute chest pain and that the newer scanners that are now available have reduced radiation exposure.	During development of the guideline the GDG appraised the evidence for the use of MSCT for emergency department triage of patients with acute chest pain and was of the opinion that there was insufficient evidence on which to make a recommendation for its use in such patients. They acknowledged that this was an evolving area, which was the subject of on-going research, but the published evidence found to date was in small cohorts of patients and further research is required. There is new evidence identified at the 2 and 4 year surveillance reviews, as well as clinical feedback, which suggests that computed tomography is effective in the assessment of people with acute chest pain, including in the triage of patients in an emergency department. There may now be sufficient new evidence on which to make a recommendation for the use of computed tomography in such patients, thus impacting on the current guideline recommendation which states: Only consider early chest computed tomography (CT) to rule out other diagnoses such as pulmonary embolism or aortic dissection, not to diagnose ACS.

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
increased the frequency of revascularisations as well as improving the detection of significant coronary stenosis in patients with acute chest pain. An RCT76 (n=60) was identified which aimed to examine the dose reduction potential of low kV triple-rule-out dual-source CT angiography (TRO-CTA) in non-obese patients with acute chest pain. The subjective image quality of the low-dose TRO-CTA was rated similar to the standard protocol TRO-CTA. There were also no differences in the signal-to-noise and contrast-to-noise ratios in different vascular segments between the two groups. However, vessel attenuation was higher in the low dose TRO-CTA group than in the standard protocol group.		
Clinical area: Investigations and diagnosis of patients with acute chest pain (research recommendation) - recommendations – 1.2.1.10, 1.2.5		
Q: What is the effectiveness and cost effectiveness of new, high-sensitivity troponin assay methods and other new cardiac biomarkers in low, medium, and high risk people with acute chest pain?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence identified from 2-year surveillance review</u> Through a focused literature search, 27 studies77-94 were identified. The new evidence indicated that high sensitive troponins are more effective than conventional cardiac troponins in the early diagnosis of acute myocardial infarction and ACS. A further four studies95-98 were identified which indicated that copeptin, together with high sensitive troponin, improves diagnostic performance in early diagnosis of patients with suspected MI. It was considered that the new evidence relating to high-sensitive troponin and copeptin could potentially impact on the current recommendations in the guideline. Six more studies99-104 were identified which looked at other biomarkers for ACS, including amino terminal pro-B-type natriuretic peptide,	At both the 2-year and 4-year review points, clinical feedback was provided which identified that there is new evidence relating to highly sensitive troponin assays for testing patients with suspected ACS. Feedback suggested that the new troponin assays are now increasingly used and have reduced the timescales from symptom onset to results from 10-12 hours to 3-6 hours. NICE currently has no plans to update MTG4. Feedback from the Newcastle and York External Assessment Centre has indicated	The clinical evidence for the following biomarkers was assessed as part of a review question in the guideline: troponin I, troponin T, creatine kinase (CK), creatine kinase-MB (CKMB), creatine kinase-MB isoforms (CKMB isoforms) and myoglobin. An additional research recommendation was made with the aim of investigating newer more sensitive troponin assays which may offer advantages over previous assays in terms of diagnostic accuracy, and allow exclusion of MI earlier than the 12 hour time frame currently required. The research recommendation also sought to assess other proposed biomarkers compared to the best available troponin assays. At the 2-year surveillance review, it was considered that the evidence relating to high sensitive

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
unbound free fatty acids, high-sensitivity C-reactive protein, pentraxin 3 and serum ischemia modified albumin. These were just single studies and it was therefore considered that more evidence would be required to support these findings before consideration for inclusion in the guideline. <u>Evidence identified from 4-year surveillance review</u> The results of an RCT105 (n=542) suggested that a rapid diagnostic pathway (including Thrombolysis in Myocardial Infarction score, electrocardiography and 0- and 2-hour troponin tests) increased the proportion of patients with chest pain discharged within 6 hours compared to a standard-care diagnostic pathway (including troponin test on arrival at hospital, prolonged observation, and a second troponin test 6-12 hours after onset of pain) for the assessment of patients with acute chest pain consistent with ACS. An RCT106 was identified which assessed changes in contemporary sensitive troponin I (TnI) levels in 7,863 patients after MI or unstable angina. The findings indicated that both baseline TnI levels and increases in TnI levels after 1 year were linked with an increased risk of CHD death and myocardial infarction. A second study, a systematic review and meta-analysis107 including 4 studies (n=2033), also found that elevated high-sensitivity troponin (hs-Tn) were associated with an increased risk of mortality. It is unlikely that this new evidence will impact on current recommendations. New Diagnostics guidance, published in October 2014, reviewed the clinical and cost-effectiveness of three types of high-sensitive troponin assay (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays) compared to standard troponin testing over 10–12 hours. The guidance recommends the Elecsys Troponin T high-sensitive assay and ARCHITECT STAT High Sensitive Troponin-I assay as options for the early rule out of non-ST-segment-elevation myocardial infarction (NSTEMI) in people presenting to an emergency department with chest pain and suspected ACS. The assays are recommended for use	that that the claimed benefits of the copeptin assay have been superseded by high-sensitivity troponin assays in terms of faster diagnosis of MI.	troponins compared to the conventional cardiac troponins to diagnose ACS in patients with acute chest pain could potentially impact on the current guideline recommendations. The new Diagnostics guidance reviewed the clinical and cost-effectiveness of high-sensitive troponins compared to standard troponin testing over 10–12 hours, and recommended the Elecsys Troponin T high-sensitive assay and ARCHITECT STAT High Sensitive Troponin-I assay as options for the early rule out of non-ST-segment-elevation myocardial infarction (NSTEMI) in people presenting to an emergency department with chest pain and suspected ACS. The assays are recommended for use with 'early rule-out protocols', which typically include a blood sample for cardiac troponin I or T taken at initial assessment in an emergency department and a second blood sample taken after 3 hours. Currently CG95 only recommends: Take a blood sample for troponin I or T measurement on initial assessment in hospital. These are the preferred biochemical markers to diagnose acute MI; and take a second blood sample for troponin I or T measurement 10–12 hours after the onset of symptoms. The evidence identified at the 2 and 4 year surveillance reviews, together with the Diagnostics Guidance and clinical feedback, indicate that high sensitive troponins are effective in the diagnosis of acute MI and ACS, and therefore may impact on the current recommendations in the guideline. Evidence was identified at the 2-year surveillance review regarding the improved diagnostic

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
with 'early rule-out protocols', which typically include a blood sample for cardiac troponin I or T taken at initial assessment in an emergency department and a second blood sample taken after 3 hours. The results of a meta-analysis108 indicated that circulating miRNAs, particularly miR-499 and miR-133a, had good diagnostic accuracy for myocardial infarction. A systematic review and meta-analysis109 (n=941) was identified which assessed the early diagnostic performance of glycogen phosphorylase isoenzyme BB (GPBB) in patients with suspected AMI. The results of the meta-analysis found that GPBB had a sensitivity of 0.854 and specificity of 0.767, although there was high heterogeneity across the included studies. The authors concluded that GPBB does not currently provide efficient diagnosis of AMI when used as a stand-alone test. Two systematic reviews and meta-analyses110,111 were identified which found that the addition of heart-type fatty acid binding protein (H-FABP) to troponin increased sensitivity but decreased specificity compared to troponin alone for the diagnosis of MI. MTG4 (NICE medical technologies guidance), published in June 2011, was identified through the intelligence gathering search for the guideline. MTG4 stated that the BRAHMS copeptin assay shows potential to reduce the time taken to rule out myocardial infarction in patients presenting with acute chest pain, when used in combination with cardiac troponin testing. However, it stated that there is currently insufficient evidence on its use in clinical practice to support the case for routine adoption of the BRAHMS copeptin assay in the NHS and recommended that further research be undertaken in the UK clinical setting to compare the BRAHMS copeptin assay in combination with cardiac troponin testing against sequential cardiac troponin testing for ruling out MI. As part of the evidence base for this guidance, two studies considered at the previous		performance of copeptin together with high sensitive troponin in patients with MI. It was considered that this evidence could potentially impact on the current guideline recommendations. However, MTG4, which was published in June 2011, reviewed the evidence for copeptin assay including two studies considered at the 2 year surveillance review. It found that whilst the assay showed potential to reduce the time taken to rule out MI when used in combination with cardiac troponin testing, there was insufficient evidence on its use in clinical practice to support the case for routine adoption in the NHS and recommended that further research be undertaken in the UK clinical setting to compare the BRAHMS copeptin assay in combination with cardiac troponin testing against sequential cardiac troponin testing for ruling out MI. Further evidence relating to copeptin was identified at the 4 year surveillance review which also showed that copeptin and troponin combined had increased sensitivity for diagnosing MI. NICE currently has no plans to update MTG4 and feedback has indicated that that the claimed benefits of the copeptin assay have been superseded by high-sensitivity troponin assays in terms of faster diagnosis of MI. Evidence was also identified in relation to other biomarkers, including heart-type fatty acid binding protein which increased the sensitivity of troponin compared to troponin alone, and miRNAs which had good diagnostic accuracy for MI. In summary, the evidence and clinical feedback

Clinical area: Assessment of patients with stable chest pain - recommendation – 1.3.1.1, 1.3.2.1, 1.3.2.2, 1.3.3.1, 1.3.3.2, 1.3.3.3, 1.3.3.4, 1.3.3.16		
surveillance review (Keller et al., 2010; Reichlin et al., 2009) were considered. Through the literature search for the 4-year surveillance review, two systematic reviews112,113 were identified which published after MTG4. The studies found that copeptin and troponin combined improved sensitivity for the diagnosis of acute MI compared with troponin alone.		relating to high sensitive troponins and other biomarkers for MI, suggest that there is potentially new evidence in this area which should be considered for inclusion in the guideline.

Ongoing research

4. The following ongoing trials relevant to this guideline were identified through clinical feedback and the literature search for the surveillance review:
   - The impact of the HEART risk score in the early assessment of patients with acute chest pain: design of a stepped wedge, cluster randomised trial. Estimated study completion date – November 2014.
   - HTA - 13/04/108: 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
   - The role of cardiovascular magnetic resonance imaging and computed tomography angiography in suspected non-ST-elevation myocardial infarction patients: design and rationale of the CARdiovascular Magnetic rEsoNance imaging and computed Tomography Angiography (CARMENTA) trial.
   - Role of multidetector computed tomography in the diagnosis and management of patients attending the rapid access chest pain clinic, The Scottish computed tomography of the heart (SCOT-HEART) trial. The study is expected to report in 2014.
   - Design and rationale of the MR-INFORM study: stress perfusion cardiovascular magnetic resonance imaging to guide the management of patients with stable coronary artery disease.
   - DETermination of the role of OXygen in suspected Acute Myocardial Infarction trial. Estimated Study Completion Date: December 2015.
   - A randomized controlled trial of oxygen therapy in acute myocardial infarction Air Verses Oxygen In myocarDial infarction study (AVOID Study).

Anti-discrimination and equalities considerations

5. Clinical feedback from the GDG indicated that there is geographical variation in access to diagnostic testing for patients with stable chest pain.

Implications for other NICE programmes

6. This guideline relates to the Quality Standard for Acute coronary syndromes (including myocardial infarction) (QS68 published September 2014) and to the Quality Standard for Stable angina (QS21 published August 2012).

7. None of the quality statements in QS68 are likely to be affected by the proposed areas for update.

8. The proposed area for update 'Assessment of patients with stable chest pain' is likely to affect Quality statement 1: Diagnostic investigation in QS21. In particular, recommendation 1.3.3.16 from CG95 was used as the guideline source for Statement 1 and recommendations 1.3.3.1, 1.3.3.16 and 1.3.4.4-7 are the sources for the definitions attached to this statement.

Triage Panel recommendation

9. The new evidence identified through the surveillance review of CG95 which may potentially impact on guideline recommendations was considered by the Triage Panel to determine the most appropriate route to commission an update.

    i. Assessment of patients with stable chest pain:

        a. What is the incremental benefit and cost effectiveness of a clinical history, cardiovascular risk factors and a physical examination in evaluation of individuals with stable chest pain of suspected cardiac origin?
        - The Triage Panel agreed that this question needs to be updated to reflect new evidence relating to a revised version of the Diamond and Forrester model. The evidence suggested that the current Diamond and Forrester model overestimates the probability of coronary artery disease (CAD). The revised model would therefore impact on the recommended appropriate first-line diagnostic investigation required based on a person's estimated likelihood of CAD. It was felt that the review question could be amended to ensure focus around diagnosing CAD.
        - **Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

    ii. Investigations and diagnosis of patients with stable chest pain suspected to be stable angina:

        a. What is the diagnostic utility of non-invasive and invasive tests for the evaluation of patients with stable chest pain of suspected cardiac origin?
        - The Triage Panel agreed that this question would need to be updated and suggested that the body of evidence on all imaging modalities, including functional imaging should be evaluated whilst the current economic model could be adapted to include more comparators.
        - **Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

iii. Investigations and diagnosis of patients with acute chest pain:

a. What is the utility and cost effectiveness of non-invasive tests in the evaluation of individuals with acute chest pain of suspected cardiac origin?

- The Triage Panel indicated that the new evidence relating to this question was less convincing. However, the group felt that if an update of Computed Tomography (CT) angiography for acute chest pain was being considered, evidence relating to functional imaging should also be evaluated. In terms of priorities, the group suggested that functional testing for acute coronary syndromes (ACS) should be a lower priority.
- **Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

b. What is the diagnostic utility of Multislice Computed Tomography (MSCT) coronary angiography in the diagnosis of patients with acute chest pain of suspected cardiac origin?

- The Triage Panel agreed that the evidence relating to this question has moved on significantly since the guideline was developed and that the guideline recommendation relating to CT scanning would need updating. It was acknowledged that there is an ongoing HTA trial (RAPID-CTCA) in this area but that this is unlikely to report for at least two years. However, in order to avoid hindering recruitment to the trial and repeating any review of evidence already undertaken, the group agreed that an update should consider the role of CT angiography in patient groups who would not be eligible for the trial.
- **Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

c. What is the effectiveness and cost effectiveness of new, high-sensitivity troponin assay methods and other new cardiac biomarkers in low, medium, and high risk people with acute chest pain?

- The Triage Panel agreed that this question needs to be updated as the guideline recommendation relating to the use of standard troponin assays has been superseded by current clinical practice and the recently published Diagnostics guidance (DG15) which recommends high-sensitivity troponin testing for the early rule out or diagnosis of acute myocardial infarction in people with acute chest pain. The Triage Panel indicated that there was potential for CG95 to cross reference to the Diagnostics guidance but that an additional check was needed to determine if any supplementary recommendations might be required.
- **Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

Conclusion

10. Through the surveillance review of CG95 new evidence which may potentially impact guideline recommendations was identified in the following areas:

    - Assessment of patients with stable chest pain
    - Investigations and diagnosis of patients with stable chest pain suspected to be stable angina
    - Investigations and diagnosis of patients with acute chest pain

11. All these areas were considered by the Triage Panel and were assessed as requiring an update at this time. It was determined that all the areas identified should be updated using the Standing Committee for Updates via the Clinical Guidelines Update Team.

12. For all other areas of the guideline no evidence was identified which would impact on recommendations.

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Centre for Clinical Practice
December 2014

A.1 Decision matrix

Surveillance and identification of triggers for updating CG95. The table below provides summaries of the evidence for key questions for which studies were identified.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
95-01: What are the education and information needs in adults presenting with chest pain to optimise their understanding of the diagnostic process and their participation in decisions about their investigations?			
No evidence identified.	An RCT114 (n=204) was identified which aimed to assess the impact on patient preferences of a decision aid showing the pre-test probability of acute coronary syndrome (ACS) and available management options. The results suggested that compared to usual care, the decision aid increased patient knowledge and reduced the proportion of patients who decided to undergo observation unit admission and cardiac stress testing, with no major adverse cardiac events.	None identified through GDG questionnaire.	The new evidence is consistent with the current guideline recommendations which state: clearly explain the options to people at every stage of investigation; make joint decisions with them and take account of their preferences; provide information about any proposed investigations using everyday, jargon-free language; and offer information about the risks of diagnostic testing.
People presenting with acute chest pain			
95-02: What is the incremental benefit and cost effectiveness of a clinical history in evaluation of individuals with acute chest pain of suspected cardiac origin? 95-03: What is the incremental benefit and cost effectiveness of assessment of cardiovascular risk factors in evaluation of individuals with acute chest pain of suspected cardiac origin?			

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
95-04: What is the incremental benefit and cost effectiveness of a physical examination in evaluation of individuals with acute chest pain of suspected cardiac origin?			
Through a high level search two systematic reviews were identified. The results of one of the studies115 showed that the Thrombolysis in Myocardial Infarction (TIMI) risk score is an effective risk stratification tool for patients in the emergency department with potential ACS but the authors concluded that it should not be used as the sole means of determining patient disposition. Another study116 found that no instrument assisting in the diagnostic investigation of patients with suspected ACS consistently fulfils the safety requirements of clinicians. Through a focused search one study117 was identified which found that individual historical and examination findings are effective in diagnosing AMI in patients with acute chest pain. This was considered to be in keeping with the current guideline recommendation.	The results of a systematic review and meta-analysis118 indicated that telemedicine systems, including early telemetry of electrocardiograms (ECG), can reduce the risk of in-hospital mortality from AMI. An RCT119 (n=7083) was identified which evaluated the impact on quality and safety of electronic risk alerts to primary care physicians for patients with chest pain. The study found that the electronic alerts made no difference in terms of risk-appropriate management of both high and low risk patients. An RCT120 (n=550) was identified which assessed the impact of providing pre-test probability estimates for both ACS and pulmonary embolism and prescriptive clinical advice on radiation exposure and health care costs. Patients with chest pain and dyspnoea, non-diagnostic ECGs, and no obvious diagnosis	None identified through GDG questionnaire.	The new evidence relating to telemedicine systems suggests that they may reduce the risk of mortality from ACS. The use of telemedicine is not specifically covered in the guideline, although the GDG's preferred option was for a pre-hospital ECG, ideally with advanced notification to hospital, providing this did not delay transfer of the patient to hospital. It is unlikely that this evidence will impact on current recommendations which state: Refer people to hospital as an emergency if an ACS is suspected 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; and take a resting 12-lead ECG as soon as possible. When people are referred, send the results to hospital before they arrive if possible. In terms of electronic risk alerts in primary care, the evidence suggests that these demonstrated no impact on the management of patients, therefore it is unlikely to impact on current guideline recommendations.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	were included. The findings indicated that pre-test probability estimates and clinical advice reduced exposure to chest radiation and health care costs, with no increase in adverse events. The findings of a secondary analysis from an RCT121 indicated that in patients with CAD, symptoms of chest pain and arm pain are more common in patients with ACS, and symptoms of shortness of breath and dizziness are more common in patients without ACS. The findings of a meta-analysis3 also indicated that the most accurate tests for diagnosing ACS were pain radiation to right arm/shoulder and palpitation, and visceral pain.		With regards to risk scores for ACS, the evidence identified at the 2-year review suggested that no single risk score or instrument was effective in diagnosing the cause of chest pain. This was considered to be in keeping with the current guideline recommendations. However, a study identified at the 4-year review suggested that the use of pre-test probability estimates reduced unnecessary diagnostic assessments for patients with symptoms suggestive of ACS but with non-diagnostic ECGs. For the assessment in hospital for people with a suspected ACS, the guideline recommends resting 12-lead ECG and troponin testing, as well as carrying out a physical examination and taking a detailed clinical history. The guideline further states: Only consider early chest computed tomography (CT) to rule out other diagnoses such as pulmonary embolism or aortic dissection, not to diagnose ACS. It is probable that pre-test likelihood estimates would take into account the information gathered by clinicians through physical examinations and in taking a clinical history. It is therefore unlikely that this evidence to would impact on the current guideline

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
			recommendations. Evidence relating to symptoms associated with ACS is consistent with the current guideline recommendations which state: Initially assess people for any of the following symptoms, which may indicate an ACS, including pain in the chest and/or other areas (for example, the arms, back or jaw) lasting longer than 15 minutes, and chest pain associated with nausea and vomiting, marked sweating or breathlessness.
95-05: Are the symptoms and description of the symptoms different in women presenting with acute chest pain of suspected cardiac origin compared with men?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-06: Are the symptoms and description of the symptoms different in Black and Ethnic Minorities presenting with acute chest pain of suspected cardiac origin compared with Caucasians?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-07: What is the diagnostic utility of pain relief with nitrates in the identification of patients with acute chest pain of cardiac origin?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-08: What is the utility and cost effectiveness of the resting ECG in evaluation of individuals with chest pain of suspected cardiac origin?			
No evidence identified.	A systematic review and meta-analysis122 was identified which found insufficient evidence to	None identified through GDG questionnaire.	The new evidence suggests that using ECG technicians can speed up the process for undertaking in-hospital ECGs

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	support the use of ECG-based signal analysis technologies for detecting ischemia or infarct in patients with ACS compared with the standard 12-lead ECG. The findings of an RCT123 (n=354) indicated that use of an ECG technician (ECG-T) reduced in-hospital first medical contact-to-ECG times compared to a control intervention.		for patients with chest pain. The current recommendation relating to ECGs states: Take a resting 12-lead ECG as soon as possible. There are no recommendations relating to who should take the ECG other than that a review of resting 12-lead ECGs should be obtained by a healthcare professional qualified to interpret them as well as taking into account automated interpretation. It is therefore unlikely that the new evidence will impact on the current recommendations.
95-09: What is the utility and cost effectiveness of non-invasive tests in the evaluation of individuals with acute chest pain of suspected cardiac origin? (new question)			
Through a focused search two studies were identified relating to stress testing in patients with acute chest pain. One study54 found that the addition of stress echocardiography to electrocardiography (ECG) was more effective than the individual tests alone in assessing patients with acute chest pain. The results of another study55 suggested that routine cardiac provocative cardiac testing added little to the diagnostic evaluation of low-risk young adult patients with ACS compared to cardiac biomarkers.	An RCT56 (n=1508) found that stress myocardial perfusion imaging (SMPI) added to a standard triage strategy (including clinical evaluation, serial ECGs, and cardiac markers) more effectively identified patients with ACS, with reduced hospital admission rates for participants who underwent SMPI compared to those who received just clinical assessment. The findings of an RCT57, including 105 intermediate-risk participants without a definite	Clinical feedback indicated that the guideline needs to be updated. One of the reasons supporting this was that cardiac imaging has moved on over the last 4 years although no further details were provided.	The evidence identified at the 2-year surveillance review found limited evidence for stress testing in the assessment of patients presenting with acute chest pain in the emergency department. The evidence was considered to be in keeping with the current recommendations relating to the evaluation of individuals with acute chest pain, which include resting 12-lead ECG and troponin testing, as well as carrying out a physical examination and taking a detailed clinical history. The new evidence identified at the 4-year review suggests that non-invasive

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	diagnosis of ACS following ECG and troponin testing, indicated that stress cardiac magnetic resonance (CMR) imaging in an observation unit reduced coronary artery revascularisation, hospital readmissions, and recurrent cardiac testing compared to usual care provided by cardiologists and internists. The results of a systematic review and meta-analysis58 (n=634) indicated that CMR had a higher sensitivity but lower specificity than low-dose dobutamine CMR for the assessment of myocardial stunning after acute myocardial infarction.		cardiac imaging, including stress myocardial perfusion imaging and stress cardiac magnetic resonance imaging, may be an alternative method for excluding other diagnoses in people with symptoms of ACS but with an uncertain diagnosis following ECG and troponin testing. Currently the guideline recommends a chest X-ray to help exclude complications of ACS, and early chest computed tomography (CT) should only be considered to rule out other diagnoses. The new evidence relating to non-invasive cardiac imaging may potentially impact on these recommendations.
95-10: What is the utility and cost effectiveness of the chest X ray in evaluation of individuals with chest pain of suspected cardiac origin?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-11: In adults presenting with acute chest pain of suspected cardiac origin, what is the clinical and cost effectiveness of giving oxygen compared with a placebo?			
No evidence identified.	An update of a systematic review124 of RCTs was identified which investigated whether routine use of inhaled oxygen in AMI improves patient-centred outcomes, including pain and	None identified through GDG questionnaire.	The evidence reviewed in the guideline suggested that supplementary oxygen may be harmful in patients with an acute MI. It was therefore recommended that: Do not routinely administer oxygen, but monitor oxygen saturation using pulse

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	death. One new trial was identified through the search for the systematic review, resulting in a total of four trials involving 430 participants. The results showed that use of oxygen increased the risk of death compared to air, although the authors concluded that this could be the results of chance due to the small number of deaths recorded. The results of an RCT125 (n=136) combined through meta-analysis with the results of two previous studies indicated that there were no differences in mortality and infarct size in patients with STEMI administered with high-concentration or titrated oxygen for 6 hours after presentation. However, there was clinical uncertainty over the results and the authors concluded that further studies would be needed.		oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to: people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94–98%; or people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88–92% until blood gas analysis is available. The new evidence was inconclusive regarding the harmful effects of oxygen in people with MI, although one study suggested that it may lead to an increased risk of mortality. The new evidence is therefore consistent with the current guideline recommendations.
95-12: In adults presenting with acute chest pain, what is the clinical and cost effectiveness of pain (e.g. sublingual and buccal nitrates, diamorphine, morphine with anti-emetic) management?			
No evidence identified.	An RCT126 (n=1763) was identified which evaluated the impact of a combination of anxiolytics and analgesics	None identified through GDG questionnaire.	The new evidence regarding pain relief is consistent with current guideline recommendations which state: Offer pain relief as soon as possible. This may be

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	(midazolam and morphine) compared to analgesics (morphine) alone in the pre-hospital treatment of patients with suspected ACS. The findings of the study indicated that combined anxiolytics and analgesics were more effective at reducing anxiety compared to analgesics alone. However, there was no difference in patients' estimation of pain between the two groups.		achieved with GTN (sublingual or buccal), but offer intravenous opioids such as morphine, particularly if an acute myocardial infarction (MI) is suspected.
95-13: In adults presenting with chest pain of suspected cardiac origin, what is the clinical and cost effectiveness of anti-platelet therapy (aspirin, clopidogrel alone or in combination) compared with a placebo?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-14: In patients presenting with suspected acute coronary syndromes, what is the clinical and cost effectiveness of early treatment with glucose-insulin-potassium compared with a placebo? (new question)			
No evidence identified.	The results of an RCT127 (n=911) suggested that there were no differences in progression to myocardial infarction or 30-day survival following out-of hospital emergency administration of glucose-insulin-potassium (GIK) in patients with suspected ACS. However, there was a reduction in the composite outcome of cardiac arrest or in-hospital mortality in patients who received GIK	None identified through GDG questionnaire.	Administration of glucose-insulin-potassium was not covered in the guideline. There was limited evidence from the study that it might improve outcomes of cardiac arrest or in-hospital mortality. However, further consistent evidence would be needed before this can be considered for inclusion in the guideline.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	compared to placebo.		
95-15: What is the utility and cost effectiveness of cardiac biomarkers in evaluation of individuals with chest pain of suspected cardiac origin?			
Three studies were identified relating to cardiac biomarkers which were all considered to support the current guideline recommendations. One study128 showed that measurement of cardiac troponin I is sufficient for diagnosis of patients with chest pain when compared to myoglobin and the MB isoenzyme of creatine kinase (CK-MB). Another study129 found that that the most clinically accurate biomarker for the early diagnosis of myocardial infarction is the use of cardiac troponin T assay alone, rather than a multiple-biomarker approach. The results of another study130 showed that point-of-care cardiac biomarker panel consisting of CK-MB, myoglobin, and troponin did not reduce health care costs.	Two studies were identified which examined point of care (POC) tests in patients with suspected of acute myocardial infarction (AMI). One RCT131 (n=2243) and economic analysis evaluated a POC panel of CK-MB(mass), myoglobin and troponin compared with standard care across 6 hospitals. There was heterogeneity in the results in terms of the difference in the proportion of patients successfully discharged and the mean cost per patient for POC assessment. Another systematic review132 examining the diagnostic accuracy of POC tests found that the negative predictive values for single biomarker testing ranged from 31 to 97%, and for a multi-marker approach from 59 to 100%, for test results within 6 hours after symptom onset or in a median time from symptoms onset to testing of 3 hours. The new evidence does not support the use of point-of-care	None identified through GDG questionnaire.	The evidence from the 2-year surveillance review on troponin supports the current recommendation in the guideline which states: Take a blood sample for troponin I or T measurement on initial assessment in hospital. These are the preferred biochemical markers to diagnose acute MI. In relation to point-of-care tests, there was no consistent evidence from both the 2 and 4 year surveillance reviews of their effectiveness.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	tests in patients due to the heterogeneity in the results in both studies.		
95-16: What is the diagnostic utility of Multislice Computed Tomography (MSCT) coronary angiography in the diagnosis of patients with acute chest pain of suspected cardiac origin?			
Through a high-level search, one systematic review59 was identified which determined that 64-section coronary computed tomography angiography (CCTA) was best for identifying patients with symptoms of ACS who can safely be discharged home rather than diagnosing patients who have positive symptoms. This evidence was considered to be in line with the current recommendations. An additional focused literature search identified 13 studies60-72 relating to computerised angiographies in patients with acute chest pain. Overall, the studies showed that various forms of computerised angiography were diagnostically effective in detecting coronary artery disease (CAD) in patients presenting with acute chest pain in emergency departments. Two of the studies also showed that computed tomography was cost effective. It was considered that this	An RCT73 comparing early CCTA and standard emergency department evaluation in patients with acute chest pain found that CCTA reduced hospital length of stay and admission rates, and lessened the increased cumulative radiation dose in women with suspected ACS compared to men. The results also indicated that there were no differences in major adverse cardiac events between CCTA and standard care, or between men and women. The results of a systematic review and meta-analysis74 indicated that CCTA led to an increase in referral rates for invasive coronary angiography and coronary revascularisation compared to usual care triage of acute chest pain in the emergency department. An RCT75 also found that CCTA increased the frequency of revascularisations as	Clinical feedback indicated that there is evolving evidence for the use of CT coronary angiography in patients with acute chest pain and that the newer scanners that are now available have reduced radiation exposure.	During development of the guideline the GDG appraised the evidence for the use of MSCT for emergency department triage of patients with acute chest pain and was of the opinion that there was insufficient evidence on which to make a recommendation for its use in such patients. They acknowledged that this was an evolving area, which was the subject of on-going research, but the published evidence found to date was in small cohorts of patients and further research is required. There is new evidence identified at the 2 and 4 year surveillance reviews, as well as clinical feedback, which suggests that computed tomography is effective in the assessment of people with acute chest pain, including in the triage of patients in an emergency department. There may now be sufficient new evidence on which to make a recommendation for the use of computed tomography in such patients, thus impacting on the current guideline recommendation which states: Only

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
evidence that may potentially change the current guideline recommendation relating to computed tomography for assessment of acute chest pain.	well as improving the detection of significant coronary stenosis in patients with acute chest pain. An RCT76 (n=60) was identified which aimed to examine the dose reduction potential of low kV triple-rule-out dual-source CT angiography (TRO-CTA) in non-obese patients with acute chest pain. The subjective image quality of the low-dose TRO-CTA was rated similar to the standard protocol TRO-CTA. There were also no differences in the signal-to-noise and contrast-to-noise ratios in different vascular segments between the two groups. However, vessel attenuation was higher in the low dose TRO-CTA group than in the standard protocol group.		consider early chest computed tomography (CT) to rule out other diagnoses such as pulmonary embolism or aortic dissection, not to diagnose ACS.
People presenting with stable chest pain			
95-17: What is the incremental benefit and cost effectiveness of a clinical history, in evaluation of individuals with stable chest pain of suspected cardiac origin? 95-18: What is the incremental benefit and cost-effectiveness of assessment of cardiovascular risk factors in evaluation of individuals with stable chest pain of suspected cardiac origin? 95-19: What is the incremental benefit and cost-effectiveness of a physical examination in evaluation of individuals with stable chest pain of suspected			

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
cardiac origin?			
One study1 was identified which found that an updated version of the Diamond–Forrester model, including age, sex, symptoms, coronary calcium scores, and cardiovascular risk factors, allowed for a more accurate estimation of the pre-test probability of CAD in stable chest pain without evidence for previous CAD. The authors concluded that this could lead to decreased referral for cardiac coronary angiography (CCA), a higher yield of angiography, and increased use of non-invasive testing for risk stratification. It was considered that this new evidence could potentially change the current guideline recommendations.	The results of meta-analysis133 (n=927) suggested that there was an increased risk of CAD in patients with breast arterial calcifications seen on a mammography. A systematic review2 assessing the diagnostic accuracy of clinical prediction models, reported that the six models identified showed good diagnostic accuracy for determining short-term outcomes in a pre-hospital population with suspected ACS. A meta-analysis3 aimed to determine the diagnostic value of single symptoms and signs for coronary heart disease (CHD) in patients with chest pain. In total, 172 studies were included covering 42 signs and symptoms. The findings indicated that the most accurate predictors for a diagnosis of stable CHD were history of CHD, known acute MI, typical angina, history of diabetes mellitus, exertional pain, history of angina pectoris, and male sex.	Clinical feedback at the 2-year surveillance review suggested that there is additional evidence for the validity of using Diamond and Forrester to assess pre-test likelihood of CAD in contemporary practice. Feedback at the 4-year surveillance review indicated that there is evidence that the Diamond-Forrester risk prediction model over-estimates disease probability in patients with suspected angina. Feedback was also provided at both review points indicating that parameters to assess the pre-test likelihood of coronary disease in patients with stable chest pain have changed. Further information was sought from the GDG regarding these changes and the following reference was provided: Genders TS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, et al. A clinical prediction rule for the	The new evidence identified relating to increased risk of CAD in patients with breast arterial calcifications is not currently covered in the guideline. However, it is unlikely that it will impact on the current recommendations for diagnosing stable angina caused by CAD which state diagnose stable angina based on clinical assessment alone or plus diagnostic testing. In terms of clinical assessment, this would include taking a detailed clinical history, including any cardiovascular risk factors, for which breast arterial calcifications seen on a mammography could be one risk factor. At the 2-year surveillance review, it was considered that the evidence relating to the use of an updated Diamond-Forrester prediction model in patients with stable chest pain could potentially have an impact on the current guideline. Although no further evidence was found relating to an updated Diamond-Forrester prediction model at the 4-year review, feedback from the GDG indicated that the Diamond-Forrester model may over estimate disease probability in suspected angina.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	These are consistent with the factors listed in the guideline.	diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J2011;32:1316-30. An assessment of the abstract indicated that the Diamond-Forrester model overestimates the probability of CAD, particularly in women. A subsequent update and extension of the model in relation to the predictive value of age, sex, and type of chest pain improved its performance.	Evidence from the 4-year surveillance review showed that 6 unspecified clinical prediction models demonstrated good diagnostic accuracy for determining short-term outcomes in a pre-hospital population with suspected ACS. Furthermore, clinical feedback indicated that the parameters to assess the pre-test likelihood of coronary disease in patients with stable chest pain have changed. Further evidence was provided which supported the view that the Diamond-Forrester model overestimates the probability of CAD, particularly in women. The evidence also suggested than an updated and extended version of the model improved its performance, supporting the evidence found at the 2-year surveillance review. The diagnostic pathway presented in the guideline for people who present with stable chest pain, states that the application of the Diamond Forrester algorithm, as modified by consideration of additional risk factors, may permit a diagnosis of angina if the probability estimate is sufficiently high. The new evidence relating to an updated version of this model may therefore impact on this statement.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
95-20: Are the symptoms and description of the symptoms different in women presenting with stable chest pain of suspected cardiac origin compared with men?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-21: Are the symptoms and description of the symptoms different in Black and Ethnic Minorities presenting with stable chest pain of suspected cardiac origin compared with Caucasians?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-22: What is the utility (incremental value) and cost effectiveness of a resting ECG in evaluation of individuals with stable chest pain of suspected cardiac origin?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-23: What is the utility (incremental value) and cost effectiveness of a chest X ray in evaluation of individuals with stable chest pain of suspected cardiac origin?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-24: What is the utility and cost effectiveness of coronary artery calcium scoring in evaluation of patients with stable chest pain?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-25: What is the diagnostic utility of non-invasive and invasive tests for the evaluation of patients with stable chest pain of suspected cardiac origin?			
Through a focused search, 29 studies4-32 were identified related to non-invasive and invasive tests for patients with stable chest pain. The evidence showed that various non-invasive techniques including stress echocardiography, PET, myocardial perfusion imaging, CT coronary	Computed coronary tomographic angiography (CCTA) A systematic review and meta-analysis33 was identified which compared CCTA versus invasive coronary angiography in the diagnosis of CHD. For the diagnosis of obstructive stenosis,	Clinical feedback indicated that there is new evidence about diagnostic assessment in patients with suspected stable angina, including the comparative effectiveness of different imaging modalities.	At the 2-year review it was considered that there was no new evidence which would invalidate the current guideline recommendations regarding assessment of patients with stable chest pain. Computed coronary tomographic angiography

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
calcium score, coronary computed tomography, single-photon emission computed tomography (SPECT) and cardiovascular magnetic resonance, were effective in diagnosing CAD when compared to coronary angiography. Other studies found that exercise stress testing, real-time three-dimensional echocardiography and coronary artery calcium were not effective in the diagnosis of CAD when compared to angiography. Overall, it was considered that there was no new evidence which would invalidate the current guideline recommendations regarding assessment of patients with stable chest pain.	compared to invasive coronary angiography as the reference standard, CCTA had high sensitivity and specificity, and at a pre-test probability of CHD of 50% or less, resulted in a lower cost per patient. However, at a pre-test probability of CHD of 70% or higher, invasive coronary angiography provided a lower cost per patient. For the diagnosis of functionally relevant stenosis, using intracoronary pressure measurement as the reference standard, CCTA had a higher sensitivity but lower specificity than invasive coronary angiography and both types of coronary angiography resulted in substantially higher cost per patient. As such, the review recommended that neither type of angiography should be used in the diagnosis of functionally relevant stenosis. The results of a meta-analysis34 (n=2567) indicated that patients undergoing CCTA as the first imaging test for the detection of CAD were more likely to undergo	It was suggested that novel imaging techniques are now more widely available, particularly CT coronary angiography and MR perfusion imaging for diagnosis of chest pain. CT coronary angiography is also able to pick up other issues with lungs and mediastinum which might be missed in the old paradigm. Radiation exposure from CT imaging is now lower with the newer scanners, so exposure will be less. It was reported that the value of zero calcium score for excluding CAD has been questioned. Furthermore, the advice to do a calcium score prior to CT angiography is now increasingly ignored because low radiation CT angiography is now available. One GDG member identified that the US guideline recommends exercise ECG as first diagnostic test for many	There was new evidence identified at the 4-year review which suggested that CCTA is an effective first line imaging test for the diagnosis of CAD, although it was not clear from all the abstracts what the level of CAD risk was in the study populations. There was also evidence relating to the diagnostic effectiveness of lower radiation CCTA. The new evidence for CCTA together with clinical feedback may potentially impact on the current guideline recommendations relating to the use of CCTA for the diagnosis of CAD in patients with stable chest pain, particularly the level of CAD risk at which to undertake CCTA. Currently the guideline only recommends 64-slice (or above) CT coronary angiography in people who have an estimated likelihood of CAD of 10–29% and have a calcium score of 1-400. For people with an estimated likelihood of CAD of 10–29% and a calcium score over 400, invasive coronary angiography is recommended. Non-invasive functional imaging is recommended for people who have an estimated likelihood of CAD of 30–60%, or for people who have an estimated likelihood of 61–90% and for whom

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	percutaneous or surgical revascularisation, and there was a reduction in the time to diagnosis and costs of care compared to non-CCTA patients. A meta-analysis35 (n=3300) was identified which compared image quality, diagnostic accuracy, and radiation dose of prospectively triggered CCTA with retrospectively gated CTA in patients with suspected or known CAD. The results indicated that the image quality and diagnostic accuracy of both types of CTA were similarly high, but with lower radiation doses provided by prospectively triggered coronary CTA. The findings of a systematic review and meta-analysis36 indicated that prospective ECG gating CCTA had high positive and negative predictive values (94% and 99% respectively) for the diagnosis of significant coronary stenosis. The authors concluded that the use of CCTA with prospective ECG gating	patients, and neither the European nor the US guidelines recommend invasive coronary angiography for patients with high probability of disease. One GDG member suggested that the right test to use in lower risk groups is individualised and does not fit into a risk profile. As such, most health care professionals will determine the right diagnostic approach on a patient by patient basis. There is also a concern that the time needed to organise tests, such as nuclear scans and CT angiography is longer and may leave some high risk patients waiting for too long.	coronary revascularisation is not being considered or invasive coronary angiography is not clinically appropriate. Invasive coronary angiography is recommended for people who have an estimated likelihood of 61–90% and for whom coronary revascularisation is being considered and invasive coronary angiography is clinically appropriate. Functional stress testing The GDG found that the diagnostic performance for diagnosing CAD did not support the use of one functional imaging test in preference to another and they concluded that the tests were generally comparable and any could be used. The new evidence from the 4 year surveillance review relating to functional imaging generally supports this conclusion and is therefore consistent with the guideline recommendation which states: 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

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	allows for a reduced radiation exposure without a sacrifice in diagnostic efficacy in a population with high disease prevalence. A pilot RCT37 (n=180) found that CCTA was associated with increased revascularisation, lower costs and lower effective radiation dose compared with myocardial perfusion single-photon emission (MPS) CT in patients presenting with stable chest pain and suspected CAD. CTA and MPS resulted in comparable improvements in angina-specific health status. A systematic review38 was identified which compared 64-slice CCTA and coronary angiography (CA). Ten studies, including 1188 patients with angina with suspected or known CAD, were included in the review. At a patient level, 64-slice CCTA had positive predictive values ranging from 86-97% and negative predictive values of 76.9-100%. The authors concluded that the findings supported the use of 64-		MR imaging for stress-induced wall motion abnormalities.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	slice CCTA as a non-invasive alternative to CA for standalone diagnosis of significant stenosis in patients with angina. The results of a systematic review and meta-analysis39 (n=3,539) indicated that "triple rule-out" computed tomography (TRO CT) had high sensitivity and specificity for diagnosing CAD, although with greater radiation exposure and contrast exposure compared to non-TRO CT. A systematic review40 was identified which assessed the clinical effectiveness and cost-effectiveness of new-generation computed tomography (NGCCT) for diagnosing CAD in patients who are difficult to image using 64-slice computed tomography (e.g. obese patients, patients with high or irregular heartbeats and patients who have high levels of coronary calcium or a previous stent or bypass graft). The results indicated that NGCCT had good diagnostic accuracy for diagnosing CAD in difficult-to-image patients.		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	An NGCCT only strategy was most cost-effective in patients with suspected CAD, whereas invasive coronary angiography after a positive NGCCT was the most cost-effective strategy in patients with known CAD. Functional stress testing A meta-analysis41 (n=761) reported that stress perfusion cardiac MRI had a high sensitivity and specificity (89.1% and 84.9% respectively) for diagnosing flow-limiting obstructive CAD. The results of two RCTs42,43 suggested that stress real-time myocardial contrast echocardiography (RTMCE) increased the detection of CAD compared to conventional stress echocardiography. The results of a meta-analysis44 (n=13304) suggested that compared to exercise tolerance testing, stress imaging with MPI and stress echocardiography were the most accurate at stratifying cardiac risk in patients over 65		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	years of age with known or suspected CAD. A systematic review45 was identified which found that referral bias reduced the sensitivity and increased the specificity of exercise echocardiography and MPI for CAD. The authors concluded that further research was needed to assess the ability of these and other tests to rule-in rather than rule-out CAD. The results of a meta-analysis46 (n=11,862) found that Positron emission tomography (PET) had higher mean sensitivity than SPECT (92.6% v 88.3%) for diagnosing >50% stenosis in patients with known or suspected CAD. A second systematic review and meta-analysis47 indicated that rubidium (Rb)-82 PET provided more accurate diagnosis of obstructive CAD in comparison to SPECT. However, the review was limited by heterogeneity among study populations and referral bias in some studies. Finally, the results of a meta-		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	analysis48 indicated that SPECT demonstrated moderate accuracy in diagnosing functional stenotic CAD, with a sensitivity and specificity of 77% and 77% respectively. The results of a meta-analysis49 suggested that cardiac magnetic resonance (CMR) had higher sensitivity for the detection of obstructive CAD than SPECT. A systematic review and meta-analysis50 was identified which aimed to assess the diagnostic accuracy of CMR imaging assessing myocardial viability in patients with chronic left ventricular (LV) dysfunction due to CAD. The review included 24 studies including 698 patients, evaluating myocardial viability using three techniques. Of the techniques assessed, Contrast delayed enhancement CMR had the highest sensitivity (95%) for predicting improved segmental LV contractile function after revascularisation, and low-dose dobutamine had the highest		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	specificity (91%). The authors concluded that integrating the two methods would increase accuracy in evaluating patients with chronic LV dysfunction. An RCT51 was identified which assessed the effect of provider-directed imaging stress testing in lower-risk chest pain patients presenting to the emergency department. Patients were randomised to receive a CMR stress test (n=60) or a provider-selected stress test (n=60) (e.g. stress echo, CMR, cardiac catheterisation, nuclear, and coronary CT). The results of the study indicated that the median cost was higher for those receiving the CMR mandated test, with no differences in other outcomes between the two groups. A systematic review and meta-analysis52 examining the diagnostic accuracy of magnetocardiography (MCG) reported that MCG had a sensitivity of 83% and a specificity of 77% for the diagnosis of CAD.		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	However, the authors reported that there was significant heterogeneity present in all meta-analyses. A systematic review and meta-analysis53 was identified which assessed the efficacy of Tissue Doppler imaging (TDI) in the diagnosis of CAD. The results showed that among CAD patients, TDI was associated with a decrease in the maximum systolic velocity at rest, and a decrease in maximum early diastolic velocity and maximum late diastolic velocity post stress. The authors concluded that TDI may have a role in the evaluation of CAD. Coronary angiography An RCT134 (n=223) was identified which assessed the impact on early complications of a simultaneous injection of trinitroglycerin (TNG) with contrast agent during angiography. The study found that frequency of nausea, coronary artery spasm and chest pain were lower in the group which received TNG with		

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	contrast agent than in the control group.		
Research recommendations			
95-RR1: 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?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-RR2: What is the effectiveness and cost effectiveness of new, high-sensitivity troponin assay methods and other new cardiac biomarkers in low, medium, and high risk people with acute chest pain?			
Through a focused literature search, 27 studies77-94 were identified. The new evidence indicated that high sensitive troponins are more effective than conventional cardiac troponins in the early diagnosis of acute myocardial infarction and ACS. A further four studies95-98 were identified which indicated that copeptin, together with high sensitive troponin, improves diagnostic performance in early diagnosis of patients with suspected MI. It was considered that the new evidence relating to high-sensitive troponin and copeptin could potentially impact on the current recommendations in the guideline.	The results of an RCT105 (n=542) suggested that a rapid diagnostic pathway (including Thrombolysis in Myocardial Infarction score, electrocardiography and 0- and 2-hour troponin tests) increased the proportion of patients with chest pain discharged within 6 hours compared to a standard-care diagnostic pathway (including troponin test on arrival at hospital, prolonged observation, and a second troponin test 6-12 hours after onset of pain) for the assessment of patients with acute chest pain consistent with ACS. An RCT106 was identified which assessed changes in contemporary sensitive troponin I (TnI) levels in 7,863 patients after	At both the 2-year and 4-year review points, clinical feedback was provided which identified that there is new evidence relating to highly sensitive troponin assays for testing patients with suspected ACS. Feedback suggested that the new troponin assays are now increasingly used and have reduced the timescales from symptom onset to results from 10-12 hours to 3-6 hours. NICE currently has no plans to update MTG4. Feedback from the Newcastle and York External Assessment Centre has indicated that that the claimed benefits of the copeptin assay have been superseded	The clinical evidence for the following biomarkers was assessed as part of a review question in the guideline: troponin I, troponin T, creatine kinase (CK), creatine kinase-MB (CKMB), creatine kinase-MB isoforms (CKMB isoforms) and myoglobin. An additional research recommendation was made with the aim of investigating newer more sensitive troponin assays which may offer advantages over previous assays in terms of diagnostic accuracy, and allow exclusion of MI earlier than the 12 hour time frame currently required. The research recommendation also sought to assess other proposed biomarkers compared to the best available troponin assays. At the 2-year surveillance review, it was considered that the evidence relating to

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
Six more studies99-104 were identified which looked at other biomarkers for ACS, including amino terminal pro-B-type natriuretic peptide, unbound free fatty acids, high-sensitivity C-reactive protein, pentraxin 3 and serum ischemia modified albumin. These were just single studies and it was therefore considered that more evidence would be required to support these findings before consideration for inclusion in the guideline.	MI or unstable angina. The findings indicated that both baseline TnI levels and increases in TnI levels after 1 year were linked with an increased risk of CHD death and myocardial infarction. A second study, a systematic review and meta-analysis107 including 4 studies (n=2033), also found that elevated high-sensitivity troponin (hs-Tn) were associated with an increased risk of mortality. It is unlikely that this new evidence will impact on current recommendations. New Diagnostics guidance, published in October 2014, reviewed the clinical and cost-effectiveness of three types of high-sensitive troponin assay (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays) compared to standard troponin testing over 10–12 hours. The guidance recommends the Elecsys Troponin T high-sensitive assay and ARCHITECT STAT High Sensitive Troponin-I assay as options for the	by high-sensitivity troponin assays in terms of faster diagnosis of MI.	high sensitive troponins compared to the conventional cardiac troponins to diagnose ACS in patients with acute chest pain could potentially impact on the current guideline recommendations. The new Diagnostics guidance reviewed the clinical and cost-effectiveness of high-sensitive troponins compared to standard troponin testing over 10–12 hours, and recommended the Elecsys Troponin T high-sensitive assay and ARCHITECT STAT High Sensitive Troponin-I assay as options for the early rule out of non-ST-segment-elevation myocardial infarction (NSTEMI) in people presenting to an emergency department with chest pain and suspected ACS. The assays are recommended for use with 'early rule-out protocols', which typically include a blood sample for cardiac troponin I or T taken at initial assessment in an emergency department and a second blood sample taken after 3 hours. Currently CG95 only recommends: Take a blood sample for troponin I or T measurement on initial assessment in hospital. These are the preferred biochemical markers to diagnose acute MI; and take a second blood sample for troponin I or T measurement 10–12 hours after the onset of symptoms. The evidence identified at the 2 and 4 year surveillance

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	early rule out of non-ST-segment-elevation myocardial infarction (NSTEMI) in people presenting to an emergency department with chest pain and suspected ACS. The assays are recommended for use with 'early rule-out protocols', which typically include a blood sample for cardiac troponin I or T taken at initial assessment in an emergency department and a second blood sample taken after 3 hours. The results of a meta-analysis108 indicated that circulating miRNAs, particularly miR-499 and miR-133a, had good diagnostic accuracy for myocardial infarction. A systematic review and meta-analysis109 (n=941) was identified which assessed the early diagnostic performance of glycogen phosphorylase isoenzyme BB (GPBB) in patients with suspected AMI. The results of the meta-analysis found that GPBB had a sensitivity of 0.854 and specificity of 0.767, although there was high heterogeneity		reviews, together with the Diagnostics Guidance and clinical feedback, indicate that high sensitive troponins are effective in the diagnosis of acute MI and ACS, and therefore may impact on the current recommendations in the guideline. Evidence was identified at the 2-year surveillance review regarding the improved diagnostic performance of copeptin together with high sensitive troponin in patients with MI. It was considered that this evidence could potentially impact on the current guideline recommendations. However, MTG4, which was published in June 2011, reviewed the evidence for copeptin assay including two studies considered at the 2 year surveillance review. It found that whilst the assay showed potential to reduce the time taken to rule out MI when used in combination with cardiac troponin testing, there was insufficient evidence on its use in clinical practice to support the case for routine adoption in the NHS and recommended that further research be undertaken in the UK clinical setting to compare the BRAHMS copeptin assay in combination with cardiac troponin testing against sequential cardiac troponin testing for ruling out MI. Further

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	across the included studies. The authors concluded that GPBB does not currently provide efficient diagnosis of AMI when used as a stand-alone test. Two systematic reviews and meta-analyses110,111 were identified which found that the addition of heart-type fatty acid binding protein (H-FABP) to troponin increased sensitivity but decreased specificity compared to troponin alone for the diagnosis of MI. MTG4 (NICE medical technologies guidance), published in June 2011, was identified through the intelligence gathering search for the guideline. MTG4 stated that the BRAHMS copeptin assay shows potential to reduce the time taken to rule out myocardial infarction in patients presenting with acute chest pain, when used in combination with cardiac troponin testing. However, it stated that there is currently insufficient evidence on its use in clinical practice to support the case for		evidence relating to copeptin was identified at the 4 year surveillance review which also showed that copeptin and troponin combined had increased sensitivity for diagnosing MI. NICE currently has no plans to update MTG4 and feedback has indicated that that the claimed benefits of the copeptin assay have been superseded by high-sensitivity troponin assays in terms of faster diagnosis of MI. Evidence was also identified in relation to other biomarkers, including heart-type fatty acid binding protein which increased the sensitivity of troponin compared to troponin alone, and miRNAs which had good diagnostic accuracy for MI. In summary, the evidence and clinical feedback relating to high sensitive troponins and other biomarkers for MI, suggest that there is potentially new evidence in this area which should be considered for inclusion in the guideline.

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	routine adoption of the BRAHMS copeptin assay in the NHS and recommended that further research be undertaken in the UK clinical setting to compare the BRAHMS copeptin assay in combination with cardiac troponin testing against sequential cardiac troponin testing for ruling out MI. As part of the evidence base for this guidance, two studies considered at the previous surveillance review (Keller et al., 2010; Reichlin et al., 2009) were considered. Through the literature search for the 4-year surveillance review, two systematic reviews112,113 were identified which published after MTG4. The studies found that copeptin and troponin combined improved sensitivity for the diagnosis of acute MI compared with troponin alone.		
95-RR3: In what circumstances should telephone advice be given to people calling with chest pain? Is the appropriateness influenced by age, sex or symptoms?			
No evidence identified.	An RCT135 (n=1944) was identified which tested an educational intervention to reduce pre-hospital delay in patients with	None identified through GDG questionnaire.	The purpose of the research recommendation was to develop a robust system for giving appropriate telephone advice to people with chest pain. The

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
	ACS. All patients received usual in-hospital care. Those in the intervention group also received an individualised education session using motivational techniques which was reinforced a month later by telephone. The findings of the study indicated that the intervention reduced the pre-hospital median delay time compared to the control group, and that those who received the intervention reported their symptoms more promptly.		guideline stated that research should be conducted to clarify if an emergency response in all circumstances is appropriate, or if there are identifiable factors such as age, sex, or associated symptoms that would allow a modified response and a more appropriate use of resources. The new evidence suggests that an educational intervention, including follow up by telephone, may reduce the time taken for an individual to seek help for potential ACS. However, the evidence does not clarify the appropriate circumstances in which telephone advice should be given. Therefor it is unlikely that the new evidence will impact on the current guideline recommendations.
95-RR4: Can a national registry of people presenting with suspected angina be established to allow cohort analysis of treatments, investigations and outcomes in this group?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-RR5: What is the clinical and cost effectiveness of multislice CT coronary angiography compared with functional testing in the diagnosis of angina in a population of people with stable chest pain who have a moderate (30–60%) pre-test likelihood of CAD?			
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.
95-RR6: 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?			

Conclusions from the 2-year surveillance review (2012)	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Conclusion of this 4-year surveillance review (2014)
No evidence identified.	No new evidence identified.	None identified through GDG questionnaire.	No relevant evidence identified.

A.2 References

1. Genders TSS, Steyerberg EW, Hunink MGM et al. (2012) Prediction model to estimate presence of coronary artery disease: Retrospective pooled analysis of existing cohorts. BMJ (Online).344 (7862) , 2012.Article Number: e3485.Date of Publication: 23 Jun 2012.
2. Nehme Z, Boyle MJ, and Brown T. (2013) Diagnostic accuracy of prehospital clinical prediction models to identify short-term outcomes in patients with acute coronary syndromes: a systematic review. [Review]. Journal of Emergency Medicine 44:946-954.
3. Haasenritter J, Stanze D, Widera G et al. (2012) Does the patient with chest pain have a coronary heart disease? Diagnostic value of single symptoms and signs--a meta-analysis. [Review]. Croatian Medical Journal 53:432-441.
4. Banerjee A, Newman DR, Van den Bruel A et al. (2012) Diagnostic accuracy of exercise stress testing for coronary artery disease: a systematic review and meta-analysis of prospective studies. [Review]. International Journal of Clinical Practice 66:477-492.
5. Adil M, Hafizullah M, Jan H et al. (2011) Diagnostic yield of stress echocardiography in coronary artery disease patients. Journal of Postgraduate Medical Institute.25 (4) (pp 331-337), 2011.Date of Publication: 2011. 331-337.
6. Yoshitani H, Takeuchi M, Mor-Avi V et al. (2009) Comparative diagnostic accuracy of multiplane and multislice three-dimensional dobutamine stress echocardiography in the diagnosis of coronary artery disease. Journal of the American Society of Echocardiography 22:437-442.
7. Arnold JR, Karamitsos TD, Pegg TJ et al. (2010) Adenosine stress myocardial contrast echocardiography for the detection of coronary artery disease: a comparison with coronary angiography and cardiac magnetic resonance. Jacc: Cardiovascular Imaging 3:934-943.
8. Kirschbaum SW, Nieman K, Springeling T et al. (24-6-2011) Non-invasive diagnostic workup of patients with suspected stable angina by combined computed tomography coronary angiography and magnetic resonance perfusion imaging. Circulation Journal 75:1678-1684.
9. Abdelmoneim SS, Dhoble A, Bernier M et al. (2009) Quantitative myocardial contrast echocardiography during pharmacological stress for diagnosis of coronary artery disease: a systematic review and meta-analysis of diagnostic accuracy studies. [Review] [33 refs]. European Journal of Echocardiography 10:813-825.

10. Greulich S, Bruder O, Parker M et al. (2012) Comparison of exercise electrocardiography and stress perfusion CMR for the detection of coronary artery disease in women. Journal of Cardiovascular Magnetic Resonance 14:36.
11. Parkka JP, Koskenvuo JW, Kervinen H et al. (2010) Diagnostic performance of cardiac magnetic resonance imaging in coronary artery disease. Clinical Physiology & Functional Imaging 30:89-97.
12. Kato S, Kitagawa K, Ishida N et al. (14-9-2010) Assessment of coronary artery disease using magnetic resonance coronary angiography: a national multicenter trial. Journal of the American College of Cardiology 56:983-991.
13. de Mello RA, Nacif MS, Dos Santos AA et al. (2012) Diagnostic performance of combined cardiac MRI for detection of coronary artery disease. European Journal of Radiology 81:1782-1789.
14. Hamon M, Fau G, Nee G et al. (2010) Meta-analysis of the diagnostic performance of stress perfusion cardiovascular magnetic resonance for detection of coronary artery disease. [Review] [51 refs]. Journal of Cardiovascular Magnetic Resonance 12:29.
15. Chattranukulchai P, Tumkosit M, Cholteesupachai J et al. (2010) Diagnostic accuracy of combined dipyridamole stress perfusion and delayed enhancement cardiovascular magnetic resonance imaging for detection of coronary artery disease. Asian Biomedicine.4 (1) (pp 19-25), 2010.Date of Publication: February 2010. 19-25.
16. Gaibazzi N, Rigo F, and Reverberi C. (2010) Detection of coronary artery disease by combined assessment of wall motion, myocardial perfusion and coronary flow reserve: a multiparametric contrast stress-echocardiography study. Journal of the American Society of Echocardiography 23:1242-1250.
17. Alessandri N, Di MA, Rondoni G et al. (2009) Heart imaging: the accuracy of the 64-MSCT in the detection of coronary artery disease. European Review for Medical & Pharmacological Sciences 13:163-171.
18. Amemiya S and Takao H. (2009) Computed tomographic coronary angiography for diagnosing stable coronary artery disease - A cost-utility and cost-effectiveness analysis. Circulation Journal.73 (7) (pp 1263-1270), 2009.Date of Publication: July 2009. 1263-1270.
19. Arbab-Zadeh A, Miller JM, Rochitte CE et al. (24-1-2012) Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary arterial calcification. The CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) International Multicenter Study. Journal of the American College of Cardiology 59:379-387.
20. Chao SP, Law WY, Kuo CJ et al. (2010) The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. European Heart Journal 31:1916-1923.
21. Cheneau E, Vahdat B, Bernard L et al. (2011) Routine use of coronary computed tomography as initial diagnostic test for angina pectoris. Archives of cardiovascular diseases 104:29-34.
22. de Graaf FR, Schuijf JD, van Velzen JE et al. (2010) Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of significant coronary artery disease. European Heart Journal 31:1908-1915.
23. Mohammadzadeh A, Shabestari AA, Mohammadzadeh M et al. (2012) Diagnostic performance of multislice CT coronary angiography in the assessment of significant coronary artery disease. Acta Medica Iranica 50:31-36.

24.Nieman K, Galema T, Weustink A et al. (2009) Computed tomography versus exercise electrocardiography in patients with stable chest complaints: real-world experiences from a fast-track chest pain clinic. Heart 95:1669-1675.

25.Selcoki Y, Yilmaz OC, Kankilic MN et al. (2010) Diagnostic accuracy of 64-slice computed tomography in patients with suspected or proven coronary artery disease. Turk Kardiyoloji Dernegi Arsivi 38:95-100.

26.Guo SL, Guo YM, Zhai YN et al. (2011) Diagnostic accuracy of first generation dual-source computed tomography in the assessment of coronary artery disease: a meta-analysis from 24 studies. [Review]. The International Journal of Cardiovascular Imaging 27:755-771.

27.Genders TS, Pugliese F, Mollet NR et al. (2010) Incremental value of the CT coronary calcium score for the prediction of coronary artery disease. European Radiology 20:2331-2340.

28.Salavati A, Radmanesh F, Heidari K et al. (2012) Dual-source computed tomography angiography for diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. [Review]. Journal of cardiovascular computed tomography 6:78-90.

29.Guner LA, Karabacak NI, Cakir T et al. (2010) Comparison of diagnostic performances of three different software packages in detecting coronary artery disease. European Journal of Nuclear Medicine & Molecular Imaging 37:2070-2078.

30.Al MM, Sun Z, and Lenzo N. (2011) Diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease: A systematic review. Biomedical Imaging & Intervention Journal 7:e9.

31.Jaarsma C, Leiner T, Bekkers SC et al. (8-5-2012) Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. Journal of the American College of Cardiology 59:1719-1728.

32.De Jong MC, Genders TS, van Geuns RJ et al. (2012) Diagnostic performance of stress myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis. European Radiology 22:1881-1895.

33.Gorenoi V, Schonermark MP, and Hagen A. (2012) CT coronary angiography vs. invasive coronary angiography in CHD. GMS Health Technology Assessment 8:Doc02.

34.D'Ascenzo F, Cerrato E, Biondi-Zoccai G et al. (2013) Coronary computed tomographic angiography for detection of coronary artery disease in patients presenting to the emergency department with chest pain: a meta-analysis of randomized clinical trials. European heart journal cardiovascular Imaging 14:782-789.

35.Menke J, Unterberg-Buchwald C, Staab W et al. (2013) Head-to-head comparison of prospectively triggered vs retrospectively gated coronary computed tomography angiography: Meta-analysis of diagnostic accuracy, image quality, and radiation dose. American Heart Journal 165:154.

36.Sun Z and Ng K-H. (2012) Diagnostic value of coronary CT angiography with prospective ECG-gating in the diagnosis of coronary artery disease: A systematic review and meta-analysis. International Journal of Cardiovascular Imaging 28:2109-2119.

37.Min JK, Koduru S, Dunning AM et al. (2012) Coronary CT angiography versus myocardial perfusion imaging for near-term quality of life, cost and radiation exposure: a prospective multicenter randomized pilot trial. Journal of cardiovascular computed tomography 6:274-283.

38. Powell H and Cosson P. (2013) Comparison of 64-slice computed tomography angiography and coronary angiography for the detection and assessment of coronary artery disease in patients with angina: A systematic review. Radiography 19:168-175.
39. Ayaram D, Bellolio MF, Murad MH et al. (2013) Triple rule-out computed tomographic angiography for chest pain: a diagnostic systematic review and meta-analysis. [Review]. Academic Emergency Medicine 20:861-871.
40. Westwood M, Al M, Burgers L et al. (2013) A systematic review and economic evaluation of newgeneration computed tomography scanners for imaging in coronary artery disease and congenital heart disease: Somatom definition flash, Aquilion ONE, Brilliance ICT and Discovery CT750 HD. Health Technology Assessment 17:1-243.
41. Desai RR and Jha S. (2013) Diagnostic performance of cardiac stress perfusion mri in the detection of coronary artery disease using fractional flow reserve as the reference standard: A meta-Analysis. American Journal of Roentgenology 201:W245-W252.
42. Porter TR, Smith LM, Wu J et al. (2013) Patient outcome following 2 different stress imaging approaches: A prospective randomized comparison. Journal of the American College of Cardiology 61:2446-2455.
43. Thomas D, Xie F, Smith LM et al. (2012) Prospective randomized comparison of conventional stress echocardiography and real-time perfusion stress echocardiography in detecting significant coronary artery disease. Journal of the American Society of Echocardiography 25:1207-1214.
44. Rai M, Baker WL, Parker MW et al. (2012) Meta-analysis of optimal risk stratification in patients >65 years of age. American Journal of Cardiology 110:1092-1099.
45. Ladapo JA, Blecker S, Elashoff MR et al. (2013) Clinical implications of referral bias in the diagnostic performance of exercise testing for coronary artery disease. Journal of the American Heart Association 2:e000505.
46. Parker MW, Iskandar A, Limone B et al. (2012) Diagnostic accuracy of cardiac positron emission tomography versus single photon emission computed tomography for coronary artery disease: A bivariate meta-analysis. Circulation: Cardiovascular Imaging 5:700-707.
47. Mc Ardle BA, Dowsley TF, Dekemp RA et al. (30-10-2012) Does rubidium-82 PET have superior accuracy to SPECT perfusion imaging for the diagnosis of obstructive coronary disease?: A systematic review and meta-analysis. [Review]. Journal of the American College of Cardiology 60:1828-1837.
48. Zhou T, Yang L-F, Zhai J-L et al. (2014) SPECT myocardial perfusion versus fractional flow reserve for evaluation of functional ischemia: A meta analysis. European Journal of Radiology 83:951-956.
49. Chen L, Wang X, Bao J et al. (2014) Direct comparison of cardiovascular magnetic resonance and single-photon emission computed tomography for detection of coronary artery disease: A meta-analysis. PLoS ONE 9.
50. Romero J, Xue X, Gonzalez W et al. (2012) CMR imaging assessing viability in patients with chronic ventricular dysfunction due to coronary artery disease: a meta-analysis of prospective trials. [Review]. Jacc: Cardiovascular Imaging 5:494-508.
51. Miller CD, Hoekstra JW, Lefebvre C et al. (2012) Provider-directed imaging stress testing reduces health care expenditures in lower-risk chest pain patients presenting to the emergency department. SO: Circulation.Cardiovascular imaging 5:111-118.

52. Agarwal R, Saini A, Alyousef T et al. (2012) Magnetocardiography for the diagnosis of coronary artery disease: a systematic review and meta-analysis. [Review]. Annals of Noninvasive Electrocardiology 17:291-298.

53. Agarwal R, Gosain P, Kirkpatrick JN et al. (2012) Tissue Doppler imaging for diagnosis of coronary artery disease: A systematic review and meta-analysis. Cardiovascular Ultrasound 10.

54. Langdorf MI, Wei E, Ghobadi A et al. (2010) Echocardiography to supplement stress electrocardiography in emergency department chest pain patients. The Western Journal of Emergency Medicine 11:379-383.

55. Hermann LK, Weingart SD, Duvall WL et al. (2009) The limited utility of routine cardiac stress testing in emergency department chest pain patients younger than 40 years. Annals of Emergency Medicine 54:12-16.

56. Lim SH, Anantharaman V, Sundram F et al. (2013) Stress myocardial perfusion imaging for the evaluation and triage of chest pain in the emergency department: A randomized controlled trial. SO: Journal of nuclear cardiology 20:1002-1012.

57. Miller CD, Case LD, Little WC et al. (2013) Stress CMR reduces revascularization, hospital readmission, and recurrent cardiac testing in intermediate-risk patients with acute chest pain. Jacc: Cardiovascular Imaging 6:785-794.

58. Romero J, Kahan J, Kelesidis I et al. (2013) CMR imaging for the evaluation of myocardial stunning after acute myocardial infarction: A meta-analysis of prospective trials. European heart journal cardiovascular Imaging 14:1080-1091.

59. Takakuwa KM, Keith SW, Estepa AT et al. (2011) A meta-analysis of 64-section coronary CT angiography findings for predicting 30-day major adverse cardiac events in patients presenting with symptoms suggestive of acute coronary syndrome. Academic Radiology 18:1522-1528.

60. Athappan G, Habib M, Ponniah T et al. (28-5-2010) Multi-detector computerized tomography angiography for evaluation of acute chest pain--a meta analysis and systematic review of literature. [Review] [44 refs]. International Journal of Cardiology 141:132-140.

61. Samad Z, Hakeem A, Mahmood SS et al. (2012) A meta-analysis and systematic review of computed tomography angiography as a diagnostic triage tool for patients with chest pain presenting to the emergency department

62. 539. Journal of Nuclear Cardiology.19 (2) (pp 364-376), 2012.Date of Publication: April 2012. 364-376.

63. Branch KR, Bresnahan BW, Veenstra DL et al. (2012) Economic outcome of cardiac CT-based evaluation and standard of care for suspected acute coronary syndrome in the emergency department: a decision analytic model. Academic Radiology 19:265-273.

64. Chow BJ, Joseph P, Yam Y et al. (15-8-2010) Usefulness of computed tomographic coronary angiography in patients with acute chest pain with and without high-risk features. American Journal of Cardiology 106:463-469.

65. Fazel P, Peterman MA, and Schussler JM. (15-8-2009) Three-year outcomes and cost analysis in patients receiving 64-slice computed tomographic coronary angiography for chest pain. American Journal of Cardiology 104:498-500.

66. Goldstein JA, Chinnaiyan KM, Abidov A et al. (27-9-2011) The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. Journal of the American College of Cardiology 58:1414-1422.

67. Hoffmann U, Bamberg F, Chae CU et al. (2009) Coronary Computed Tomography Angiography for Early Triage of Patients With Acute Chest Pain. The ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) Trial. Journal of the American College of Cardiology.53 (18) (pp 1642-1650), 2009.Date of Publication: 05 May 2009. 1642-1650.

68. Hoffmann U, Truong QA, Schoenfeld DA et al. (26-7-2012) Coronary CT angiography versus standard evaluation in acute chest pain. New England Journal of Medicine 367:299-308.

69. Kim J, Lee H, Song S et al. (2010) Efficacy and safety of the computed tomography coronary angiography based approach for patients with acute chest pain at an emergency department: one month clinical follow-up study. Journal of Korean Medical Science 25:466-471.

70. Maffei E, Seitun S, Martini C et al. (2010) CT coronary angiography and exercise ECG in a population with chest pain and low-to-intermediate pre-test likelihood of coronary artery disease. Heart 96:1973-1979.

71. Ueno K, Anzai T, Jinzaki M et al. (2009) Diagnostic capacity of 64-slice multidetector computed tomography for acute coronary syndrome in patients presenting with acute chest pain. Cardiology 112:211-218.

72. van Velzen JE, de Graaf FR, Kroft LJ et al. (2012) Performance and efficacy of 320-row computed tomography coronary angiography in patients presenting with acute chest pain: results from a clinical registry. The International Journal of Cardiovascular Imaging 28:865-876.

73. Litt HI, Gatsonis C, Snyder B et al. (12-4-2012) CT angiography for safe discharge of patients with possible acute coronary syndromes. New England Journal of Medicine 366:1393-1403.

74. Truong QA, Hayden D, Woodard PK et al. (25-6-2013) Sex differences in the effectiveness of early coronary computed tomographic angiography compared with standard emergency department evaluation for acute chest pain: the rule-out myocardial infarction with Computer-Assisted Tomography (ROMICAT)-II Trial. Circulation 127:2494-2502.

75. Hulten E, Pickett C, Bittencourt MS et al. (26-2-2013) Outcomes after coronary computed tomography angiography in the emergency department: a systematic review and meta-analysis of randomized, controlled trials. Journal of the American College of Cardiology 61:880-892.

76. Linde JJ, Kofoed KF, Sorgaard M et al. (2013) Cardiac computed tomography guided treatment strategy in patients with recent acute-onset chest pain: Results from the randomised, controlled trial: CArdiac cT in the treatment of acute CHest pain (CATCH). SO: International journal of cardiology 168:5257-5262.

77. Krissak R, Henzler T, Prechel A et al. (2012) Triple-rule-out dual-source CT angiography of patients with acute chest pain: dose reduction potential of 100 kV scanning. European Journal of Radiology 81:3691-3696.

78. Aldous SJ, Florkowski CM, Crozier IG et al. (2011) Comparison of high sensitivity and contemporary troponin assays for the early detection of acute myocardial infarction in the emergency department. Annals of Clinical Biochemistry 48:3-8.

79. Christ M, Popp S, Pohlmann H et al. (2010) Implementation of high sensitivity cardiac troponin T measurement in the emergency department. American Journal of Medicine 123:1134-1142.

80. Cuda G, Lentini M, Gallo L et al. (2012) High sensitive troponin T in individuals with chest pain of presumed ischemic origin. Frontiers in Bioscience 4:2322-2327.

81. Eggers KM, Venge P, and Lindahl B. (11-7-2012) High-sensitive cardiac troponin T outperforms novel diagnostic biomarkers in patients with acute chest pain. Clinica Chimica Acta 413:1135-1140.

82. Freund Y, Chenevier-Gobeaux C, Bonnet P et al. (2011) High-sensitivity versus conventional troponin in the emergency department for the diagnosis of acute myocardial infarction. Critical Care (London, England) 15:R147.

83. Giannitsis E, Becker M, Kurz K et al. (2010) High-sensitivity cardiac troponin T for early prediction of evolving non-ST-segment elevation myocardial infarction in patients with suspected acute coronary syndrome and negative troponin results on admission. Clinical Chemistry 56:642-650.

84. Keller T, Zeller T, Peetz D et al. (27-8-2009) Sensitive troponin I assay in early diagnosis of acute myocardial infarction. New England Journal of Medicine 361:868-877.

85. Khan DA, Sharif MS, and Khan FA. (2011) Diagnostic performance of high-sensitivity troponin T, myeloperoxidase, and pregnancy-associated plasma protein A assays for triage of patients with acute myocardial infarction. Korean Journal Of Laboratory Medicine 31:172-178.

86. Kurz K, Giannitsis E, Becker M et al. (2011) Comparison of the new high sensitive cardiac troponin T with myoglobin, h-FABP and cTnT for early identification of myocardial necrosis in the acute coronary syndrome. Clinical Research in Cardiology 100:209-215.

87. Lindahl B, Venge P, and James S. (2010) The new high-sensitivity cardiac troponin T assay improves risk assessment in acute coronary syndromes.[Erratum appears in Am Heart J. 2011 Feb;161(2):425]. American Heart Journal 160:224-229.

88. Melki D, Lind S, Agewall S et al. (2011) Diagnostic value of high sensitive troponin T in chest pain patients with no persistent ST-elevations. Scandinavian Cardiovascular Journal.45 (4) (pp 198-204), 2011.Date of Publication: August 2011. 198-204.

89. Pracon R, Kruk M, Jakubczak B et al. (2012) Superior early diagnostic performance of a sensitive cardiac troponin assay as compared to a standard troponin test in the diagnosis of acute myocardial infarction. Kardiologia Polska 70:131-138.

90. Reichlin T, Hochholzer W, Bassetti S et al. (27-8-2009) Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. New England Journal of Medicine 361:858-867.

91. Reiter M, Twerenbold R, Reichlin T et al. (2011) Early diagnosis of acute myocardial infarction in the elderly using more sensitive cardiac troponin assays. European Heart Journal 32:1379-1389.

92. Saenger AK, Beyrau R, Braun S et al. (11-4-2011) Multicenter analytical evaluation of a high-sensitivity troponin T assay. Clinica Chimica Acta 412:748-754.

93. Sanchis J, Bardaji A, Bosch X et al. (2012) Usefulness of high-sensitivity troponin T for the evaluation of patients with acute chest pain and no or minimal myocardial damage. American Heart Journal 164:194-200.

94. Weber M, Bazzino O, Navarro Estrada JL et al. (2011) Improved diagnostic and prognostic performance of a new high-sensitive troponin T assay in patients with acute coronary syndrome. American Heart Journal 162:81-88.

95. Body R, Carley S, McDowell G et al. (20-9-2011) Rapid exclusion of acute myocardial infarction in patients with undetectable troponin using a high-sensitivity assay. Journal of the American College of Cardiology 58:1332-1339.

96. Reichlin T, Hochholzer W, Stelzig C et al. (30-6-2009) Incremental value of copeptin for rapid rule out of acute myocardial infarction. Journal of the American College of Cardiology 54:60-68.

97. Keller T, Tzikas S, Zeller T et al. (11-5-2010) Copeptin improves early diagnosis of acute myocardial infarction. Journal of the American College of Cardiology 55:2096-2106.

98. Giannitsis E, Kehayova T, Vafaie M et al. (2011) Combined testing of high-sensitivity troponin T and copeptin on presentation at prespecified cutoffs improves rapid rule-out of non-ST-segment elevation myocardial infarction. Clinical Chemistry 57:1452-1455.

99. Giavarina D, Carta M, Fortunato A et al. (2011) Copeptin and high sensitive troponin for a rapid rule out of acute myocardial infarction? Clinical Laboratory 57:725-730.

100. Bhardwaj A, Truong QA, Peacock WF et al. (2011) A multicenter comparison of established and emerging cardiac biomarkers for the diagnostic evaluation of chest pain in the emergency department. American Heart Journal 162:276-282.

101. Diercks DB, Kirk JD, Naser S et al. (2011) Value of high-sensitivity C-reactive protein in low risk chest pain observation unit patients. International Journal of Emergency Medicine 4:37.

102. Hjortshoj S, Venge P, and Ravkilde J. (30-1-2011) Clinical performance of a new point-of-care cardiac troponin I assay compared to three laboratory troponin assays. Clinica Chimica Acta 412:370-375.

103. Kume N, Mitsuoka H, Hayashida K et al. (2011) Pentraxin 3 as a biomarker for acute coronary syndrome: comparison with biomarkers for cardiac damage. Journal of Cardiology 58:38-45.

104. Takhshid MA, Kojuri J, Tabei SMB et al. (2010) Early diagnosis of acute coronary syndrome with sensitive troponin I and ischemia modified albumin. Iranian Cardiovascular Research Journal.4 (4) (pp 144-151), 2010.Date of Publication: December 15, 2010. 144-151.

105. Truong QA, Bayley J, Hoffmann U et al. (2012) Multi-marker strategy of natriuretic peptide with either conventional or high-sensitivity troponin-T for acute coronary syndrome diagnosis in emergency department patients with chest pain: from the "rule out myocardial infarction using computer assisted tomography" (ROMICAT) trial. American Heart Journal 163:972-979.

106. Than M, Aldous S, Lord SJ et al. (2014) A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. JAMA Internal Medicine 174:51-58.

107. White HD, Tonkin A, Simes J et al. (4-2-2014) Association of contemporary sensitive troponin I levels at baseline and change at 1 year with long-term coronary events following myocardial infarction or unstable angina: results from the LIPID Study (Long-Term Intervention With Pravastatin in Ischaemic Disease). Journal of the American College of Cardiology 63:345-354.

108. Chatterjee S, Kim J, Dahhan A et al. (2013) Use of high-sensitivity troponin assays predicts mortality in patients with normal conventional troponin assays on admission - Insights from a meta-analysis. Clinical Cardiology 36:649-653.

109. Cheng C, Wang Q, You W et al. (2014) MiRNAs as biomarkers of myocardial infarction: A meta-analysis. PLoS ONE 9.

110. Lippi G, Mattiuzzi C, Comelli I et al. (2013) Glycogen phosphorylase isoenzyme BB in the diagnosis of acute myocardial infarction: a meta-analysis. Biochemia Medica 23:78-82.

111. Carroll C, Al KM, Stevens JW et al. (2013) Heart-type fatty acid binding protein as an early marker for myocardial infarction: systematic review and meta-analysis. [Review]. Emergency Medicine Journal 30:280-286.

112. Lippi G, Mattiuzzi C, and Cervellin G. (2013) Critical review and meta-analysis on the combination of heart-type fatty acid binding protein (H-FABP) and troponin for early diagnosis of acute myocardial infarction. [Review]. Clinical Biochemistry 46:26-30.

113. Lipinski MJ, Escarcega RO, D'Ascenzo F et al. (1-5-2014) A systematic review and collaborative meta-analysis to determine the incremental value of copeptin for rapid rule-out of acute myocardial infarction. [Review]. American Journal of Cardiology 113:1581-1591.

114. Raskovalova T, Twerenbold R, Collinson PO et al. (2014) Diagnostic accuracy of combined cardiac troponin and copeptin assessment for early rule-out of myocardial infarction: a systematic review and meta-analysis. European Heart Journal Acute Cardiovascular Care 3:18-27.

115. Hess EP, Knoedler MA, Shah ND et al. (2012) The chest pain choice decision aid: a randomized trial. Circulation Cardiovascular:251-259.

116. Hess EP, Agarwal D, Chandra S et al. (13-7-2010) Diagnostic accuracy of the TIMI risk score in patients with chest pain in the emergency department: a meta-analysis. CMAJ Canadian Medical Association Journal 182:1039-1044.

117. Steurer J, Held U, Schmid D et al. (2010) Clinical value of diagnostic instruments for ruling out acute coronary syndrome in patients with chest pain: a systematic review. [Review]. Emergency Medicine Journal 27:896-902.

118. Body R, Carley S, Wibberley C et al. (2010) The value of symptoms and signs in the emergent diagnosis of acute coronary syndromes. Resuscitation 81:281-286.

119. de WC, Cadeddu C, Gualano MR et al. (2012) Telemedicine for the reduction of myocardial infarction mortality: a systematic review and a meta-analysis of published studies. [Review]. Telemedicine Journal & E-Health 18:323-328.

120. Sequist TD, Morong SM, Marston A et al. (2012) Electronic risk alerts to improve primary care management of chest pain: a randomized, controlled trial. Journal of General Internal Medicine 27:438-444.

121. Kline JA, Jones AE, Shapiro NI et al. (2014) Multicenter, randomized trial of quantitative pretest probability to reduce unnecessary medical radiation exposure in emergency department patients with chest pain and dyspnea. Circulation Cardiovascular:66-73.

122. Pelter MM, Riegel B, McKinley S et al. (2012) Are there symptom differences in patients with coronary artery disease presenting to the ED ultimately diagnosed with or without ACS? SO: American journal of emergency medicine 30:1822-1828.

123. Leisy PJ, Coeytaux RR, Wagner GS et al. (2013) ECG-based signal analysis technologies for evaluating patients with acute coronary syndrome: a systematic review. [Review]. Journal of Electrocardiology 46:92-97.

124. Tulder R, Roth D, Weiser C et al. (2012) An electrocardiogram technician improves in-hospital first medical contact-to-electrocardiogram times: a cluster randomized controlled interventional trial. SO: American journal of emergency medicine 30:1729-1736.

125. Cabello JB, Burls A, Emparanza JI et al. (2013) Oxygen therapy for acute myocardial infarction. [Review][Update of Cochrane Database Syst Rev. 2010;(6):CD007160; PMID: 20556775]. Cochrane Database of Systematic Reviews 8:CD007160.

126. Ranchord AM, Argyle R, Beynon R et al. (2012) High-concentration versus titrated oxygen therapy in ST-elevation myocardial infarction: a pilot randomized controlled trial. SO: American heart journal 163:168-175.

127. Sundstrom BW, Bang A, Karlsson T et al. (2013) Anxiolytics in patients suffering a suspected acute coronary syndrome: Multi-centre randomised controlled trial in Emergency Medical Service. SO: International journal of cardiology 168:3580-3587.

128. Selker HP, Beshansky JR, Sheehan PR et al. (2012) Out-of-hospital administration of intravenous glucose-insulin-potassium in patients with suspected acute coronary syndromes: the IMMEDIATE randomized controlled trial. SO: JAMA 307:1925-1933.

129. Collinson P, Goodacre S, Gaze D et al. (2012) Very early diagnosis of chest pain by point-of-care testing: comparison of the diagnostic efficiency of a panel of cardiac biomarkers compared with troponin measurement alone in the RATPAC trial. Heart 98:312-318.

130. Apple FS, Smith SW, Pearce LA et al. (2009) Assessment of the multiple-biomarker approach for diagnosis of myocardial infarction in patients presenting with symptoms suggestive of acute coronary syndrome. Clinical Chemistry 55:93-100.

131. Fitzgerald P, Goodacre SW, Cross E et al. (2011) Cost-effectiveness of point-of-care biomarker assessment for suspected myocardial infarction: the randomized assessment of treatment using panel Assay of cardiac markers (RATPAC) trial. Academic Emergency Medicine 18:488-495.

132. Bradburn M, Goodacre SW, Fitzgerald P et al. (2012) Interhospital variation in the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers). SO: Emergency medicine journal 29:233-238.

133. Bruins Slot MH, van der Heijden GJ, Stelpstra SD et al. (15-10-2013) Point-of-care tests in suspected acute myocardial infarction: a systematic review. International Journal of Cardiology 168:5355-5362.

134. Rafeh NA, Castellanos MR, Khoueiry G et al. (2012) Association between coronary artery disease diagnosed by coronary angiography and breast arterial calcifications on mammography: Meta-analysis of the data. Journal of Women's Health 21:1053-1058.

135. Heidari R, Sadeghi M, Sanei H et al. (2012) The effects of trinitroglycerin injection on early complications of angiography. ARYA Atherosclerosis 8:50-53.

136. Mooney M, McKee G, Fealy G et al. (2014) A randomized controlled trial to reduce prehospital delay time in patients with acute coronary syndrome (ACS). SO: Journal of emergency medicine 46:495-506.

Appendix B: Declarations of interest

The September 2014 version of the NICE code of practice for declaring and dealing with conflicts of interest policy was applied to this guideline.

Jonathan Mant (Chair)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	Received a fee from BMS for interview on atrial fibrillation.	Non-specific personal financial	Declared and participated
	Consultancy work for Expert-24: Communications company that manage a health website that provides information on life expectancy.	Non-specific personal financial	Declared and participated
	Holds grants as chief investigator awarded by NIHR and Stroke Association/British Heart Foundation.	Non-specific non-personal financial	Declared and participated
	Brother works for Quintiles.	Non-specific personal family	Declared and participated
Second GC meeting 09/03/16	Running a trial funded by the Stroke Association and the British Heart Foundation. Ferrer provided the interventional drug at no charge.	Non-specific non-personal financial	Declared and participated
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Peter Bolton (Lay Member)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A

GC meeting	Declaration of interest	Classification	Action taken
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Liz Clark (Lay Member)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	Lay member of the Scot-Heart Steering Committee reviewing the role of multi-detector computed tomography at rapid access chest pain clinic. No payment was received.	Non-specific personal non-financial	Declared and participated
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Stephen Hoole (Consultant Interventional Cardiologist)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	Received speaker fee honoraria from AstraZeneca (Ticagrelor).	Non-specific personal financial	Declared and participated
	Received speaker fee honoraria from Abbott Vascular (Bioresorbable scaffolds).	Non-specific personal financial	Declared and participated
	Received professional (proctoring) fees from Abbott Vascular.	Non-specific personal financial	Declared and participated
	Received research grant support from AstraZeneca	Non-specific personal financial	Declared and participated

GC meeting	Declaration of interest	Classification	Action taken
	(Ticagrelor In STEMI). Received research grant support from Gore Medical (PFO closure). Received travel grants from Boston Scientific and Abbott Vascular to lecture and present at cardiology meetings.	Non-specific personal financial Reasonable travel expenses	Declared and participated Declared and participated
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 18/05/16	No change to existing declarations.	N/A	N/A

Anita McSorley (Consultant Physician Acute Medicine)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Sarah Mounsey (Cardiac Advance Nurse Practitioner)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	MSc dissertation on high sensitivity troponin triple test. This study has been used as a	Specific personal non-financial	Declared and participated

GC meeting	Declaration of interest	Classification	Action taken
	pilot for an unfunded larger study being undertaken by the medical registrar in the same department. Sarah doesn't have any involvement in this larger study.		
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Naveen Mudalagiri (Consultant Cardiologist and Intervantionalist)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Charles Peebles (Consultant Radiologist)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	Received £800 payment for lecture seminars on the use of cardiac imaging and MR equipment (not diagnosis).	Non-specific personal financial	Declared and participated
	Sponsorship to the department from contrast companies (Medtronic, Bayer and Gurvee) for MRI	Specific non-personal financial	Declared and participated

GC meeting	Declaration of interest	Classification	Action taken
	departmental course.		
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Carl Roobottom (Consultant Radiologist)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	Involved in providing lectures on a CT accreditation course run by GE for nearly 10 years which is based in the Peninsula Radiology Academy in Plymouth. Takes annual leave to deliver the course and is paid a lecture fee (via a separate company called ATC). The course is non-vendor specific and was designed to ensure high standards of CT reporting in the UK. Declared this interest when involved in the CG95 and DG3 NICE guidance and it was not felt to be an issue as recommendations on CT are non-vendor-specific. No pending publications on acute chest pain or associations with any manufacturers of Tn assays.	Non-specific personal financial	Declared and participated
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting	No change to existing declarations.	N/A	N/A

GC meeting	Declaration of interest	Classification	Action taken
11/04/16			

Graham Stiff (General Practitioner)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Neil Swanson (Consultant Radiologist)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	Occasionally responded to market research surveys that relate to personal opinions on the management of some acute chest pain conditions. In a year, this is estimated to be under £100. No payments/sponsorships received from any industry directly involved in the management of any cardiac conditions.	Non-specific personal financial	Declared and participated
	Money is paid to Neil's department from industry for the employment of clinical fellows, but he is not involved in that and does not know how much money is paid. He is not involved in the selection of such trainees.	Non-specific non-personal financial	Declared and participated
	Money is paid to Neil's research department for research trials from a variety of companies which have a commercial interest in the	Specific non-personal financial	Declared and participated

GC meeting	Declaration of interest	Classification	Action taken
	treatments for acute chest pain. None of this money is paid to /spent by Neil. He is site principal investigator for a clinical trial (Re dual) sponsored by the makers of dabigatran. This trial recruits patients with acute chest pain (for example due to non ST elevation MI). Money is paid to the department for each patient recruited. Neil has no control over that money or how it is spent (mostly to pay for retention of research nurses). He does not know the exact amount but think it will be in the order of £20,000/year. Unpaid member of the British Cardiovascular Society Guidelines committee.	Specific non-personal financial	Declared and participated
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Paul Wallman (Consultant Emergency Physician)

GC meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	None.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting	No change to existing declarations.	N/A	N/A

GC meeting	Declaration of interest	Classification	Action taken
21/04/16			
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

NGC team

GDG meeting	Declaration of interest	Classification	Action taken
First GC meeting 20/01/16	In receipt of NICE commissions.	N/A	N/A
Second GC meeting 09/03/16	No change to existing declarations.	N/A	N/A
Third GC meeting 11/04/16	No change to existing declarations.	N/A	N/A
Fourth GC meeting 21/04/16	No change to existing declarations.	N/A	N/A
Fifth GC meeting 11/04/16	No change to existing declarations.	N/A	N/A

Appendix C: Clinical review protocols

C.1 High sensitivity cardiac troponins

Table 1: Review protocol: High sensitivity troponins – test and treat

Component	Description
Rationale	The chest pain of recent onset (acute) guideline (CG95) was reviewed in 2014 as part of NICE's routine surveillance programme to decide whether the guideline requires updating. The surveillance programme identified new evidence on the use of highly sensitive troponins compared to the conventional cardiac troponins to diagnose ACS in patients with acute chest pain. High-sensitivity cardiac troponin (hs-cTn) assays may allow rapid rule-out of AMI (acute myocardial infarction) and avoidance of unnecessary hospital admissions and anxiety. Ruling in an ACS in a timely manner is also a high priority, as early intervention in patients with ACS has been shown to lead to better outcomes.
Review question	In low, medium and high risk people under investigation for acute chest pain of suspected cardiac origin, what is the clinical and cost-effectiveness of high-sensitivity troponin assay methods compared to standard cardiac troponins to identify/rapidly rule-out NSTEMI/unstable angina and to improve patient outcomes?
Objectives	To evaluate the clinical and cost-effectiveness of high-sensitivity troponin assay methods compared to conventional cardiac troponins in diagnosing/rapid rule out of NSTEMI/unstable angina.
Population and target condition	Target condition and presentation: Adults (age ≥18 years) presenting with acute chest pain/discomfort of suspected cardiac origin. Acute chest pain is defined as 'pain, discomfort or pressure in the chest, epigastrium, neck, jaw, or upper limb without an apparent non-cardiac source[77] attributed to a suspected, but not confirmed AMI.' Strata (as defined by study): • High risk people • Medium risk people • Low risk people
Index diagnostic test + treatment	High-sensitivity cardiac troponin (hs-cTn) assays: The recommended definition of a hs-cTn assay uses 2 criteria: • The total imprecision, coefficient of variation (CV), of the assay should be ≤10% at the 99th percentile value of a healthy reference population. • The limit of detection (LoD) of the assay should be such as to allow measurable concentrations to be attainable for at least 50% (ideally >95%) of healthy individuals
Comparator index diagnostic tests + treatment or treatment alone (no test)	• Tn T or I measurement on presentation and 10–12 hours after the onset of symptoms • any other hs-cTn test, as specified above, or no comparators • no test.
Outcomes	Efficacy outcomes: • all-cause mortality during 30 days and 1 year follow-up period (or closest time point) • cardiovascular mortality during 30 days and 1 year follow-up period (or closest time point) • myocardial infarction during 30 day follow-up period • percutaneous coronary intervention (PCI) during 30-day follow-up period • coronary artery bypass graft (CABG) during 30-day follow-up period

	• hospitalisation during 30-day follow-up period for cardiac causes (or closest time point) • hospitalisation during 30-day follow-up for non-cardiac causes (or closest time point) • patient satisfaction or HRQoL measures at one year • incidence of MACE (major adverse cardiac events [cardiac death, non-fatal AMI, revascularisation or hospitalisation for myocardial ischaemia]) during follow-up period. Process outcomes: • time to discharge • early discharge (≤4 hours after initial presentation) without MACE during follow-up • re-attendance at or re-admission to hospital during follow-up • referral rates for invasive coronary angiography and/or coronary revascularisation • repeat testing/additional testing. Secondary accuracy outcomes: • sensitivity/specificity and other test accuracy measures.
Study design	Test-and-treat RCTs (CCTs will be considered if no RCTs are identified), systematic reviews of test-and-treat RCTs
Exclusions to consider	Studies not fulfilling the inclusion criteria will be excluded. A full list of reasons for exclusions will be given in the appendix. Exclusions to consider: • studies which do not contain a concurrent control group • studies with population of traumatic chest injury without cardiac symptoms • studies with population in whom the cause of their chest pain/discomfort is known to be related to another condition, without cardiac symptoms • studies from non-OECD countries. Other exclusions to consider: • the test does not lead directly to treatment, for example triage tests – consider including but assess risk of bias and indirectness • there are different treatments for the 2 randomised groups • not all patients in the trial are followed up regardless of test results (that is, including those that were not treated) – consider including but assess risk of bias • may exclude comparisons of the index test and treat versus the reference standard and treat.
Search Strategy	The search strategy will be based on intervention (high-sensitivity Tn assays) and target condition • The databases to be searched are: ○ Medline, Embase, The Cochrane Library • Date limits for search: ○ no date cut-off • Language: English only
Review Strategy	<u>Data synthesis:</u> For the effectiveness data: • Data synthesis of RCT data. Meta-analysis where appropriate will be conducted. <u>Stratification – groups that cannot be combined</u>: Analyses will be conducted separately for each of the three hs-cTn assays. Analyses will be stratified according to whether the study evaluated:

	• target condition • timing of collection of blood sample for testing • the threshold used to define a positive hs-cTn result. For timing and threshold, stratified analysis will be conducted for all timepoints for which sufficient data are available. • risk stratification: low, moderate and high pre-test probability of disease compared with each other if data allows. Pre-probability of disease (determined by clinical judgement based on cardiovascular risk factors, type of chest pain, physical findings and ECG abnormalities). Subgroup analysis and investigation of heterogeneity: In the event of significant heterogeneity, we plan to explore possible causes by looking at the characteristics of the included studies. Possible sources of heterogeneity in this review may include: • age ≥70 years compared with age ≤70 years; <40 years versus ≥40 years • patients with pre-existing CAD at baseline compared with patients without pre-existing CAD • without previous AMI compared with pre-existing AMI • mixed populations compared with those that excluded patients with STEMI • time from symptom onset to presentation <3 hours compared with >3 hours • time from symptom onset to presentation <6 hours compared with >6 hours • renal function • gender • age • ethnicity • socioeconomic status • people with disabilities. Are there any equality issues to consider? • see above • variation in access to diagnostic testing . Quality assessment: • The methodological quality of each RCT or CCT will be assessed using the Evibase checklist and GRADE. MIDs Any reduction in mortality was clinically important. A 25% reduction or increase was used for all other outcomes. A 5% change in adverse events was seen as clinically important.

Table 2: Review protocol: High sensitivity troponins – diagnostic accuracy

Component	Description
Rationale	The chest pain of recent onset (acute) guideline (CG95) was reviewed in 2014 as part of NICE's routine surveillance programme to decide whether the guideline requires updating. The surveillance programme identified new evidence on the use of highly sensitive troponins compared to the conventional cardiac troponins to diagnose ACS in patients with acute chest pain. High-sensitivity cardiac troponin (hs-cTn) assays may allow rapid rule-out of AMI (acute myocardial infarction) and avoidance of unnecessary hospital admissions and anxiety. Ruling in an ACS in a timely manner is also a high

	priority, as early intervention in patient with ACS has been shown to lead to better outcomes.
Review question	In low, medium and high risk people under investigation for acute chest pain of suspected cardiac origin, what is the accuracy of high-sensitivity troponin assay to identify NSTEMI/unstable angina?
Objectives	To evaluate the accuracy of high-sensitivity troponin assays in diagnosing NSTEMI/unstable angina.
Study design	• cross-sectional studies and cohort studies (including both retrospective and prospective analyses), and systematic reviews of diagnostic cohort studies • case-control studies to be included only if no other evidence is identified.
Population [with target condition]	Target condition and presentation: Adults (age ≥18 years) presenting with acute chest pain/discomfort of suspected cardiac origin. Acute chest pain is defined as 'pain, discomfort or pressure in the chest, epigastrium, neck, jaw, or upper limb without an apparent non-cardiac source[77] attributed to a suspected, but not confirmed AMI.' Include studies that compare different risks and studies that report accuracy for different risk stratifications. • High risk • Medium risk • Low risk For papers which do not report TIMI, GRACE or other validated risk tool scores we will map prevalence to the risks reported in TIMI.
Setting	Emergency department and other hospital settings (for example coronary care unit)
Index tests	High-sensitivity cardiac troponin (hs-cTn) assays: The recommended definition of a hs-cTn assay uses 2 criteria: • The total imprecision, coefficient of variation (CV), of the assay should be ≤10% at the 99th percentile value of a healthy reference population. • The limit of detection (LoD) of the assay should be such as to allow measurable concentrations to be attainable for at least 50% (ideally >95%) of healthy individuals.
Reference standards	Composite reference standard on the contemporary universal definition of myocardial infarction.[679] Reference assays used to diagnose myocardial necrosis, for example: • serial high sensitivity troponin assays • standard troponin T or I assays or a combination of them
Statistical measures	Test accuracy: • 2 x 2 tables (the numbers of TP, FN, FP and TN test results) • sensitivity, specificity, positive likelihood ratios, negative likelihood ratios
Other exclusions	Studies not fulfilling the inclusion criteria will be excluded. A full list of reasons for exclusions will be given in the appendix. For example: • studies which do not contain a concurrent control group • studies with population of traumatic chest injury without cardiac symptoms • studies with population in whom the cause of their chest pain/discomfort is known to be related to another condition, without cardiac symptoms (for example gastro-oesophageal reflux, panic disorder, cocaine-associated chest pain) • studies evaluating prognosis only and not reporting diagnostic accuracy • studies from non-OECD countries • studies published prior to 1999 • studies including patients with STEMI and where then results are not reported separately.
Search strategy	The search strategy will be based on intervention (high-sensitivity Tn assays) and target

	condition . • The databases to be searched are: ○ Medline, Embase, The Cochrane Library • Date limits for search: ○ studies published before 1999 • Language: English language only
Review strategy	Data synthesis: • Priority will be given to results as presented by AUCs (discriminatory analysis) and results of multivariate analysis (OR or RRs [95% CI]). Stratification – groups that cannot be combined: Analyses will be conducted separately for each hs-cTn assay. Analyses will be stratified according to whether the study evaluated: • target condition • timing of collection of blood sample for testing • the threshold used to define a positive hs-cTn result. For timing and threshold stratified analysis will be conducted for all timepoints for which sufficient data is available. • risk stratification: low, moderate and high pre-test probability of disease compared with each other if data allows. Pre-probability of disease (determined by clinical judgement based on cardiovascular risk factors, type of chest pain, physical findings and ECG abnormalities). Subgroups where diagnostic tests may be more or less accurate – to investigate heterogeneity: In the event of significant heterogeneity, we plan to explore possible causes by looking at the characteristics of the included studies. Possible sources of heterogeneity in this review may include: • age <70 years compared with age ≥70 years; <40 years versus ≥40 years • patients with pre-existing CAD at baseline compared with patients without pre-existing CAD • without previous AMI compared with pre-existing AMI • low to moderate pre-test probability of disease compared with high pre-test probability of disease (determined by clinical judgement based on cardiovascular risk factors, type of chest pain, physical findings and ECG abnormalities) • mixed populations compared with those that excluded patients with STEMI • time from symptom onset to presentation <3 hours compared with >3 hours • time from symptom onset to presentation <6 hours compared with >6 hours • renal function • diabetes • obesity • gender • ethnicity • socioeconomic status • people with disabilities. Are there any equality issues to consider? • see above • variation in access to diagnostic testing.

	Appraisal of methodological quality: The methodological quality of included DTA studies will be assessed using the QUADAS-2 checklist (per target condition).

C.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Table 3: Review protocol: Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Component	Description
Review question	In people under investigation for acute chest pain of suspected cardiac origin, what is the clinical and cost-effectiveness of non-invasive imaging compared to standard practice, when each is followed by the appropriate treatment for NSTEMI/unstable angina, in order to improve patient outcomes?
Rationale	The chest pain of recent onset guideline published in March 2010 (CG95) was reviewed in 2014 as part of NICE's routine surveillance programme to decide whether the guideline required updating. New evidence identified suggested that non-invasive cardiac imaging, including stress myocardial perfusion imaging, stress cardiac magnetic resonance imaging and multi-detector computed tomography, may afford early identification of people with NSTEMI/unstable angina in people presenting with acute chest pain and uncertain diagnosis following ECG and troponin testing. Currently the guideline recommends a chest X-ray to help exclude other causes of chest pain, and early chest computed tomography should only be considered to rule out other diagnoses. The new evidence relating to non-invasive cardiac imaging may potentially impact on these recommendations.
Objectives	To evaluate the clinical effectiveness of non-invasive imaging when followed up by treatment for NSTEMI/unstable angina.
Population and target condition	All adults (age ≥18 years) with acute chest pain/discomfort of suspected cardiac origin under investigation for NSTEMI/unstable angina, who have had initial triage including: • clinical history • signs and symptoms assessment • physical examination • ECG • high sensitivity troponin I or T, or standard sensitivity troponin I or T.

Index diagnostic tests + treatment	Index diagnostic tests:
	• coronary computed tomography angiography (coronary CT)
	  ○ multi-detector CT (MDCT) (≥64-slice CT scanner)
	  ○ dual X-ray source MDCT
	• myocardial perfusion scintigraphy (MPS):
	  ○ single photon emission CT (SPECT)
	  ○ positron emission tomography (PET)
	• cardiac magnetic resonance imaging (cardiac MRI)
	• stress perfusion cardiac MRI
	• echocardiography
	  ○ resting
	  ○ stress.
	Treatment:
	• standard practice

	To include: • aspirin • ticagrelor/clopidogrel • beta blocker • ACE inhibitor • statin • anticoagulant, for example fondaparinux, low molecular weight heparin, prasugrel • revascularisation where warranted.
Comparator + treatment or treatment alone (no test)	Comparator: • standard practice • one index test versus a second index test. Treatment: • standard practice (as above).
Outcomes	Efficacy outcomes: • all-cause mortality at 30-day and 1-year follow-up (or closest time point) • cardiovascular mortality at 30-day and 1 year follow-up (or closest time point) • myocardial infarction at 30-day follow-up • percutaneous coronary intervention (PCI) at 30-day follow-up • coronary artery bypass graft (CABG) at 30-day follow-up • hospitalisation at 30-day follow-up for cardiac causes (or closest time point) • hospitalisation at 30-day follow-up for non-cardiac causes (or closest time point) • quality of life at one year • adverse events related to index non-invasive test at 30 days • adverse events related to treatment: major bleeding at 30 days. Process outcomes: • number of people receiving treatment • length of hospital stay. Secondary accuracy outcomes: • sensitivity/specificity and other test accuracy measures.
Study design	RCTs
Exclusions	• studies with population of traumatic chest injury without cardiac symptoms • studies with population in whom the cause of their chest pain/discomfort is known to be related to another condition, without cardiac symptoms, for example gastro-oesophageal reflux, panic disorder, cocaine-associated chest pain • studies where there are different treatments for the 2 randomised groups • studies conducted in developing countries • studies published prior to 1999.
Search Strategy	The search strategy will be based on intervention (non-invasive tests listed) and target condition. • The databases to be searched are: ○ Medline, Embase, The Cochrane Library • Language: English only
Review Strategy	Stratification – population groups that cannot be combined: • low risk of CAD • intermediate risk of CAD • high risk of CAD

	○ risk stratification based on pre-test likelihood of CAD determined by cardiovascular risk factors, signs and symptoms, and clinical examination. Stratification – prior investigations: • standard troponin I or T • high sensitivity troponin I or T. <u>Subgroups (where diagnostic tests may be more or less accurate – to investigate heterogeneity):</u> • In the event of significant heterogeneity, we plan to explore possible causes by looking at the characteristics of the various included studies. Possible sources of heterogeneity in this review may include: ○ age, for example <70 years versus ≥70 years, ≤40 years versus >40 years ○ diabetes ○ ethnicity ○ gender ○ impaired renal function ○ obesity ○ people with disabilities ○ pre-existing CAD compared with no prior history of CAD. Equality issues • access to diagnostic testing. Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate. Extraction of data to include (where available): • timing of non-invasive test • troponin I or T test results • information on population risk of CAD. MIDs: Any different in mortality was clinically important, a 25% reduction or increase for all other outcomes. A 10% increase in adverse events was clinically important.

C.3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

Table 4: Review protocol: Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

Component	Description
Review question	In people under investigation for acute chest pain of suspected cardiac origin are non-invasive imaging tests more accurate compared to standard practice to identify whether NSTEMI/unstable angina is present, as indicated by the reference standard?
Rationale	The chest pain of recent onset (acute) guideline published in March 2010 (CG95) was reviewed in 2014 as part of NICE's routine surveillance programme to decide whether the guideline required updating. New evidence identified suggested that non-invasive cardiac imaging, including stress myocardial perfusion imaging, stress cardiac magnetic resonance imaging and multidetector computed tomography, may afford early identification of people with NSTEMI/unstable angina in people presenting with acute chest pain and uncertain diagnosis following ECG and troponin testing. Currently the guideline recommends a chest X-ray to help exclude other causes of chest pain, and early chest computed tomography should only be considered to rule out other diagnoses. The new evidence relating to non-invasive cardiac imaging may potentially impact on these recommendations.
Objective	To evaluate the accuracy of non-invasive imaging tests in diagnosing NSTEMI/unstable angina.
Study design	• cross-sectional studies and cohort studies (including both retrospective and prospective analyses) • case-control studies to be included only if no other evidence is identified.
Population	All adults (age ≥18 years) with acute chest pain/discomfort of suspected cardiac origin under investigation for NSTEMI/unstable angina, and have had initial triage including: • clinical history • signs and symptoms assessment • physical examination • ECG • high sensitivity troponin I or T, or standard sensitivity troponin I or T.
Settings	Emergency department and other hospital settings (for example coronary care unit)
Index tests	• coronary computed tomography angiography (coronary CT) ○ multidetector CT (MDCT) (≥64-slice CT scanner) ○ dual X-ray source MDCT • myocardial perfusion scintigraphy (MPS): ○ single photon emission CT (SPECT) ○ positron emission tomography (PET) • cardiac magnetic resonance imaging (cardiac MRI) • stress perfusion cardiac MRI • echocardiography ○ resting ○ stress
Comparator test	• standard practice To include: • aspirin • ticagrelor/clopidogrel • beta blocker • ACE inhibitor • statin • anticoagulant, for example fondaparinux, low molecular weight heparin, prasugrel • revascularisation where warranted

	• one index test versus a second index test
Reference standard(s)	• coronary angiography • ACS (NSTEMI/unstable angina) as defined by the American College of Cardiology/American Heart Association Guidelines • ACS (NSTEMI/unstable angina) as defined by European Society of Cardiology Guidelines
Statistical measures	• 2×2 tables • specificity • sensitivity • ROC curve or area under curve (AUC) • positive predictive value • negative predictive value • positive likelihood ratio • negative likelihood ratio
Other exclusions	• studies with population of traumatic chest injury without cardiac symptoms • studies with population in whom the cause of their chest pain/discomfort is known to be related to another condition, without cardiac symptoms, for example gastro-oesophageal reflux, panic disorder, cocaine-associated chest pain • studies conducted in developing countries • studies published prior to 1999.
Search strategy	The search strategy will be based on intervention (non-invasive tests listed) and target condition . • The databases to be searched are: ○ Medline, Embase, The Cochrane Library • Language: English only
Review strategy	<u>Stratification – population groups that cannot be combined:</u> • ≤10% prevalence of NSTEMI and/or unstable angina • >10% to 20% prevalence of NSTEMI and/or unstable angina • >20% to 50% prevalence of NSTEMI and/or unstable angina • >50% prevalence of NSTEMI and/or unstable angina ○ risk stratification based on prevalence of NSTEMI and/or unstable angina in individual study population <u>Stratification – prior investigations:</u> • standard troponin I or T • high sensitivity troponin I or T. <u>Subgroups (where diagnostic tests may be more or less accurate – to investigate heterogeneity):</u> • In the event of significant heterogeneity, we plan to explore possible causes by looking at the characteristics of the various included studies. Possible sources of heterogeneity in this review may include: ○ age, for example <70 years versus ≥70 years, ≤40 years versus >40 years ○ diabetes ○ ethnicity ○ gender ○ impaired renal function ○ obesity ○ people with disabilities

	○ pre-existing CAD compared with no prior history of CAD. Equality issues • access to diagnostic testing. Appraisal of methodological quality: • The methodological quality of each study will be assessed using the QUADAS-2 checklist (per target condition). Synthesis of data: • Diagnostic meta-analysis will be conducted where appropriate using hierarchical methods. Extraction of data to include (where available): • timing of non-invasive test • troponin I or T test results • information on population risk of CAD.

Appendix D: Health economic review protocol

Table 5: Health economic review protocol

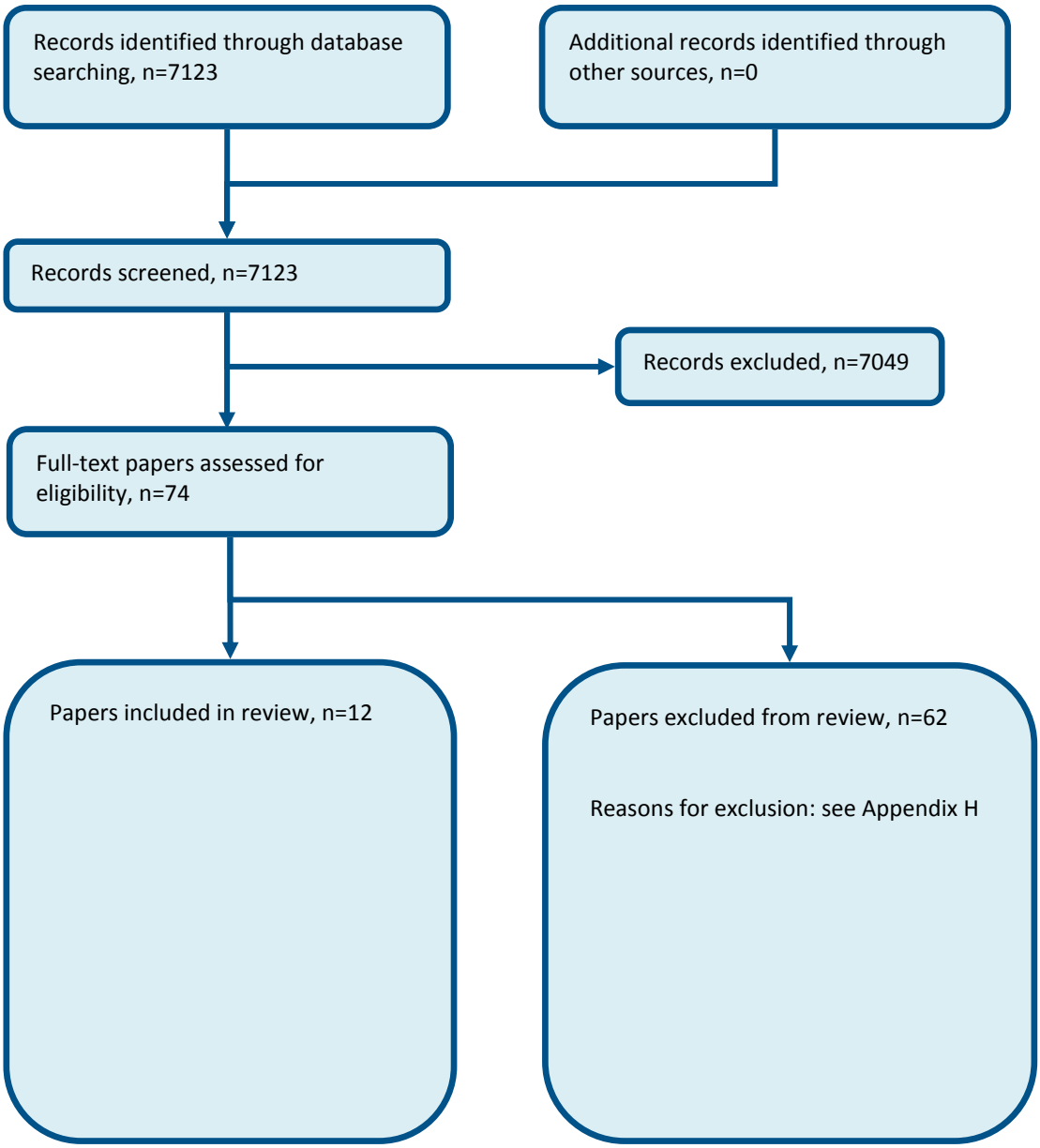
Review question	All questions – health economic evidence
Objectives	To identify economic evaluations relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G [in the Full guideline].
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 1999, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the NICE guidelines manual (2012).[528] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the GDG if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix M. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France,

	Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will have been excluded before being assessed for applicability and methodological limitations. *Economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will have been excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 1999 or later but that depend on unit costs and resource data entirely or predominantly from before 1999 will be rated as 'Not applicable'. • Studies published before 1999 will have been excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix E: Clinical study selection

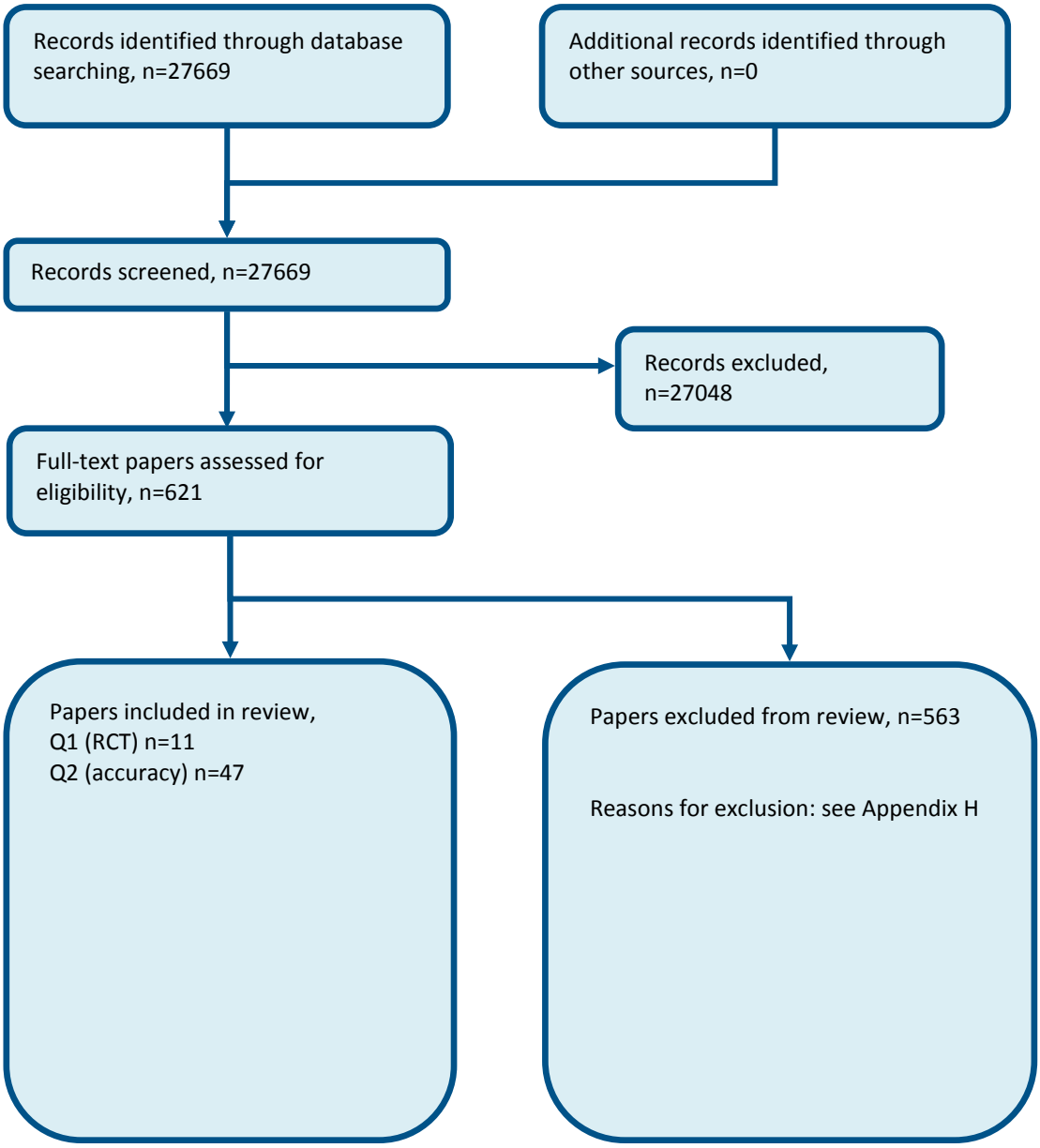
D1 High sensitivity cardiac troponins

Figure 1: Flow chart of clinical study selection for the review of high sensitivity troponins



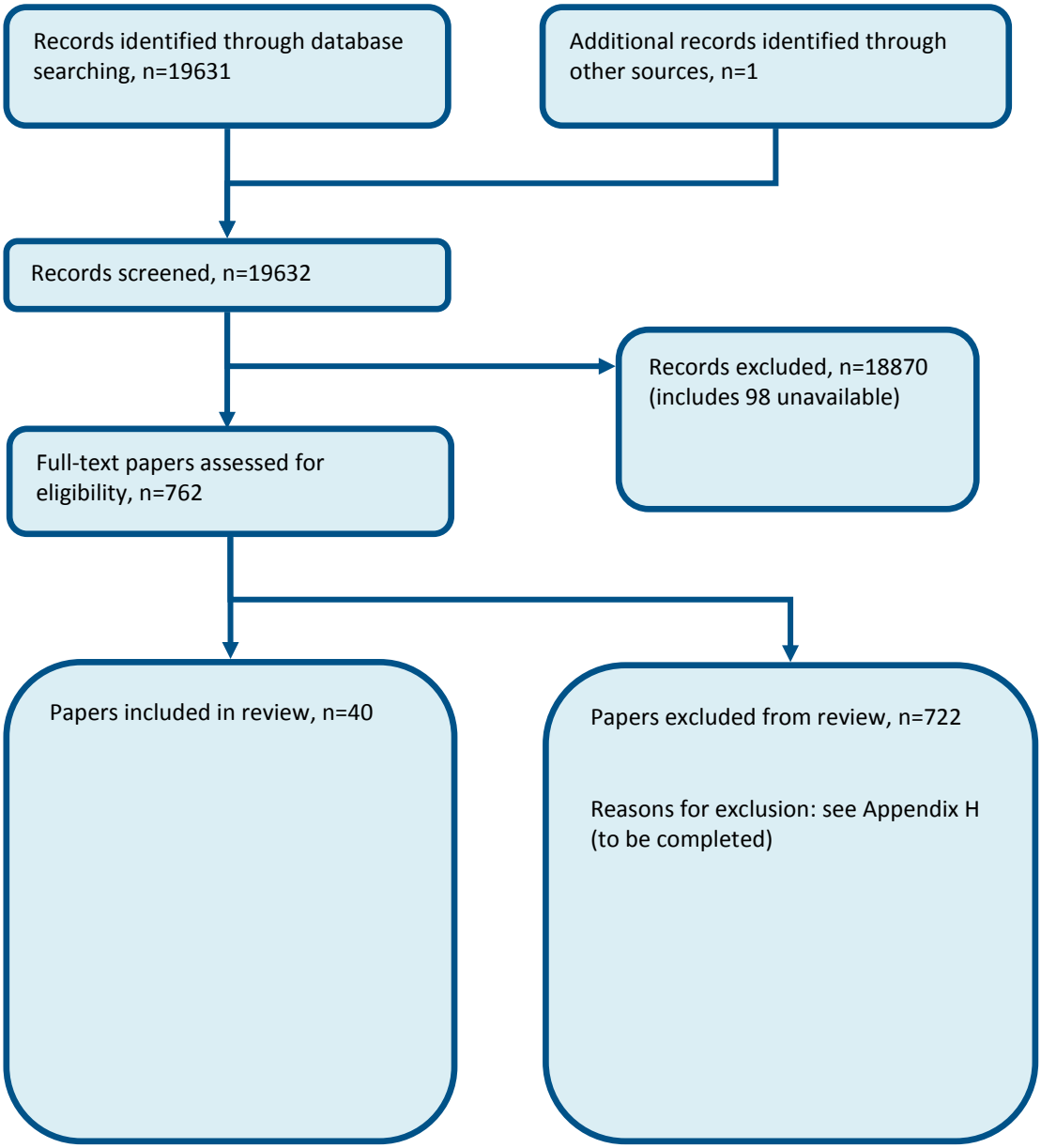
D2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Figure 2: Flow chart of clinical study selection for the review of non-invasive imaging for the identification of people with NSTEMI/unstable angina

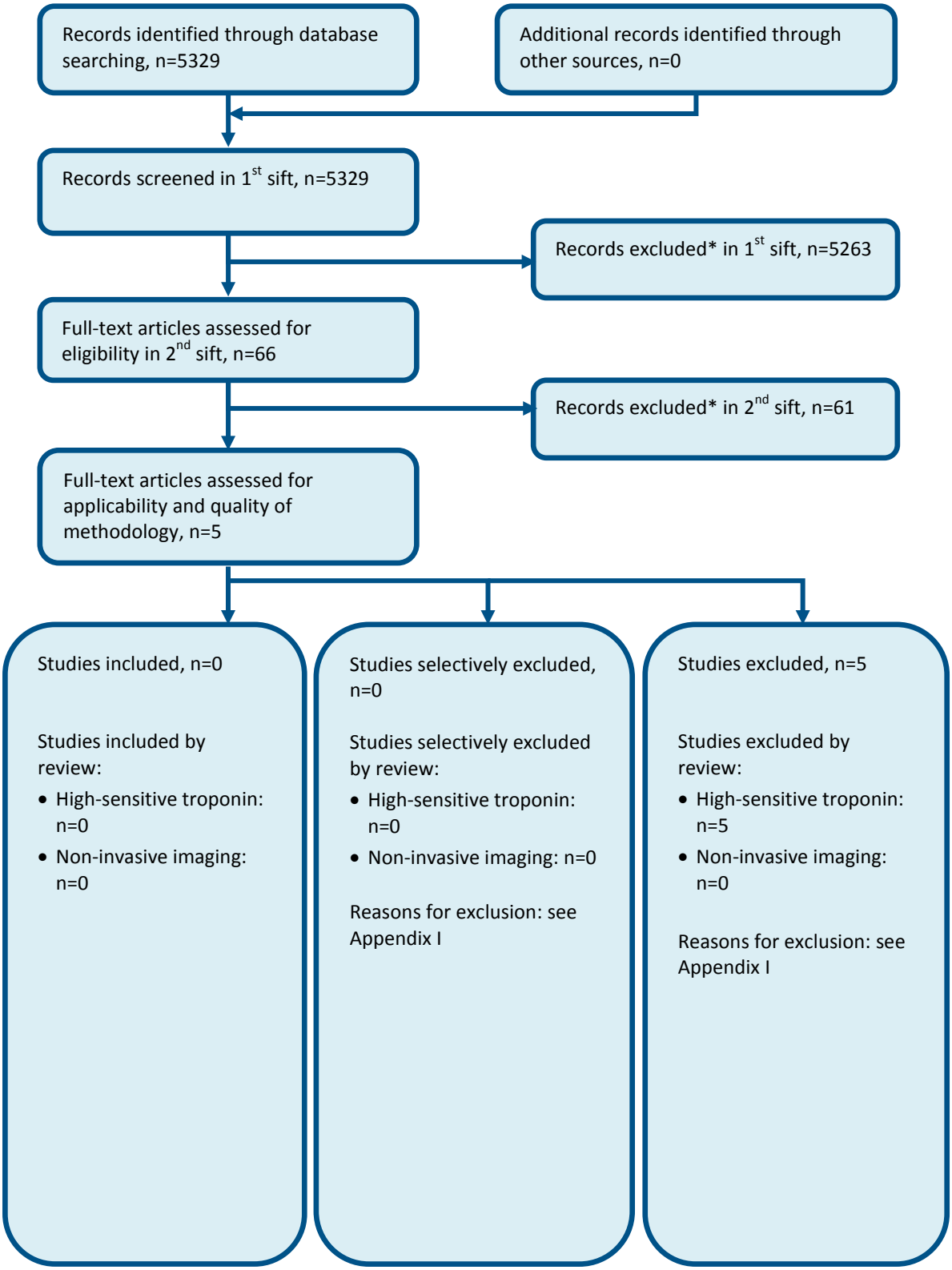


D3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

Figure 3: Flow chart of clinical study selection for the review of non-invasive imaging for the identification of people with NSTEMI/unstable angina



Appendix F: Health economic study selection



Appendix G: Literature search strategies

G.1 Contents

Search strategies used for the acute chest pain guideline are outlined below and were run in accordance with the methodology in the NICE guidelines manual (2014).[527] All searches were run up to 10 May 2016 unless otherwise stated. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text. Electronic, ahead of print or 'online early' publications are not routinely searched for. Where possible searches were limited to retrieve material published in English.

Table 6: Database date parameters

Database	Dates searched
Medline	1946 – 10 May 2016
Embase	1974 – 10 May 2016
The Cochrane Library	Cochrane Reviews to 2016 Issue 4 of 12 CENTRAL to 2015 Issue 2 of 12 DARE to 2016 Issue 4 of 4 HTA to 2016 Issue 2 of 4 NHSEED to 2015 Issue 2 of 4

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library (Wiley).

Searches for **intervention and diagnostic studies** were usually constructed using a PICO format where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Searches for the health economic reviews were run in Medline, Embase, the NHS Economic Evaluations Database (NHS EED) and the Health Technology Assessment (HTA). NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD).

For Medline and Embase an economic filter (instead of a study type filter) was added to the same clinical search strategy.

G.2 Population search strategies

G.2.1 Standard acute chest pain population

Medline search terms

1.	exp Chest Pain/
2.	chest pain.ti,ab.
3.	exp Angina Pectoris/
4.	angina.ti,ab.
5.	((unstable or acute) adj3 coronary).ti,ab.
6.	acute coronary syndrome*.ti,ab.
7.	exp Myocardial Infarction/
8.	(acute adj3 (heart or myocardial) adj (infarct* or ischaemi* or ischemi*)).ti,ab.
9.	(coronary adj (heart or arter*) adj (disease or syndrome*)).ti,ab.
10.	or/1-9

Embase search terms

1.	exp Thorax Pain/
2.	chest pain.ti,ab.
3.	exp Angina Pectoris/
4.	angina.ti,ab.
5.	((unstable or acute) adj3 coronary).ti,ab.
6.	acute coronary syndrome*.ti,ab.
7.	exp Heart Infarction/
8.	(acute adj3 (heart or myocardial) adj (infarct* or ischaemi* or ischemi*)).ti,ab.
9.	exp Coronary Artery Disease/
10.	(coronary adj (heart or arter*) adj (disease or syndrome*)).ti,ab.
11.	or/1-10

Cochrane search terms

#1.	MeSH descriptor: [Chest Pain] explode all trees
#2.	chest pain:ti,ab
#3.	MeSH descriptor: [Angina Pectoris] explode all trees
#4.	angina:ti,ab
#5.	((unstable or acute) next/3 coronary):ti,ab
#6.	acute coronary syndrome:ti,ab
#7.	MeSH descriptor: [Myocardial Infarction] explode all trees
#8.	(acute next/3 (heart or myocardial) next (infarct* or ischaemi* or ischemi*)):ti,ab
#9.	(coronary next (heart or arter*) next (disease or syndrome*)):ti,ab
#10.	{or #1-#9}

CRD search terms

#1.	MeSH DESCRIPTOR Chest Pain EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Angina Pectoris EXPLODE ALL TREES
#3.	(angina)
#4.	((unstable or acute) ADJ3 (chest pain or coronary))
#5.	(acute coronary syndrome)
#6.	MeSH DESCRIPTOR myocardial infarction EXPLODE ALL TREES
#7.	(acute ADJ3 (heart or myocardial) ADJ (infarct* or ischaemi* or ischemi*))
#8.	(coronary ADJ (heart or arter*) ADJ (disease or syndrome*))
#9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

G.3 Study filter search terms

G.3.1 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1.	letter/
2.	editorial/
3.	news/
4.	exp historical article/
5.	anecdotes as topic/
6.	comment/
7.	case report/
8.	(letter or comment*).ti.
9.	or/1-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animals/ not humans/
13.	exp animals, laboratory/
14.	exp animal experimentation/
15.	exp models, animal/
16.	exp rodentia/
17.	(rat or rats or mouse or mice).ti.
18.	or/11-17

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7

9.	animal/ not human/
10.	nonhuman/
11.	exp animal experiment/
12.	exp experimental animal/
13.	animal model/
14.	exp rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

G.3.2 Randomised controlled trials (RCT)

Medline search terms

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ti,ab.
4.	placebo.ab.
5.	randomly.ab.ti
6.	clinical trials as topic.sh.
7.	trial.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	single blind procedure/
8.	randomized controlled trial/
9.	double blind procedure/
10.	or/1-9

G.3.3 Systematic reviews (SR)

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

11.	or/1-10

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

G.3.4 Health economic studies (HE)

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.
11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp fee/
5.	budget/
6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.

10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

G.3.5 Diagnostic test accuracy studies (DIAG)

Medline search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	likelihood function/
7.	(roc curve* or auc).ti,ab.
8.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
9.	gold standard.ab.
10.	or/1-9

Embase search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	(roc curve* or auc).ti,ab.
7.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
8.	diagnostic accuracy/
9.	diagnostic test accuracy study/
10.	gold standard.ab.
11.	or/1-10

G.4 Searches for specific questions

G.4.1 Non-invasive testing

- In people under investigation for acute chest pain of suspected cardiac origin, what is the clinical and cost-effectiveness of non-invasive imaging compared to standard practice, when each is followed by the appropriate treatment for NSTEMI/unstable angina, in order to improve patient outcomes?

Medline search terms

1.	Standard population [G.2.1]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2

4.	Limit 3 to English language
5.	Echocardiography, Stress/
6.	((echocardiogra* or echo) adj3 (stress or resting or nonstress or 2d or 2 dimension* or two dimension* or contrast)).ti,ab.
7.	(cardiac adj3 stress).ti,ab.
8.	Exercise Test/
9.	((exercise or treadmill or bicycle or stress) adj3 test*).ti,ab.
10.	((physical or chemical or pharmacolog* or nuclear) adj2 stress).ti,ab.
11.	exp magnetic resonance imaging/
12.	magnet* resonance.ti,ab.
13.	(MR*1 or NMR*1 or cmr* or (magnet* adj3 (tomogra* or imag* or scan* or perfusion or angiograph*))).ti,ab.
14.	exp Chest Pain/ri [Radionuclide Imaging]
15.	Myocardial Perfusion Imaging/
16.	(myocardial adj2 (perfusion or scintigraphy)).ti,ab.
17.	((myocardial or mp or mps) adj3 (imag* or scan*)).ti,ab.
18.	exp Positron-Emission Tomography/
19.	((photon or positron) adj3 (emission or tomograph*)).ti,ab.
20.	(spect or mpi or pet or petscan*).ti,ab.
21.	Tomography, X-Ray Computed/
22.	((x-ray or radiograph* or compute*) adj3 tomograph*).ti,ab.
23.	Coronary Angiography/
24.	(compute* or ct or tomograph*).ti,ab.
25.	49 and 50
26.	((compute* or ct or tomograph*) adj3 angiograph*).ti,ab.
27.	Multidetector Computed Tomography/
28.	((multislice or multi slice or multisection or multidetect*) adj2 (ct or compute* or tomograph*)).ti,ab.
29.	('64' adj3 (scan* or ct or compute* or tomograph*)).ti,ab.
30.	((heart or cardiac or myocardial or imag* or scan* or diagnos*) adj2 (ct or cat)).ti,ab.
31.	(cta or ccta or tro-cta or msct).ti,ab.
32.	or/5-22,25-31
33.	4 and 31
34.	Study filters RCT [G.3.2] or SR [G.3.3] or DIAG [G.3.5]
35.	33 and 34
	Date parameters: 1999 - 10 May 2016

Embase search terms

1.	Standard population [G.2.1]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	exercise electrocardiography/
6.	((echocardiogra* or echo) adj3 (stress or resting or nonstress or 2d or 2 dimension* or two dimension* or contrast)).ti,ab.
7.	(cardiac adj3 stress).ti,ab.

8.	exercise test/
9.	((exercise or treadmill or bicycle or stress) adj3 test*).ti,ab.
10.	((physical or chemical or pharmacolog* or nuclear) adj2 stress).ti,ab.
11.	exp nuclear magnetic resonance imaging/
12.	magnet* resonance.ti,ab.
13.	(MR*1 or NMR*1 or cmr* or (magnet* adj3 (tomogra* or imag* or scan* or perfusion or angiograph*))).ti,ab.
14.	myocardial perfusion imaging/
15.	(myocardial adj2 (perfusion or scintigraphy)).ti,ab.
16.	((myocardial or mp or mps) adj3 (imag* or scan* or stress)).ti,ab.
17.	exp positron emission tomography/
18.	((photon or positron) adj3 (emission or tomograph*)).ti,ab.
19.	(spect or mpi or pet or petscan*).ti,ab.
20.	tomography/
21.	((x-ray or radiograph* or compute*) adj3 tomograph*).ti,ab.
22.	angiocardiography/
23.	(ct or computer* or tomograph*).ti,ab.
24.	47 and 48
25.	((compute* or ct or tomograph*) adj2 angiograph*).ti,ab.
26.	multidetector computed tomography/
27.	((multislice or multi slice or multisection or multidetect*) adj2 (ct or computer* or tomograph*)).ti,ab.
28.	('64' adj3 (scan* or ct or compute* or tomograph*)).ti,ab.
29.	((heart or cardiac or myocardial or imag* or scan* or diagnos*) adj2 (ct or cat)).ti,ab.
30.	(cta or ccta or tro-cta or msct).ti,ab.
31.	or/5-21,24-30
32.	4 and 31
33.	Study filters RCT [G.3.2] or SR [G.3.3] or DIAG [G.3.5]
34.	32 and 33
	Date parameters: 1999 - 10 May 2016

Cochrane search terms

#1.	Standard population [G.2.1]
#2.	MeSH descriptor: [Echocardiography, Stress] this term only
#3.	((echocardiogra* or echo) next/3 (stress or resting or nonstress or 2d or 2 dimension* or two dimension* or contrast)):ti,ab
#4.	(cardiac next/3 stress):ti,ab
#5.	MeSH descriptor: [Exercise Test] this term only
#6.	((exercise or treadmill or bicycle or stress) next/3 test*):ti,ab
#7.	((physical or chemical or pharmacolog* or nuclear) next/2 stress):ti,ab
#8.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#9.	magnet* resonance:ti,ab
#10.	MRI or MRS or NMRI or cmr*:ti,ab
#11.	(magnet* next/3 (tomogra* or imag* or scan* or perfusion or angiograph*)):ti,ab
#12.	MeSH descriptor: [Chest Pain] explode all trees and with qualifier(s): [Radionuclide imaging - RI]

#13.	MeSH descriptor: [Myocardial Perfusion Imaging] this term only
#14.	(myocardial next/2 (perfusion or scintigraphy)):ti,ab
#15.	((myocardial or mp or mps) next/3 (imag* or scan* or stress)):ti,ab
#16.	MeSH descriptor: [Positron-Emission Tomography] this term only
#17.	((photon or positron) next/3 (emission or tomograph*)):ti,ab
#18.	(spect or mpi or pet or petscan*):ti,ab
#19.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#20.	((x-ray or radiograph* or compute*) next/3 tomograph*):ti,ab
#21.	MeSH descriptor: [Coronary Angiography] this term only
#22.	(compute* or ct or tomograph*):ti,ab
#23.	#21 and #22
#24.	((compute* or ct or tomograph*) next/2 angiograph*):ti,ab
#25.	MeSH descriptor: [Multidetector Computed Tomography] this term only
#26.	((multislice or multi slice or multisection or multidetect*) next/2 (ct or compute* or tomograph*)):ti,ab
#27.	((heart or cardiac or myocardial or imag* or scan* or diagnos*) next/2 (ct or cat)):ti,ab
#28.	(cta or ccta or tro-cta or msct):ti,ab
#29.	{or #2-#20, #23-#28}
#30.	#1 and #29
	Date parameters: 1999 – 10 May 2016

G.4.2 High-sensitivity troponins

- In low, medium and high risk people under investigation for acute chest pain of suspected cardiac origin, what is the accuracy of high-sensitivity troponin assay methods compared to conventional cardiac troponins to identify/rapidly rule out NSTEMI/unstable angina compared to standard cardiac troponins?

Medline search terms

1.	Standard population [G.2.1]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Troponin/
6.	troponin i/ or troponin t/
7.	(sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive).ti,ab.
8.	(5 or 6) and 7
9.	((troponin* or tnt or ctnt or tropt or trop t or tni or ctni or tropI or trop I) adj2 (sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive)).ti,ab.
10.	(troponin* adj5 (architect or elecsys or accutni or accu-tni or access or unicel)).ti,ab.
11.	(hs?tnt or hs-?tnt or tnt-hs or tnths or ctnths or ctnt-hs).ti,ab.
12.	(hs?tni or hs-?tni or tni-hs or tnihs or ctnihs or ctni-hs or ctni-ultra or accutni or accu-tni).ti,ab.
13.	Myoglobin/
14.	(myoglobin* adj5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)).ti,ab.
15.	Creatine Kinase/

16.	(creatine kinase* adj5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)).ti,ab.
17.	Creatine Kinase, MB Form/
18.	(ck mb* or ck 2 or (mb* adj3 (isoenzyme* or enzyme* or isoform*))).ti,ab.
19.	or/8-18
20.	4 and 19
21.	Study filters RCT [G.3.2] or SR [G.3.3] or DIAG [G.3.5]
22.	20 and 21

Embase search terms

1.	Standard population [G.2.1]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	troponin/
6.	troponin c/ or troponin t/
7.	(sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive).ti,ab.
8.	(5 or 6) and 7
9.	((troponin* or tnt or ctnt or tropt or trop t or tni or ctni or tropI or trop I) adj2 (sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive)).ti,ab.
10.	(troponin* adj5 (architect or elecsys or accutni or accu-tni or access or unicel)).ti,ab.
11.	(hs?tnt or hs-?tnt or tnt-hs or tnths or ctnths or ctnt-hs).ti,ab.
12.	(hs?tni or hs-?tni or tni-hs or tnihs or ctnihs or ctni-hs or ctni-ultra or accutni or accu-tni).ti,ab.
13.	myoglobin/
14.	(myoglobin* adj5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)).ti,ab.
15.	creatine kinase/
16.	(creatine kinase* adj5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)).ti,ab.
17.	creatine kinase MB/
18.	(ck mb* or ck 2 or (mb* adj3 (isoenzyme* or enzyme* or isoform*))).ti,ab.
19.	or/8-18
20.	4 and 19
21.	Study filters RCT [G.3.2] or SR [G.3.3] or DIAG [G.3.5]
22.	20 and 21

Cochrane search terms

#1.	Standard population [G.2.1]
#2.	MeSH descriptor: [Troponin] explode all trees
#3.	MeSH descriptor: [Troponin I] this term only
#4.	MeSH descriptor: [Troponin T] this term only
#5.	(sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive):ti,ab,kw
#6.	(#2 or #3 or #4) and #5

#7.	((troponin* or tnt or ctnt or tropt or trop t or tni or ctni or tropI or trop I) near/2 (sensitiv* or hs or early or initial or rapid or present* or ultra or high performance or ultrasensitive)):ti,ab,kw
#8.	(troponin* near/5 (architect or elecsys or accutni or accu-tni or access or unicel)):ti,ab,kw
#9.	(hs*tnt or hs-*tnt or tnt-hs or tnths or ctnths or ctnt-hs):ti,ab,kw
#10.	(hs*tni or hs-*tni or tni-hs or tnihs or ctnihs or ctni-hs or ctni-ultra or accutni or accu-tni):ti,ab,kw
#11.	MeSH descriptor: [Myoglobin] this term only
#12.	(myoglobin* near/5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)):ti,ab,kw
#13.	MeSH descriptor: [Creatine Kinase] this term only
#14.	(creatine kinase* near/5 (analys* or analyze* or test* or investigat* or evaluat* or examin* or check* or assess* or measur* or diagnos* or identif* or verif* or assay or biological marker* or biomarker* or bio marker*)):ti,ab,kw
#15.	MeSH descriptor: [Creatine Kinase, MB Form] this term only
#16.	(ck mb* or ck 2 or (mb* near/3 (isoenzyme* or enzyme* or isoform*))):ti,ab,kw
#17.	44-#16
#18.	#1 and #17

G.5 Health economics search terms

G.5.1 Health economic (HE) reviews

Economic searches were conducted in Medline, Embase and CRD databases.

Medline & Embase search terms

1.	Standard population [G.2.1]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: March 2009 – 10 May 2016

CRD search terms

#1.	Standard population [G.2.1]
	Date parameters: Inception to 10 May 2015

Appendix H: Clinical evidence tables

H.1 High sensitivity cardiac troponins

Study	**Aldous 2011, 2012[45,46]**
Study type	Cohort
Number of studies (number of participants	n=939
Country and setting	New Zealand
Funding	Non-industry funded
Duration of study	November 2007–December 2010
Age, gender, ethnicity	Median age (IQR): 65 (56, 76) Male (%): 60 White (%): 89 Previous CAD (%): 52 Previous family history (%): 60 Previous revascularisation (%): 30 Diabetes (%): 17 Smoking (%): 61 Hypertension (%): 61 Dyslipidaemia (%): 58 Median BMI (IQR): 28(25, 31) Median (IQR) time to presentation (hours): 6.3 (3.3, 13.3)
Patient characteristics	Inclusion criteria: Adults (≥18 years) with symptoms suggestive of cardiac ischemia (acute chest, epigastric, neck, jaw or arm pain or

Study	Aldous 2011, 2012[45,46]
	discomfort or pressure without an apparent non-cardiac source) Exclusion criteria: ST-segment elevation on ECG; unable to provide informed consent; would not be available to follow-up
Index test	Roche Elecsys hs-cTnT LOD: 5 99th centile: 14 Coefficient of variation: <10% at 13
Reference standard	AMI was diagnosed if there was a rise and/or fall of the cTnI (≥20)% with ≥1 value at the 99th percentile Conventional troponins were measured using Abbott Diagnostics TnI (LoD 10 ng/l, 99th centile 28 ng/l, CV <10% at 32 ng/l, decision threshold 30 ng/l) Timing: On presentation, and at 2 hours and 6–12 hours
Target condition	NSTEMI
Results: 2012 Threshold: 14 Timing: On presentation TP FP FN TN Sensitivity% Specificity%	 181 134 24 600 83 82

Study	Aldous 2011, 2012[45,46]
Threshold: 5 Timing: On presentation	
TP	192
FP	305
FN	13
TN	429
Sensitivity%	93
Specificity%	58
Threshold: 3 Timing: On presentation	
TP	9196
FP	383
FN	9
TN	351
Sensitivity%	95
Specificity%	48
Threshold: 14 Timing: 2 hours	
TP	189
FP	149
FN	16
TN	585

Study	Aldous 2011, 2012[45,46]
Sensitivity% Specificity% Threshold: 5 Timing: 2 hours TP FP FN TN Sensitivity% Specificity% Threshold: 3 Timing: 2 hours TP FP FN TN Sensitivity% Specificity% 2011 Threshold: Peak 14 Timing: 0-2 hours	92 80 196 340 9 394 95 54 201 424 4 310 98 42

Study	Aldous 2011, 2012[45,46]
TP	189
FP	149
FN	11
TN	590
Sensitivity%	94
Specificity%	80
Threshold: Peak 14 and change 20% Timing: 0-2 hours	
TP	99
FP	43
FN	101
TN	696
Sensitivity%	50
Specificity%	94
Threshold: Peak 14 and change 20% Timing: 0-2 hours	
TP	195
FP	260
FN	5
TN	479
Sensitivity%	97
Specificity%	65

Study	Aldous 2011, 2012[45,46]
General limitations (according to QUADAS-2)	Patient flow and timing, patient selection and reference standard

Study	Borna 2016[160]
Study type	Cohort
Number of studies (number of participants	n=477
Country and setting	Sweden
Funding	Non-industry
Duration of study	Not stated
Age, gender, ethnicity	Median (IQR) age: 82 (77–85) Male (%): 53 White (%): NR Previous CAD (%): 59 Previous family history (%): NR Previous revascularisation (%):47 Diabetes (%): 24 Smoking (%): NR

Study	Borna 2016[160]
	Hypertension (%): 59 Dyslipidaemia (%): 48 Mean (SD) BMI: NR Time to presentation: NR
Patient characteristics	Inclusion criteria: All patients ≥75 years with chest pain suspicious of ACS if they were admitted to the ED or the medical observation unit. Exclusion criteria: Patients identified as low risk and discharged home from the ED. STEMI patients
Index test	The HScTnT analyses were performed with the use of the Elecsys 2010 system (Roche) with a limit of detection of 2 ng/l, a 99th percentile cut-off of 14 ng/l, and a coefficient of variation of less than 10 at 13 ng/l
Reference standard	AMI was diagnosed according to the joint European Society of Cardiology/American College of Cardiology/ American Heart Association/World Heart Federation Task Force. In addition, all diagnoses and ECGs were reviewed by 2 cardiologists. In patients with a HScTnT >14 ng/l, a 20% rise or fall was considered sufficient for an AMI diagnosis together with a clinical course suggestive of ACS.
Target condition	NSTEMI

Study	Borna 2016[160]
Results:	
Threshold: 14	
Timing: On presentation	
TP	117
FP	198
FN	12
TN	150
Sensitivity%	91
Specificity%	43
Threshold: 14	
Timing: 3-4h	
TP	129
FP	212
FN	0
TN	136
Sensitivity%	100
Specificity%	39
Threshold: 20	
Timing: 3-4hours	
TP	200
FP	143
FN	9
TN	205

Study	Borna 2016[160]
Sensitivity% Specificity% Threshold: 30 Timing: 3-4hours TP FP FN TN Sensitivity% Specificity% General limitations (according to QUADAS-2)	93 59 116 87 13 261 90 75 Patient flow and timing and reference standard

Study	Collinson 2013[227]
Study type	UK
Number of studies (number of participants	n=850
Country and setting	UK
Funding	Non-industry
Duration of study	Not stated
Age, gender, ethnicity	Median age (IQR): 54 (44, 64) Male (%): 60

Study	Collinson 2013[227]
	Previous AMI (%): 40 Previous family history (%): Previous revascularisation (%): 1 Diabetes (%): 8 Smoking (%): 28 Hypertension (%): 35 Dyslipidaemia (%): 24
Patient characteristics	Patients presenting to the ED with chest pain due to suspected, but not, proven AMI. Exclusion criteria: ECG changes diagnostic for AMI or high risk ACS (>1 mm ST deviation, or >3 mm inverted T waves); known CAD with prolonged (>1 hour) or recurrent typical cardiac-type pain; proven or suspected serious non-cardiac pathology (for example PE); co-morbidity or social problems requiring hospital admission even if AMI ruled out; obvious non-cardiac cause of chest pain (for example pneumothorax or muscular pain); presentation >12 hours after most significant episode of pain.
Index test	Roche Elecsys hs-cTnT LOD: 3 99th Centile: 14 Coefficient of variation: <10% at30 ng/l
Reference standard	The universal definition of myocardial infarction was used to categorise patients into those with or without an AMI utilising clinical, ECG, trial and local laboratory-derived cardiac troponin values and troponin measurements subsequently performed in the trial central laboratory on the admission and 90 minute samples using the Siemens Ultra assay as the predicate troponin method. Patients were classified as having an AMI on the basis of appropriate clinical features, electrocardiographic changes and the presence of a rise in troponin level above the diagnostic discriminant of the relevant assay in use locally and no alternative clinical cause of a troponin rise. Patients with a troponin rise consistent with an AMI and a final diagnosis of ACS or an AMI were classified as having an AMI. Patients with no troponin rise consistent with an AMI and a final diagnosis that was neither ACS nor an AMI were classified as not having an AMI. Patients with a final

Study	Collinson 2013[227]
	diagnosis of ACS or an AMI but no troponin rise were assessed by a single reviewer blind to treatment group who reviewed the initial and next-day ECG and categorised these patients as having an AMI only if an ECG showed ST-segment elevation and coronary reperfusion was performed. Patients with a troponin rise and a final diagnosis other than ACS or an AMI were assessed by 2 reviewers blinded to treatment group who reviewed case details and decided whether or not an AMI was the most likely diagnosis. Disagreements were resolved by discussion and patients classified as having an AMI or not. All patients with a cTnI (measured on the Siemens Ultra assay) exceeding the 99th percentile or a troponin measurement from the local laboratory exceeding the 99th percentile were reviewed and the final diagnosis confirmed.
Target condition	NSTEMI
Results: Threshold: 14 Timing: On presentation TP FP FN TN Sensitivity% Specificity% Threshold: Peak 14 Timing: On presentation and at 1.5 hours TP FP FN	 57 43 11 736 79 96 57 43 11 736

Study	Collinson 2013[227]
TN	83
Sensitivity%	94
Specificity%	
General limitations (according to QUADAS-2)	Patient flow and timing, patient selection and reference standard

Study	Eggers 2012[255,267,328]
Study type	Cohort
Number of studies (number of participants	n=360
Country and setting	Sweden
Funding	Non-industry funded
Duration of study	May 2000 (FAST II), October 2002 (FASTER I) – March 2001 (FAST II), August 2003 (FASTER I)
Age, gender, ethnicity	Male (%): 66 Previous AMI (%): 38 Previous revascularisation (%): 18 Diabetes (%): 18 Smoking (%): 18 Hypertension (%): 43 Dyslipidaemia (%): 38

Study	Eggers 2012[255,267,328]
	Delay <4 hours (%): 40
Patient characteristics	Inclusion criteria: Chest pain with ≥15 minute duration within the last 24 hours (FAST II-study), or the last 8 hours (FASTER I-study). Analysis restricted to patients with symptom onset <8 hours. Exclusion criteria: ST-segment elevation on the admission 12-lead ECG leading to immediate reperfusion therapy or its consideration was used as exclusion criterion.
Index test	Roche Elecsys hs-cTnT LOD: 3 99th centile: 14 Coefficient of variation: <10% at 13
Reference standard	Diagnosis was made based on the ESC/ACC consensus document. cTnI (Stratus CS, Siemens Healthcare Diagnostics, Deerfield, IL, USA). Non-STEMI defined as: cTnI above the 99th percentile of 0.07 µg/l at least at one measurement together with a ≥20% rise and/or fall and an absolute change ≥0.05 µg/l within 24 hours. To allow for the calculation of relative changes, cTnI was set to 0.02 µg/l (that is, a concentration below the lowest level of detection) when reported as 0.00 or 0.01 µg/l. Timing: eight time points during the first 24 hours following enrolment. Patients with typical angina pain at rest in combination with ST-segment depression but not fulfilling biochemical criteria for non-STEMI were considered to suffer from unstable angina.
Target condition	NSTEMI

Study	Eggers 2012[255,267,328]
Results: Threshold: 14 Timing: On presentation	
TP	101
FP	59
FN	27
TN	173
Sensitivity%	79
Specificity%	74
Threshold: 45.7 Timing: On presentation	
TP	65
FP	11
FN	63
TN	221
Sensitivity%	51
Specificity%	95
General limitations (according to QUADAS-2)	Patient selection, reference standard, flow and timing, patient selection and reference standard

Study	Freund
Study type	Cohort

Study	Freund
Number of studies (number of participants	317
Country and setting	France
Funding	Industry
Duration of study	1 year 5 months
Age, gender, ethnicity	Mean (SD) age: 56 (17) Male (%): 64 White (%): NR Previous CAD (%): 22 Previous family history (%): 30 Previous revascularisation (%):NR Diabetes (%): 12 Smoking (%): 38 Hypertension (%): 34 Dyslipidaemia (%): 33 Mean (SD) BMI: NR
Patient characteristics	August 2005–January 2007 Inclusion criteria: Consecutive hospital outpatients (>18 years of age) who presented to the ED with chest pain suggestive of ACS with the onset or peak occurring within the previous 6 hours. No STEMI included in the sub-group extracted. Exclusion: Chronic Kidney Disease requiring dialysis.
Index test	cTnI (Siemens Healthcare Diagnostica Inc., NewaRK, USA or Access analyser Beckman Coulter Inc., Brea, USA). Threshold for Siemens assay 140 ng/l, CV ≤10%

Study	Freund
	Threshold for Beckman assay 60 ng/l, CV 10% Timing: On presentation and at 3–9 hours if needed
Reference standard	AMI was diagnosed according to the joint European Society of Cardiology/American College of Cardiology/ American Heart Association/World Heart Federation Task Force redefinition of MI guidelines. Diagnosis of AMI required a cTnI increase above the 10% coefficient of variation (CV) value associated with at least one of the following: symptoms of ischaemia, new ST-T changes or a new Q wave on an electrocardiogram, imaging of new loss of viable myocardium or normal cTnI on admission. Unstable angina was diagnosed in patients with constant normal cTnI levels and a history or clinical symptoms consistent with ACS. cTnI (Siemens Healthcare Diagnostica Inc., NewaRK, USA or Access analyser Beckman Coulter Inc., Brea, USA). Threshold for Siemens assay 140 ng/l, CV ≤10% Threshold for Beckman assay 60 ng/l, CV 10% Timing: On presentation and at 3–9 hours if needed
Target condition	NSTEMI
Results: Low pre-test probability Threshold: 14 Timing: On presentation TP FP FN TN Sensitivity% Specificity% General limitations (according to QUADAS-2)	 22 12 1 24 89 (70–97) 85 (79–89) Patient selection and reference standard

Study	Hochholzer 2011[328]
Study type	Cohort
Number of studies (number of participants	n=724
Country and setting	Country: Switzerland, Spain, USA and Germany
Funding	Non-industry funded
Duration of study	Date recruited: April 2006–April 2008
Age, gender, ethnicity	Median age (IQR): 63 (50–75) Male (%): 66 Previous AMI (%): 25 Previous CAD (%): 35 Previous revascularisation (%): 28 Impaired rental function (GFR <60 ml/minute): 12 Diabetes (%): 16 Smoker (current) (%): 25 Hypertension (%): 61 Dyslipidaemia (%): 43 Median BMI (IQR): 26 (24–29)
Patient characteristics	Inclusion criteria: Consecutive adults presenting to the ED with symptoms suggestive of AMI at rest or minor exertion within the last 12 hours. Exclusion criteria: Positive troponin test prior to presentation, cardiogenic shock, terminal kidney failure requiring dialysis, or anaemia requiring transfusion.
Index test	Roche Elecsys hs-cTnT LOD: 2 ng/l 99th centile: 14 ng/l

Study	Hochholzer 2011[328]
	Coefficient of variation: <10% at 13 ng/l
Reference standard	Joint ESC, ACC, AHA and WHF[(a)] Conventional troponins were measured using Roche cTnT 4th generation assay (CV <10% at 35 ng/l), Beckman Coulter Accu cTnI (CV <10% at 60 ng/l), or Abbott Axsym cTnI ADV (CV <10% at 160 ng/l). A positive test was defined as change ≥30% of 99th centile or 10% CV level, within 6–9 hours. Timing: On presentation and at 6–9 hours. Final diagnoses were adjudicated by 2 independent cardiologists blind to hsTnT results. Where there was disagreement a third cardiologist was consulted.
Target condition	NSTEMI
Results: On presentation, 11 ng/L TP FP FN TN Sensitivity (95% CI) Specificity (95% CI) General limitations (according to QUADAS-2)	 90 177 3 454 96 (90, 99) 72 (68, 75) Flow and timing and patient selection

Study	Irfan 2013[350]
Study type	
Number of studies (number of participants	n=830

Study	Irfan 2013[350]
Country and setting	Country: Switzerland, Spain, USA and Germany
Funding	Industry and non-industry funded
Duration of study	Date recruited: April 2006–June 2009
Age, gender, ethnicity	Median age (IQR): 64 (51–75) Male (%): 67 Previous AMI (%): 25 Previous CAD (%): 36 Renal insufficiency (%): 11 Diabetes (%): 20 Hypertension (%): 64 Hypercholesterolemia (%): 47 Median BMI (IQR): 26 (24–30)
Patient characteristics	Inclusion criteria: Consecutive adults presenting to the ED with symptoms suggestive of AMI (for example acute chest pain, angina pectoris) within an onset or peak within the last 12 hours. Exclusion criteria: Acute trauma and terminal kidney failure requiring dialysis.
Index test	Roche Elecsys hs-cTnT LOD: 3 ng/l 99th centile: 14 ng/l Coefficient of variation: <10% at 13 ng/l Beckman Coulter hs-cTnI LOD: 2 ng/l 99th centile: 9 ng/l Coefficient of variation: lower than 99th centile

Study	Irfan 2013[350]
Reference standard	Joint ESC, ACC, AHA and WHF[(a)] Conventional troponins were measured using Roche cTnT 4th generation assay (CV <10% at 35 ng/l), Beckman Coulter Accu cTnI (CV <10% at 60 ng/l), or Abbott Axsym cTnI ADV (CV <10% at 160 ng/l). A positive test was defined as change ≥30% of 99th centile or 10% CV level, within 6–9 hours. Timing: On presentation and at 6–9 hours. Final diagnoses were adjudicated by 2 independent cardiologists blind to hsTnT results. Where there was disagreement a third cardiologist was consulted.
Target condition	NSTEMI
Results: <u>On presentation and at 1 hour, Δ 17% ng/L</u> TP FP FN TN Sensitivity (95% CI) Specificity (95% CI) <u>On presentation and at 1 hour, Δ 27% ng/L</u> TP FP FN TN Sensitivity (95% CI)	 65 202 43 520 60 (51, 69) 72 (69, 75) 68 245 40 477 63 (53, 71)

Study	Irfan 2013[350]
Specificity (95% CI)	66 (63, 69)
General limitations (according to QUADAS-2)	Flow and timing and patient selection

Study	Kurz[399]
Study type	Cohort
Number of studies (number of participants	94
Country and setting	Germany
Funding	Industry supplied assays
Duration of study	May 2008–December 2008 7 months
Age, gender, ethnicity	Mean (SD) age: 65.6 (10.8) Male (%): 71.3 White (%): NR Previous CAD (%): 50 Previous family history (%): 31.9 Previous revascularisation (%): CABG -17

Study	Kurz[399]
	Diabetes (%): 30.9 Smoking (%): 22.3 Hypertension (%): 77.7 Dyslipidaemia (%): 64.9 Mean (SD) BMI: 28.1 (4.1)
Patient characteristics	Inclusion criteria: Consecutively, patients with symptoms suggestive of ACS admitted to the chest pain unit. Exclusion criteria: Patients with ST-segment elevation.
Index test	All laboratory measurements on the new high sensitive cardiac troponin T assay (TnThs) were performed in the research laboratory of Roche Diagnostics in Penzberg, Germany.
Reference standard	Unstable angina and non-ST-segment elevation myocardial infarction (non-STEMI) were diagnosed using the joint European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation Task Force redefinition of myocardial infarction guidelines. Patients with cTnT concentrations at presentation below the 10% CV diagnostic cut-off (0.03 lg/l) received a final diagnosis of unstable angina or evolving non-STEMI depending on the presence of an elevated cTnT concentration in at least one of the consecutive samples collected within 24 hours after index event.
Target condition	

Study	Kurz[399]
Results:	
Threshold: 9.5	
Timing: On presentation	
TP	38
FP	11
FN	8
TN	27
Sensitivity%	82 (69–90)
Specificity%	77 (63–86)
Threshold: 14	
Timing: On presentation	
TP	16
FP	7
FN	10
TN	14
Sensitivity%	61 (42–77)
Specificity%	77 (60–88)
Threshold: 14	
Timing: 3hours of presentation	
TP	
FP	26
FN	7
TN	0

Study	Kurz[399]
	23
Sensitivity%	98 (84–100)
Specificity%	76 (58–87)
Threshold: 14 and 20% change Timing: On presentation and within 3 hours	
TP	11
FP	27
FN	15
TN	3
Sensitivity%	43 (26–61)
Specificity%	11 (4–72)
General limitations (according to QUADAS-2)	Patient selection, patient selection and reference standard

Study	Melki 2011[476]
Study type	Cohort
Number of studies (number of participants	n=233
Country and setting	Sweden

Study	Melki 2011[476]
Funding	Industry and non-industry funded
Duration of study	August 2006–January 2008
Age, gender, ethnicity	Median age (IQR): 65 (55, 76) Male (%): 67 Previous AMI (%): 30 Previous revascularisation (%): 21 Diabetes (%): 23 Smoking (%): 17 Hypertension (%): 50 Mean symptom onset (95% CI/range/IQR, hours): 5 (3, 8)
Patient characteristics	Inclusion criteria: Patients admitted to a coronary care unit with chest pain or other symptoms suggestive of ACS within 12 hours of admission. Exclusion criteria: Patients with persistent ST-segment elevation.
Index test	Roche Elecsys hs-cTnT LOD: 2 99th centile: 14 Coefficient of variation: <10% at 13
Reference standard	An acute MI was defined using the universal definition. Conventional troponin Roche 4th generation TnT (LoD 10 ng/l, 10% CV at 35 ng/l), or Beckman Coulter Access AccuTnI (LoD 10 ng/l, 99th centile 40 ng/l, CV <10% at 60 ng/l) Timing: On presentation and 9–12 hours later. Final diagnosis determined by the individual cardiologist, then adjudicated by 2 independent evaluators; all three were blinded to hs-TnT results.

Study	Melki 2011[476]
Target condition	
Results: Threshold: 14 Timing: On presentation TP FP FN TN Sensitivity% Specificity% Threshold: 14 Timing: 2 hours TP FP FN TN Sensitivity% Specificity% General limitations (according to QUADAS-2)	 112 21 2 98 98 82 114 25 0 94 100 79 Patient selection

Study	Reichlin (2011)[571]

Study	Reichlin (2011)[571]
Study type	Cohort
Number of studies (number of participants	n= 590
Country and setting	Country: Switzerland, Spain, USA and Germany
Funding	Industry and non-industry
Duration of study	Date recruited: April 2006–June 2009
Age, gender, ethnicity	Median age (IQR): 64 (51–67) Male (%): 67 Previous AMI (%): 25 Previous CAD (%): 37 Diabetes (%): 22 Smoker (current and past) (%): 60 Hypertension (%): 64 Hypercholesterolemia (%): 47 Median BMI (IQR): 27 (24–30)
Patient characteristics	Inclusion criteria: Consecutive adults presenting to the ED with symptoms suggestive of AMI (for example acute chest pain, angina pectoris) within an onset or peak within the last 12 hours. Exclusion criteria: Terminal kidney failure requiring dialysis.
Index test	Roche Elecsys hs-cTnT LOD: 3 99th centile: 14 Coefficient of variation: <10% at 13
Reference standard	Joint ESC, ACC, AHA and WHF[(a)] Conventional troponins were measured using Roche cTnT 4th generation assay (CV <10% at 35 ng/l), Beckman Coulter Accu cTnI (CV <10% at 60 ng/l), or Abbott Axsym cTnI ADV (CV <10% at 160 ng/l).

Study	Reichlin (2011)[571]
	A positive test was defined as change ≥30% of 99th centile or 10% CV level, within 6–9 hours. Timing: On presentation and at 6–9 hours. Final diagnoses were adjudicated by 2 independent cardiologists blind to hsTnT results. Where there was disagreement a third cardiologist was consulted.
Target condition	NSTEMI
Results: <u>On presentation and at 2 hours, Δ 30% ng/L</u> TP FP FN TN Sensitivity (95% CI) Specificity (95% CI) General limitations (according to QUADAS-2)	 43 84 24 439 64 (52, 74) 84 (80, 87) Flow and timing and patient selection

Study	Santalo (2013)[598]
Study type	Cohort
Number of studies (number of participants	n=358
Country and setting	Spain
Funding	Industry

Study	Santalo (2013)[598]
Duration of study	Not reported
Age, gender, ethnicity	Mean age (range): 69 (27, 93) Male (%): 68 Previous CAD (%): 35 Diabetes (%): 26 Hypertension (%): 62 Presentation within 3 hours: 46.2%
Patient characteristics	Date recruited: NR Country: Spain Inclusion criteria: Adults (>18 years) described as presenting with acute coronary syndromes and symptom duration ≥5 minutes; population included 174 people with a final diagnosis of non-acute coronary syndromes. Exclusion criteria: ST-segment elevation; new left bundle branch block; pre-admission thrombolytic therapy; defibrillation or cardioversion before sampling; pregnancy; renal failure requiring dialysis; unstable angina within 2 months; CABG within 3 months.
Index test	Roche Elecsys hs-cTnT LOD: NR 99th centile: 14 Coefficient of variation: <10% at 9.3
Reference standard	National Academy of Clinical Biochemistry and International Federation of Clinical Chemistry Committee[(b)] Roche cTnT; NSTEMI was defined as cTnT >10 ng/L and ΔcTnT >20% Timing: 30 minutes after arrival and at 2,4 and 6–8 hours or until discharge. Final diagnosis was made by an adjudication committee.
Target condition	NSTEMI

Study	Santalo (2013)[598]
Results:	
<u>On presentation, 14ng/L</u>	
TP	71
FP	80
FN	8
TN	199
Sensitivity (95% CI)	89 (81, 94)
Specificity (95% CI)	71 (66, 76)
<u>On presentation and at 2, 4 and 6-8 hours or until discharge, Δ 20% ng/L</u>	
TP	79
FP	94
FN	0
TN	185
Sensitivity (95% CI)	99 (94, 100)
Specificity (95% CI)	66 (61, 72)
General limitations (according to QUADAS-2)	Reference standard

Study	Sebbane 2013[620]
Study type	

Study	Sebbane 2013[620]
Number of studies (number of participants	n=248
Country and setting	France
Funding	Industry
Duration of study	December 2009–November 2011
Age, gender, ethnicity	Median age (IQR): 61 (48, 75) Male (%): 63
Patient characteristics	Inclusion criteria: Adults presenting to the ED with chest pain of recent onset (within 12 hours of presentation). Exclusion criteria: Traumatic causes of chest pain. STEMI was defined by the persistent elevation of the ST segment of at least 1 mm in 2 contiguous ECG leads or by the presence of a new left bundle-branch block with positive cardiac enzyme results. Patients with STEMI were excluded from the analysis for our review.
Index test	Roche Elecsys hs-cTnT LOD: 5 99th centile: 14 Coefficient of variation: <10% at 13
Reference standard	Diagnosis if acute MI was made on using the universal definition. Patients with clinical signs and symptoms consistent with acute ischemia associated with ECG changes and/or at least 1 positive cTnI result together with a rise or fall within the last 6 hours of admission were categorised as having an AMI. cTnI measured using the Access2 analyser (Access Immunosystem, Beckman Instruments, France). The LoD was <10 ng/l and the decision threshold was 40 ng/l. Timing: Conventional cardiac troponin (cTnI) on presentation, 6 hours later and beyond as needed. Two independent emergency department physicians, blinded to hs-cTnT results.

Study	Sebbane 2013[620]
Target condition	NSTEMI
Results: Threshold: 14 Timing: On presentation or taken pre-hospital TP FP FN TN Sensitivity% Specificity% Threshold: 18 Timing: On presentation or pre-hospital TP FP FN TN Sensitivity% Specificity% General limitations (according to QUADAS-2)	 19 25 6 142 75 85 19 17 6 150 75 90 Patient selection, flow and timing and reference standard

H.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Study	**ACRIN-PA 2012[430]**
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=1370)
Countries and setting	Conducted in USA; setting: 5 sites
Line of therapy	2nd line
Duration of study	Intervention time: index hospital length of stay median (IQR), h, MDCT 18.0 (7.6 to 27.2), standard practice 24.8 (19.2 to 30.5) Follow-up at 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: negative ECG and low risk on TIMI risk score
Stratum	Level of risk: Low (TIMI risk score ≤2)
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged ≥30 years with signs or symptoms that were consistent with possible ACS, no acute ischemia on initial ECG, Thrombolysis in Myocardial Infarction TIMI risk score of 0 to 2.
Exclusion criteria	Symptoms clearly non-cardiac in origin, co-existing condition that necessitated admission, normal findings on MDCT or invasive angiography in the previous year, or had contraindications to MDCT.
Recruitment/selection of patients	July 2009–November 2011
Age, gender and ethnicity	Age – mean (SD): 49 (13) MDCT group versus 50 (10) standard practice group. Gender (M:F): 49%/51%. Ethnicity: MDCT group versus standard practice group (%): White 40 versus 35, Black 58 versus 62, American Indian or Alaska Indian 1 versus 1, Native Hawaiian or other Pacific Islander >1 versus 0, Unknown 1 versus 1.

<table>
<tr><td>Further population details</td><td>MDCT group versus standard practice group (%): diabetes 14 versus 14, hypertension 51 versus 50, smokers 32 versus 34, history of MI 1 versus 1, hypercholesterolemia 27 versus 26.</td></tr>
<tr><td>Extra comments</td><td>Timing of non-invasive test: not reported
Troponin I or T test results: not reported
Length of index hospital length of stay median (IQR), h, MDCT 18.0 (7.6 to 27.2), standard practice 24.8 (19.2 to 30.5)
Hospitalisation or admission at to observation unit at index visit, n/total, %:
MDCT: 458/908 (50)
Standard practice: 357/462 (77)

<table>
<tr><td colspan="3">ECG findings at presentation and TIMI risk score</td></tr>
<tr><td>Characteristic</td><td>MDCT n=908</td><td>Standard practice n= 462</td></tr>
<tr><td>Electrocardiographic findings at presentation: n (%)</td><td></td><td></td></tr>
<tr><td>Normal</td><td>584 (64)</td><td>299 (65)</td></tr>
<tr><td>Non-specific</td><td>208 (23)</td><td>111 (24)</td></tr>
<tr><td>Early repolarization</td><td>23 (3)</td><td>14 (3)</td></tr>
<tr><td>Non-diagnostic abnormalities</td><td>68 (7)</td><td>24 (5)</td></tr>
<tr><td>Ischaemia</td><td></td><td></td></tr>
<tr><td>Known to have been present previously</td><td>11 (1)</td><td>6 (1)</td></tr>
<tr><td>Not known to have been present previously</td><td>10 (1)</td><td>7 (2)</td></tr>
<tr><td>ST elevation consistent with previous acute myocardial infarction</td><td>2 (<1)</td><td>0</td></tr>
<tr><td>Other or unknown</td><td>1 (<1)</td><td>1 (<1)</td></tr>
<tr><td>TIMI risk score: n (%)</td><td></td><td></td></tr>
<tr><td>0</td><td>461 (51)</td><td>234 (51)</td></tr>
<tr><td>1</td><td>325 (36)</td><td>166 (36)</td></tr>
<tr><td>≥2</td><td>122 (13)</td><td>62 (13)</td></tr>
</table>
</td></tr>
<tr><td>Indirectness of population</td><td>No indirectness</td></tr>
</table>

Interventions	(n=908) Intervention 1: MDCT. (n=462) Intervention 2: Standard practice.
Funding	Commonwealth of Pennsylvania Department of Health and the American College of Radiology Imaging Network Foundation
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MDCT VERSUS STANDARD PRACTICE Protocol outcome 1: Cardiovascular mortality at 30-day follow-up MDCT 0/908, Standard practice 0/462: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Myocardial infarction at 30-day follow-up MDCT 10/908, Standard practice 5/462: Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	All-cause mortality at 30-day and 1-year follow-up, cardiovascular mortality at 1 year follow-up, PCI at 30-day follow-up, CABG at 30-day follow-up, hospitalisation at 30-day follow-up for cardiac causes, hospitalisation at 30-day follow-up for non-cardiac causes, quality of life, adverse events related to related to index non-invasive test, major bleeding.

Study	**BEACON 2016[243]**
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=500)
Countries and setting	Conducted in The Netherlands; setting: 2 university and 5 community hospitals and primary care
Line of therapy	2nd line
Duration of study	Median (IQR) duration hospitalisation index visit, h : MDCT 6.3 (4.8 to 11.1) versus standard practice 6.3 (4.5 to 25.5) Median (IQR) time to diagnosis from randomisation, h: MDCT 3.4 (2.3 to 14.8) versus standard practice 15.0 (7.3 to 20.2)

	Primary care follow-up: 30 day
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: clinical history and examination, ECG and cardiac biomarkers
Stratum	Low risk
Subgroup analysis within study	Not applicable
Inclusion criteria	Acute chest pain or symptoms suggestive of ACS warranting further diagnostic evaluation, aged ≥30 years with a maximum age of 75 years for men and 80 years for women.
Exclusion criteria	Symptoms clearly of non-cardiac origin or a co-existing condition already necessitating hospital admission, history of CAD, clinical need for urgent invasive coronary angiography, clinical instability, serum troponin levels above 3 times the upper limit of the 99th percentile of the local assay, impaired renal function (estimated glomerular filtration rate <60% of age-corrected normal values), pregnancy, known allergy to iodinated contrast agent, severe arrhythmias, and body mass index >40 kg/m^2.
Recruitment/selection of patients	July 2011–January 2014
Age, gender and ethnicity	Age – mean (SD), years: MDCT group 55 (10); standard practice group 53 (9). Gender (M: F%): MDCT group 51/49, Standard practice group 55/45. Ethnicity: not reported.
Further population details	Baseline characteristics: MDCT group versus standard practice group, %: diabetes 12 versus 13, hypertension 17 versus 17, hypercholesterolemia 10 versus 14, family history of CAD 45 versus 39, smoker 37 versus 31. Prior randomisation ED investigations: ECG and blood analysis including high sensitivity troponin.
Extra comments	Timing of MDCT: immediately after initial clinical work-up in ED after randomisation. Troponin I or T test results: MDCT versus standard practice (ONLINE TABLE). Length of stay from ED presentation to admission or discharge, median (IQR), h: MDCT group: 5.3 4.0 to 7 versus standard practice group: 4.7 (3.4 to 6.4) Hospitalisation at index visit, n/total, %: MDCT: 109/1126 (9.7%) Standard practice: 55/564 (9.8%), risk difference = -0.1 (95%CI -3.2 to 2.8)

Mediation during follow-up, n (%) and TIMI and GRACE risk score		
	MDCT n=250	Standard practice n=250
Statin	65 (26)	51 (20)
Aspirin	48 (19)	35 (14)
Beta-blocker	41 (16)	40 (16)
ACE inhibitor	29 (12)	29 (12)
Angiotensin-receptor blocker	18 (7)	17 (7)
Calcium-channel blocker	18 (7)	19 (8)
Diuretic agent	36 (14)	23 (9)
Oral antidiabetic agent	22 (9)	24 (10)
TIMI risk score, n		
0	74	83
1	84	91
≥2	92	76
GRACE risk score, n (%)		
Low	211 (84)	208 (83)
Intermediate	31 (12)	39 (16)
High	8 (3)	3 (1)

	Discharge admission, diagnostic testing during index visit, n (%) MDCT n=250 / Standard care n=250 Discharge status Discharge from emergency department: 159 (65) / 144 (59) Admitted to hospital: 86 (35) / 101 (41) Exercise ECG at index visit: 23 (9) / 130 (53) Exercise <30 days: 32 (13) / 143 (58) SPECT at index visit: 2 (1) / 7 (3) SPECT <30 days: 2 (1) / 16 (7) MRI at index: 1 (0) / 1 (0) MRI <30 days: 1 (0) / 3 (1) MDCT after index visit: 1 (0) / 2 (1) Outpatient diagnostic testing <30 days: 10 (4) / 26 (11)
Indirectness of population	No indirectness
Interventions	(n=245) Intervention 1: 64-slice or higher MDCT immediately in ED after randomisation. Follow-up: 30 days MDCT angiography criteria: positive criteria ≥50% stenosis in one or more coronary arteries (n=245) Intervention 2: Standard practice: attending physicians made clinical decisions regarding further testing, including repeated cardiac marker assessment, hospital admission, non-invasive tests, and referral to invasive coronary angiography, according to European 2011 and AHA/ACC 2014 guidelines for management of NSTEMI. Follow-up: 30 days.
Funding	The Erasmus University Medical Centre

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NON-INVASIVE IMAGING (MDCT) VERSUS STANDARD PRACTICE

Protocol outcome 1: All-cause mortality at 30 days
Group 1 Non-invasive imaging: 0/245, Group 2 Standard practice: 0/245; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: PCI at 30 days Group 1 Non-invasive imaging: 22/245, Group 2 Standard practice: 13/245; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: CABG at 30 days Group 1 Non-invasive imaging: 0/245, Group 2 Standard practice: 4/245; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	All-cause mortality at 1 year, CVD mortality at 30 days and 1 year, PCI at 30 days, CABG at 30 days, re-admission to hospital for cardiac causes at 30 days, re-admission to hospital for non-cardiac causes at 30 day, adverse events due to index test at 30 days, adverse events due to medication (major bleeding) at 30 days, quality of life.

Study	**CATCH 2013[426]**
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=600)
Countries and setting	Conducted in Denmark; setting: Hvidovre University Hospital and primary care
Line of therapy	2nd line
Duration of study	Median (IQR) duration hospitalisation index visit, h: not applicable Median (IQR) time to diagnosis from randomisation, h: not applicable
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: clinical history, risk factors (structured interview), physical examination, ECG and cardiac biomarkers
Stratum	Level of risk: Low determined by physician base on risk factor profile, clinical evaluation, ECG and troponin findings

Pre-test risk according to Diamond and Forrester		
	MDCT n=285	Standard practice n=291
Pre-test risk, mean ± SD	44 (15.4)	36 (12.4)

	Pre-test risk group Low, n (%) Intermediate, n (%) High, n (%)	 35 (12.3) 110 (38.6) 140 (49.1)	 34 (11.7) 116 (39.9) 141 (48.5)
Subgroup analysis within study	Not applicable		
Inclusion criteria	Suspicion of NSTEMI in ED, but with a normal or non-diagnostic ECG, normal troponins and discharged within 24 hours without recurrence of chest pain. Treating physician found clinical indication for further non-invasive, outpatient, cardiac evaluation, based on the risk factor profile, symptom description and an overall clinical assessment. Following hospital discharge, eligible participants contacted by the study team within 7 days of initial admittance and consenting participants were randomised.		
Exclusion criteria	New diagnostic ECG changes with ST-segment elevation or depression >0.5 mm or T-wave inversion >4 mm in ≥2 contiguous leads, increased levels of plasma-troponins, age <18 years, women of childbearing age, not using approved contraception, patients with geographical residence or mental or physical conditions that could complicate follow-up, known allergy to iodinated contrast agents, serum creatinine >130 mg/l, abnormal chest x-ray or blood test tests that could explain the chest pain, prior CABG.		
Recruitment/selection of patients	Consecutive from January 2010–January 2013		
Age, gender and ethnicity	Age – mean (SD), years: MDCT group 56.4 (12.2); standard practice group 54.9 (12.2). Gender (M: F %): MDCT group 56.5/43.5; standard practice group 57.7/42.3. Ethnicity: not reported.		
Further population details	Baseline characteristics MDCT group versus standard practice group, %: diabetes 47.4 versus 36.4, hypertension 47.4 versus 36.4, hyperlipidaemia 41.1 versus 34.7, family history of CAD 24.2 versus 26.1, smoker (active or former) 60.4 versus 60.0. Prior randomisation ED investigations: clinical history and examination, ECG and cardiac biomarkers.		
Extra comments	Timing of MDCT: following discharge from ED Troponin I or T test results: not reported		

	Medication use during follow-up: not reported
Indirectness of population	No indirectness
Interventions	(n=299) Intervention 1: 320-slice MDCT (participants assigned within 1 week of ED discharge). Follow-up 120 days. MDCT angiography criteria: positive criteria >50% stenosis in left main artery or ≥70% in other large artery. Participants with coronary stenosis between 50% to 70% or a non-diagnostic MDCT, underwent further evaluation plan based on an integrated evaluation of coronary lesion location (proximal versus distal), stress test results and indices of clinical presentation. (n=301) Intervention 2: Standard practice (participants assigned within 1 week of ED discharge). Participants with signs of ischaemia on exercise bicycle ECG were referred for invasive coronary angiography. Participants with a non-diagnostic test (participants not able to reach at least 85% of expected heart rate) were referred for SPECT examination. Participants with reversible perfusion defects on SPECT or non-diagnostic test results (intolerance to dipyridamol, technical failure or supranormal liver uptake) were referred for invasive coronary angiography. All patients underwent both MSCT and functional test (bicycle exercise-ECG and/or MPI) in addition to a clinical evaluation to ensure blinding of patients and clinical staff until completion of tests, MDCT results remained blinded in standard practice group.

Functional test results		
	MSCT n=285	Standard practice n=291
n	285	291
Exercise bicycle stress ECG, n (%)	213 (75)	221 (76)
Positive for ischaemia, n (%)	16 (8)	14 (6)
Based on: ECG only	7 (44)	5 (36)
-ECG + chest pain	5 (31)	8 (57)
-Chest pain only	4 (25)	1 (7)
Non diagnostic, n (%)	19 (9)	15 (7)
Normal, n (%)	178 (84)	192 (87)
SPECT, n (%)	64 (22)	63 (22)
Reversible defects, n (%)	14 (22)	15 (24)

	No reversible defects, n (%)	50 (78)	48 (76)
	No functional stress performed, n (%)	8 (3)	7 (2)
Funding	Danish Heart Foundation, John and Birthe Meyer Foundation, the AP Møller and Chastine Mc-Kinney Møller Foundation and the Toyota Foundation.		
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NON-INVASIVE IMAGING (MDCT) VERSUS STANDARD PRACTICE Protocol outcome 1: Cardiac mortality at 120 days Group 1 Non-invasive imaging: 0/285, Group 2 Standard practice: 1/291; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: MI at 120 days Group 1 Non-invasive imaging: 0/285, Group 2 Standard practice: 3/291; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Hospitalisation due to cardiac causes Group 1 Non-invasive imaging: 7/285, Group 2 Standard practice: 11/291; Risk of bias: High; Indirectness of outcome: No indirectness			
Protocol outcomes not reported by the study	Length of hospital stay (not applicable), all-cause mortality at 1 year, CVD mortality at 30 days and 1 year, PCI at 30 days, CABG at 30 days, re-admission to hospital for cardiac causes at 30 days, re-admission to hospital for non-cardiac causes at 30 days, adverse events due to index test at 30 days, adverse events due to medication (major bleeding) at 30 days, quality of life.		

Study	**CT-COMPARE**[317]
Study type	RCT (patient randomised; parallel) n=562
Number of studies (number of participants)	1 (n=562)
Countries and setting	Conducted in Australia; setting: hospital and primary care
Line of therapy	2nd line

Duration of study	Hospital stay, h : MDCT 13.5 h (95%CI 11.2 to 15.7) versus standard practice 20.7 (95%CI 17.9 to 23.1) Follow-up at 30 days and 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ECG no evidence of ischaemia, negative troponin
Stratum	Level of risk: Intermediate risk CAD according to Cardiac Society of Australia and New Zealand guidelines, TIMI risk score >4
Subgroup analysis within study	Not applicable
Inclusion criteria	Males ≥30 and females ≥40 years of age presenting to ED with acute undifferentiated chest pain, intermediate probability of coronary artery disease according to Cardiac Society of Australia and New Zealand guidelines, initial 12-lead ECG without evidence of acute ischaemia, TIMI risk score <4, negative first serum sensitive troponin-I with a 99th centile at 0.04 ng/ml (Access 2 immunoassay, Beckman-Coulter).
Exclusion criteria	Previous diagnosis of CAD, confirmed pregnancy or lactating female, history of severe reactive airway disease or current exacerbation allergy or contraindication to iodinated contrast or beta-blockade medications, current atrial fibrillation, renal impairment (eGFR <50 ml/minute using the MDRD equation).
Recruitment/selection of patients	January 2010–2011
Age, gender and ethnicity	Age – mean (SD), years: MDCT group 52.2 (10.7); Standard practice group 52.3 (9.8). Gender (M: F %): MDCT group 59/41, Standard practice group 59/42. Ethnicity: not reported.
Further population details	Baseline characteristics MDCT group versus standard practice group, %: diabetes 7 versus 6, hypertension 31 versus 31, hyperlipidaemia 25 versus 24, family history of CAD 33 versus 33, smoker 24 versus 23. Prior ED investigations: ECG and troponin.
Extra comments	Timing of MDCT/exercise ECG: not reported Troponin I or T test results: not reported MDCT: not reported Follow-up medication not reported
Indirectness of population	No indirectness

Interventions	(n=322) Intervention 1: MDCT. MDCT angiography criteria: moderate stenosis, 50 to 69%, severe stenosis >70% (n=240) Intervention 2: Exercise ECG Discharge home: no evidence of ischaemia on ECG
Funding	Queensland Emergency Medicine Research Foundation, the Smart Futures Fellowship Early Career Grant, The Washington-Queensland Trans-Pacific Fellowship fund, National Center for Research Resources (component of the National Institutes of Health [NIH] and NIH Roadmap for Medical Research)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NON-INVASIVE IMAGING (MDCT) VERSUS ECG Protocol outcome 1: All-cause mortality at 30 days Group MDCT: 0/322, Group 2 Exercise ECG: 0/240; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: All-cause mortality at 1 year Group 1 MDCT: 2/322, Group 2 Exercise ECG: 1/240; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	CVD mortality at 30 days and 1 year, PCI at 30 days, CABG at 30 days, re-admission to hospital for cardiac causes at 30 days, re-admission to hospital for non-cardiac causes at 30 days, adverse events due to index test at 30 days, adverse events due to medication (major bleeding) at 30 days.

Study	**CT-STAT 2011[299]**
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=699)
Countries and setting	Conducted in USA; setting: 11 university and 5 community hospital sites
Line of therapy	2nd line

Duration of study	Median (IQR) hospitalisation index visit, h: not reported Median (IQR) time to diagnosis from randomisation, h: MDCT 2.9 (2.1 to 4.0) versus SPECT 15.0 (4.2 to 19.0) Follow-up: in-hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Level of risk: Low, determined by TIMI risk score. TIMI risk score, mean (SD): MDCT group versus SPECT group, 0.99 (0.84) versus 1.04 (0.7)
Subgroup analysis within study	Not applicable
Inclusion criteria	Chest pain suspicious for angina based on an ED physician's history taking and physical examination, age ≥25 years, time from onset of chest pain to presentation ≤12 hours, time from ED presentation to randomization ≤12 hours, normal or non-diagnostic rest ECG at the time of enrolment without ECG evidence of ischaemia (that is, ST-segment elevation or depression ≥1 mm in 2 or more contiguous leads, and/or T-wave inversion ≥2 mm), TIMI risk score ≤4 for unstable angina or NSTEMI.
Exclusion criteria	Attending physician clinical decision for immediate invasive evaluation, electrographic evidence of ischaemia, including acute NSTEMI or STEMI with ST segment elevation or depression equal to or greater than 1 mm in two or more contiguous leads, and/or T wave inversion greater than or equal to 2 mm, positive cardiac biomarkers (troponin, CK, and/or CK-MB) compatible with AMI on initial laboratory testing, based on site standard laboratory values, presence of pre-existing CAD, including prior MI, prior angiographic evidence of significant CAD (≥25% stenosis), history of CABG, renal insufficiency (creatinine greater than 1.5 mg/dl) or renal failure requiring dialysis, atrial fibrillation or other markedly irregular rhythm, psychological unsuitability or extreme claustrophobia, pregnancy or unknown pregnancy status, clinical instability including cardiogenic shock, hypotension (systolic blood pressure <90 mmHg), refractory hypertension (systolic blood pressure >180 mmHg on therapy), sustained ventricular or atrial arrhythmia requiring intravenous medications, known allergy to iodine or iodinated contrast, inability to tolerate beta-blocker medication, iodinated contrast administration or x-ray scan within the past 48 hours, use of any erectile dysfunction medications, BMI ≥39 kg/m^2, use of biguanides in past 48 hours.
Recruitment/selection of patients	June 2007–November 2008

Age, gender and ethnicity	Age – mean (SD), years: MDCT group 50 (10); SPECT 50 (10). Gender (M:F %): MDCT group 45.2/44.8, SPECT 47/53. Ethnicity: not reported.
Further population details	Baseline characteristics MDCT group versus SPECT, %: diabetes 5.5 versus 8.3, hypertension 35.5 versus 38.8, dyslipidemia 31.0 versus 36.1, family history of CAD 30.8 versus 30.0, smoker 25.2 versus 19.5. Prior ED investigations: physician's history taking and physical examination ECG, cardiac biomarkers.
Extra comments	Timing of MDCT: not reported Timing of SPECT: not reported Troponin I or T test results: not reported Follow-up medication: not reported MDCT: 262/297 (88.2%) discharged home within 6 hours SPECT: index testing was normal or probably normal in 304/338 (89.9%), 271 of 301 (89.1%) were discharged home within 6 hours
Indirectness of population	No indirectness
Interventions	(n=361) Intervention 1: 64- to 320-slice MDCT. Participants with coronary arterial stenoses 0% to 25% and/or calcium score <100 Agatston units were eligible for discharge. Participants with stenoses >70% were referred for invasive coronary angiography. Participants with intermediate lesions (stenosis 26% to 70% or calcium score >100 Agatston units) or uninterpretable scans were recommended to cross over for a rest-stress MPI. MDCT angiography criteria: categories used: 0=no stenosis; 1=1% to 25% stenosis; 2=26% to 50% stenosis; 3=51% to 70% stenosis; 4=71% to 99% stenosis; and 5=total occlusion. Discharge home: coronary arterial narrowings >25% or calcium score over 100 Agatston U Referral for invasive angiography: stenosis >70% Referral for further testing: intermediate lesions (stenosis 26% to 70% or calcium score over 100 Agatston U) or non-diagnostic scans (for example severe coronary calcifications, excessive motion artifact, or poor contrast-to-noise signals) (n=338) Intervention 2: Resting SPECT or stress SPECT if results were normal (standard exercise treadmill or pharmacologic (adenosine or dipyridamole) SPECT criteria: classified as normal, probably normal, equivocal, probably abnormal and abnormal, on basis of stress/rest perfusion imaging and functional data as well as haemodynamic response to stress, including symptoms

	(typical angina pectoris during exercise), ECG response (>1 mm flat or downsloping ST-segment depression 80 ms after the J point, >1 mm of ST-segment elevation 80 ms after the J point, or sustained ventricular tachycardia), exercise duration when applicable, and blood pressure response.
Funding	Bayer Pharmaceuticals
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MDCT VERSUS SPECT 1: All-cause mortality during index visit (30 day outcome) Group 1 MDCT: 0/361, Group 2 MPS: 0/338; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: MI during index visit (30 day outcome) Group 1 MDCT: 1/361, Group 2 MPS: 5/338; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: PCI during index visit (30 day outcome) Group 1 MDCT: 9/361, Group 2 MPS: 8/338; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: CABG during index visit (30 day outcome) Group 1 MDCT: 4/361, Group 2 MPS: 0/338; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	CVD mortality at 30 days and 1 year, re-admission to hospital for cardiac causes at 30 days, re-admission to hospital for non-cardiac causes at 30 days, adverse events due to medication (major bleeding) at 30 days, quality of life.

Study	**Goldstein 2007**
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=197)
Countries and setting	Conducted in USA; setting: single centre, William Beaumont Hospital, Michigan

Line of therapy	2nd line
Duration of study	Median (IQR) duration hospitalisation index visit, h: not reported Median (IQR) time to diagnosis from randomisation, h: MDCT 3.4 (2.3 to 14.8) versus standard practice 15.0 (7.3 to 20.2)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: clinical history and examination, ECG and cardiac biomarkers
Stratum	Level of risk: Low, (physician reference to (a) L. Goldman, E.F. Cook, P.A. Johnson, D.A. Brand, G.W. Rouan, T.H. Lee. Prediction of the need for intensive care in patients who come to emergency departments with acute chest pain, N Engl J Med, 334 (1996), pp. 1498–1504; (b) B.M. Reilly, A.T. Evans, J.J. Schaider, et al. Impact of a clinical decision rule on hospital triage of patients with suspected acute cardiac ischemia in the emergency department. JAMA, 288 (2002), pp. 342–350). TIMI risk score, mean (SD): MDCT group versus standard practice group, 1.24 (0.8) versus 1.33 (0.8). Goldman Riley criteria of very low risk: MDCT group very low, 100%; standard practice group very low risk 100%.
Subgroup analysis within study	Not applicable
Inclusion criteria	Chest pain or angina equivalent symptoms compatible with ischaemia during the past 12 hours, age ≥25 years, and a prediction of a low risk of infarction and/or complications according to established criteria.
Exclusion criteria	Known coronary artery disease, ECG diagnostic of cardiac ischaemia and/or infarction (significant Q waves, ST-segment deviations >0.5 mm, or T-wave inversion), elevated serum biomarkers including creatine kinase-MB, myoglobin, and/or cardiac troponin I on initial and 4-hour testing, previously known cardiomyopathy (with estimated ejection fraction ≤45%), contraindication to iodinated contrast and/or beta-blocking drugs; atrial fibrillation or markedly irregular rhythm, body mass index ≥39 kg/m^2; renal insufficiency (creatinine ≥1.5 mg/dl), CT imaging or contrast administration within the past 48 hours.
Recruitment/selection of patients	March 2005–September 2005
Age, gender and ethnicity	Age – mean (SD), years: MDCT group 48 (11); standard practice group 51 (12). Gender (M:F %): MDCT group 43/57, standard practice group 56/48. Ethnicity: not reported.

Further population details	Baseline characteristics: MDCT group versus standard practice group, %: diabetes 8.2 versus 12.2, hypertension 39 versus 38, hyperlipidaemia 34 versus 38, family history of CAD 40 versus 44, smoker 15 versus 20. Prior randomisation ED investigations: Time 0-hour and 4-hour electrocardiograms and serum biomarkers.
Extra comments	Timing of MDCT: not reported Troponin I or T test results: not reported MDCT: Admitted 8 (straight to invasive coronary angiography), discharge 67, repeat testing/further tests 24 (SPECT: 3 admitted for angiography, 21 discharge), admitted not requiring treatment (false positives) 1 Standard practice: Admitted 3 (straight to invasive coronary angiography), discharge 95, repeat testing/further tests none, admitted not requiring treatment (false positives) 2
Indirectness of population	No indirectness
Interventions	(n=99) Intervention 1: 64-slice MDCT. MDCT angiography criteria: maximal luminal diameter stenosis according to a qualitative severity scale: 0=no stenosis, 1=1% to 25% stenosis, 2=26% to 50%, 3=51% to 70%, 4=71% to 99%, and 5=total occlusion. Discharge home: coronary arterial narrowings >25% or calcium score over 100 Agatston U Referral for invasive angiography: stenosis >70% Referral for further testing: intermediate lesions (stenosis 26% –70% or calcium score over 100 Agatston U) or non-diagnostic scans (for example severe coronary calcifications, excessive motion artifact, or poor contrast-to-noise signals) Follow-up: 6 months. Medication/care during follow-up: not reported. (n=98) Intervention 2: Standard practice; serial ECG and cardiac biomarkers (creatine kinase-MB, troponin I, and myoglobin; Advia Centaur assay, Bayer Healthcare, Tarrytown, New York) at 4 and 8 hours after their baseline studies. Cardiac biomarker results were classified as abnormal for: creatine kinase-MB >5 ng/ml, troponin I ≥1.5 ng/ml, and myoglobin ≥98 ng/ml. Standard same-day rest-stress SPECT. SPECT angiography criteria: categorized according to standard criteria (1) symptoms (typical angina pectoris during

	exercise); (2) electrocardiographic response (>1 mm flat or downsloping ST-segment depression 80 minutes after the J point or >1 mm of ST-segment elevation 80 minutes after the J point or sustained ventricular tachycardia); and (3) single-SPECT perfusion defects with qualitative and semiquantitative visual analysis and a standard 17-segment model. Nuclear SPECT categorized as: (1) definitely normal, (2) probably normal, (3) probably abnormal, or (4) definitely abnormal. Discharge home: normal serial electrocardiograms, cardiac biomarkers, and stress test Referral for invasive angiography: electrocardiogram (ECG) abnormalities, elevated biomarkers, or abnormal nuclear stress studies Follow-up: 6 months. Medication/care during follow-up: not reported.
Funding	Minestrelli Advanced Cardiac Research Imaging
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NON-INVASIVE IMAGING (MDCT) VERSUS STANDARD PRACTICE Protocol outcome 1: All-cause mortality in-hospital Group 1 Non-invasive imaging: 0/99, Group 2 Standard practice: 0/98; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: MI in-hospital Group 1 Non-invasive imaging: 0/99, Group 2 Standard practice: 0/98; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: PCI in-hospital Group 1 Non-invasive imaging: 3/99, Group 2 Standard practice: 1/98; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: CABG in-hospital Group 1 Non-invasive imaging: 2/99, Group 2 Standard practice: 0/98; Risk of bias: Very high, High, Low; Indirectness of outcome: No indirectness Protocol outcome 4: Index test complications Group 1 Non-invasive imaging: 0/99, Group 2 Standard practice: 0/99; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	CVD mortality at 30 days and 1 year, PCI at 30 days, CABG at 30 days, re-admission to hospital for cardiac causes at 30 days, re-admission to hospital for non-cardiac causes at 30 days, adverse events due to medication (major bleeding) at

30 days, quality of life.

Study	Lim 2013[421]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=1508)
Countries and setting	Conducted in Singapore; setting: single centre, general hospital and primary care
Line of therapy	2nd line
Duration of study	Intervention time: index hospital length of stay not reported Follow-up at 30 days and 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Level of risk: not reported
Subgroup analysis within study	Not applicable
Inclusion criteria	Negative findings during first 6 hour monitoring, initial 12-lead ECG non-diagnostic for myocardial ischemia or AMI (defined as new Q waves, ST elevation or depression greater than 1 mm or 0.1 mV in two or more contiguous leads). No lower age limit for participants with coronary risk factors such as diabetes mellitus, otherwise aged ≥25 years. Protocol in first 6 hours prior to randomisation: continuous ECG monitoring, 12-lead ECG, creatine kinase-MB isoenzyme (Elecsys CK-MB STAT) and troponin T (3rd generation Elecsys Troponin T STAT) testing at 0, 3 and 6 hours.
Exclusion criteria	Congestive cardiac failure or hypotension associated with chest pain, unequivocal non-cardiac chest pain based on clinical assessment, or a clinical syndrome of persistent chest pain consistent with unstable angina, including patients with a past history of proven CAD, whose current chest pain was more severe or frequent than previous angina episodes.
Recruitment/selection of patients	August 2000–May 2002
Age, gender and ethnicity	Age – mean (SD): 52.02 (12.43) stress SPECT group versus 51.8 (12.8) standard practice group. Gender (M:F): 61%/49%. Ethnicity: stress SPECT group versus standard practice group (%): Chinese 70.0 versus 68.3, Malay 10.5 versus 12.7, Indian 17.8 versus 17.3, others 1.6 versus 1.8.
Further population details	Stress SPECT group versus standard practice group (%): diabetes 17.9 versus 17.9, hypertension 43.2 versus 39.3, smokers 33.0 versus 30.74, history of MI 1.0 versus 1.6, history of CAD 4.1 versus 4.4.

Extra comments	Timing of non-invasive test: not reported Troponin I or T test results: not reported Length of stay: not reported Hospitalisation during index visit: not reported
Indirectness of population	No indirectness
Interventions	(n=1004) Intervention 1: SPECT performed 30 minutes of exercise stress or 1 hour after pharmacological stress. (n=504) Intervention 2: Standard practice.
Funding	National Medical Research Council, Ministry of Health, Singapore
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STRESS SPECT VERSUS STANDARD PRACTICE Protocol outcome 1: Cardiac death at 30-day follow-up Stress SPECT 0/1004, Standard practice 0/504: Risk of bias: Very High; Indirectness of outcome: No indirectness Protocol outcome 1: Cardiac death at 1-year follow-up Stress SPECT 3/1004, Standard practice 0/504: Risk of bias: Very High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	All-cause mortality at 30-day and 1-year follow-up, myocardial infarction at 30-day follow-up, percutaneous coronary intervention at 30-day follow-up, coronary artery bypass graft at 30-day follow-up, hospitalisation at 30-day follow-up for cardiac causes, hospitalisation at 30-day follow-up for non-cardiac causes, quality of life, adverse events related to related to index non-invasive test, major bleeding, length of hospital stay, quality of life.

Study	Miller 2013[486]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in the USA: setting: 1 site, tertiary care hospital
Line of therapy	2nd line
Duration of study	Follow up at 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: excludes +ECGs and raised initial troponin I level. Clinical impression or TIMI risk score ≥2.
Stratum	Level of risk: mixed: Low <2, medium 2 to 5, high >5 on the TIMI score. Author classes it as a non-low risk study population.
Subgroup analysis within study	Not applicable
Inclusion criteria	Intermediate or high probability for experiencing acute coronary syndrome (ED care provider's clinical impression or a Thromobolysis in Myocardial Infarction risk score ≥2, aged 21 years or older, symptoms of possible ACS, care provider impression that inpatient evaluation was required and ability to be discharged if cardiac disease was excluded.
Exclusion criteria	Initial increased troponin I level, new ST-segment elevation (≥1 mV) or depression (≥2 mV), inability to lie flat, systolic blood pressure <90 mmHg, contraindications to MRI, refusal of follow-up procedures, terminal diagnosis with less than 3 months to live, pregnancy, renal insufficiency, chronic liver disease, or a history of heart, liver or kidney transplant.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	OU-CMR versus standard practice group: age, CO CMR median (IQR); 54 (45–91) versus 59 (40–76), gender (M/F): 53% versus 55%, ethnicity: White race 56% versus 70%.
Further population details	OU-CMR versus standard practice group (%): diabetes 31 versus 30, hypertension 71 versus 85, history of MI 17 versus 30, hypercholesterolemia NR, hyperlipidemia 63 versus 74
Extra comments	Timing of non-invasive test (MRI): Cardiac imaging was performed in 91% of usual care and in all patients in OU MRI. Median time to completion in usual care 22h (IQR 19 to 26 h) and in (timing of first test) OU MRI 21 h (16 to 23 h) Troponin I or T test results: Not reported Length of index hospital length of stay OU MRI versus usual care, median (IQR): 21 (15 to 25) versus 26 (23 to 45) Hospitalisation or admission to an observation unit at index visit, n/total, %: reported as hospitalization (transfer to an

	inpatient bed): 21% versus 95%		
	ECG and risk stratification characteristics	Cardiac MRI group n=53	Standard care group (inpatient care) n=52
	Normal	29 (56)	34 (64)
	Non-specific ST-T wave changes	8 (15)	12 (23)
	Early repolarization only	1 (2)	1 (2)
	Abnormal but not diagnostic of ischaemia	6 (12)	3 (53)
	Infarction or ischaemia known to be old	6 (12)	1 (2)
	Infarction or ischaemia not known to be old	2 (4)	3 (6)
	Suggestive of acute MI	0 (0)	0 (0)
	TIMI risk score		
	0	1 (2)	1 (2)
	1	2 (4)	8 (15)
	2	29 (56)	21 (40)
	3	17 (33)	19 (36)

	4 5	52(4) 1 (2)	3 (6) 1 (2)
Indirectness of population	No indirectness.		
Interventions	(n=52) Intervention 1: Cardiac MRI (n=53) Intervention 2: Standard care (inpatient care)		
Funding	Funded by the Translational Science Institute of Wake Forest University School of Medicine and the National Heart, Lung and Blood Institute.		
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CARDIAC MRI VERSUS STANDARD PRACTICE Protocol outcome 1: All-cause mortality Cardiac MRI 0/52, Standard practice 0/53: Risk of bias: Low; Indirectness of outcome: No indirectness			
Protocol outcomes not reported by the study	All-cause mortality at 1-year follow-up, cardiovascular mortality at 30 days and 1 year, myocardial infarction hospitalisation at 30-day follow-up for cardiac causes, hospitalisation at 30-day follow-up for non-cardiac causes, quality of life, PCI, CABG, adverse events related to related to index non-invasive test, adverse events related to treatment: major bleeding.		

Study	Miller 2010[487]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=110)
Countries and setting	Conducted in the USA: setting: 1 site, tertiary care hospital
Line of therapy	2nd line
Duration of study	Intervention time: length of hospital stay (Median, IQR): 29.9 (26.7–35.7) inpatient care, 25.7 (20.7–31.3) observation care unit cardiac MRI (OU-CMR) Follow up at 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: excludes +ECGs and raised initial troponin I level. Clinical impression or TIMI risk score ≥2.
Stratum	Level of risk: mixed: low <2, medium 2 to 5, high >5 on the TIMI score. Author classes it as a non-low risk study population.
Subgroup analysis within study	Not applicable
Inclusion criteria	Intermediate or high probability for experiencing acute coronary syndrome (ED care provider's clinical impression or a Thromobolysis in Myocardial Infarction risk score ≥2, aged 18 years or older, symptoms of possible ACS, care provider impression that inpatient evaluation was required and ability to be discharged if cardiac disease was excluded).
Exclusion criteria	Initial increased troponin I level, new ST-segment elevation (≥1 mV) or depression (≥ 2 mV), inability to lie flat, systolic blood pressure <90 mmHg, contraindications to MRI, refusal of follow-up procedures, terminal diagnosis with less than 3 months to live, pregnancy, renal insufficiency, chronic liver disease, or a history of heart, liver or kidney transplant.
Recruitment/selection of patients	January 2008–March 2009
Age, gender and ethnicity	OU-CMR versus standard practice group: age, median (IQR); 55 (48–61) versus 57 (47–64), gender (M/F): 47%:53% versus 53%:47%, ethnicity: White race; 66% versus 70%.
Further population details	OU-CMR versus standard practice group (%): diabetes 38 versus 40, hypertension 68 versus 75, smokers 34 versus 32, history of MI 15 versus 26, hypercholesterolemia NR, hyperlipidemia 74 versus 77

Extra comments	Timing of non-invasive test (MRI): stress cardiac MRI testing in 92%, with testing occurring in a median 53 minutes (IQR: 44-58 minutes) Troponin I or T test results: not reported Length of index hospital length of stay, median (IQR): 29.9 (26.7–35.7) Inpatient care, 25.7 (20.7–31.3) observation care unit cardiac MRI (OU-CMR) Hospitalisation or admission to an observation unit at index visit, n/total, %: reported as hospitalization (transfer to an inpatient bed): 21% versus 95% Note: four patients had MRI ordered but wasn't completed (leaving against medical advice, troponin level increase, VT before testing and car provider discretion), 3 MRI's were stopped (vomiting, patient request, tachycardia with adenosine infusion).		
	ECG and risk stratification characteristics	Cardiac MRI group n=53	Standard care group (inpatient care) n=57
	Normal	25 (47)	24 (42)
	Non-specific ST-T wave changes	17 (32)	22 (39)
	Early repolarization only	0 (0)	1 (2)
	Abnormal but not diagnostic of ischaemia	4 (8)	3 (5)
	Infarction or ischaemia known to be old	3 (6)	3 (5)
	Infarction or ischaemia not known to be old	4 (8)	4 (7)
	Suggestive of acute MI	0 (0)	0 (0)
	TIMI risk score		

	0	1 (2)	1 (2)
	1	8 (15)	10 (18)
	2	22 (42)	18 (32)
	3	16 (30)	17 (30)
	4	5 (9)	11 (19)
	5	1 (2)	0 (0)
Indirectness of population	No indirectness.		
Interventions	(n=53) Intervention 1: Cardiac MRI (n=57) Intervention 2: Standard care (inpatient care)		
Funding	Funded by the Translational Science Institute of Wake Forest University School of Medicine. Author received research support from Biosite, Schering-Plough, Siemens and Heartscape Technologies Inc, consultant for Molecular Insight, speaker for SanofiAventis (indirect sponsor of a CME event), other author had research support from Heartscape Technologies Inc.		
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CARDIAC MRI VERSUS STANDARD PRACTICE Protocol outcome 1: Cardiovascular mortality at 30-day follow-up Cardiac MRI 0/53, Standard practice 0/57: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Non-fatal MI at 30-day follow-up Cardiac MRI 1/53, Standard practice 1/57: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: PCI at 30-day follow-up Cardiac MRI 1/53, Standard practice 5/57: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: CABG at 30-day follow-up Cardiac MRI 1/53, Standard practice 0/57: Risk of bias: Low; Indirectness of outcome: No indirectness			

Protocol outcomes not reported by the study	All-cause mortality at 30-day and 1-year follow-up, cardiovascular mortality at 1 year, hospitalisation at 30-day follow-up for cardiac causes, hospitalisation at 30-day follow-up for non-cardiac causes, quality of life, adverse events related to related to index non-invasive test, adverse events related to treatment: major bleeding.

Study	ROMICAT-II[332,333]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 study (n=1000), 2 papers
Countries and setting	Multicentre; setting: 9 hospitals in the United States (7 sites had a chest pain observation unit and 2 admitting patients to the internal medicine floor).
Line of therapy	2nd line
Duration of study	Intervention time: index hospital length of stay; mean +/-SD, median (IQR), hours. CCTA 23.2+/-37.0, 8,6 (6.4–27.6), Standard practice 30.8 +/-28.0, 26.7 (21.4-–0.6). Follow up at 28 days.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: without ischaemic ECG changes or elevated initial troponin
Stratum	Level of risk: mixed. The number of cardiovascular risk factors were 0 or 1, 2 or 3 or ≥4. The authors class it as an intermediate risk population.
Subgroup analysis within study	Not applicable
Inclusion criteria	40–74 years old, presented to the ED with chest pain (or the angina equivalent) of at least 5 minutes' duration within 24 hours before presentation in the ED, were in sinus rhythm, and warranted further risk stratification to rule out acute coronary syndromes, as determined by an attending physician in the ED. Able to provide written informed consent, able to hold their breath for at least 10s.
Exclusion criteria	History of known coronary artery disease, new diagnostic ischaemic changes on the initial ECG, an initial troponin level in excess of the 99th percentile of the local assay, impaired renal function (creatinine level, >1.5 mg per decilitre [132.6μmol per litre], haemodynamic or clinical instability, known allergy to an iodinated contrast agent, a BMI >40 or currently symptomatic asthma. Documented or self-reported cocaine use within the past 48 hours, on metformin therapy and unable/unwilling to discontinue for 48 hours after CT scan, contraindication to beta blockers (taking daily anti-asthmatic medication)- only applies to patients with a HR>65 beats/minute at sites using a non-dual source CT scanner. No telephone or cell phone number (preventing follow up), with a positive pregnancy test.
Recruitment/selection of patients	23 April 2010–30 January 2012
Age, gender and ethnicity	Age – mean (SD): 54 (8) CCTA group versus 54 (8) standard practice group. Gender (M/F): 52%:48% versus 54%:46%. Ethnicity %; Black: 28% versus 28%, White; 66% versus 66%, Asian; 4% versus 3%, Other; 2% versus 4%, Non-Hispanic; 87% versus 85%.

Further population details	CCTA group versus standard practice group (%): diabetes;17 versus 17, hypertension; 54 versus 54, smokers (former or current); 50 versus 49, history of MI- not reported; family history of premature coronary disease; 50 versus 49, hypercholesterolemia; not reported. Dyslipidemia; 46 versus 45. Prior medication: aspirin; 23 versus 23, beta-blocker; 18 versus 16, statin; 28 versus 30.		
Extra comments	Timing of non-invasive test: not reported Troponin I or T test results: not reported Length of index hospital length of stay ITT: Mean +/- SD, median (IQR); 23.2 +/-37.0, 8.6 (6.4–27.6) CCTA group versus 30.8 +/- 28.0, 26.7 (21.4–30.6) standard care group Hospitalisation or admission to observation unit at index visit: 30% CCTA versus 60% standard practice group for admission to observation unit, 21% versus 25% for admission to hospital. ECG findings/TIMI scores		
	Cardiovascular risk factors	CCTA (n=501)	Standard practice group (n=499)
	0 or 1	36	38
	2 or 3	54	52
	≥ 4	10	10
Indirectness of population	No indirectness.		
Interventions	(n=501) Intervention 1: CCTA (n=499) Intervention 2: Standard practice		
Funding	Study was funded by the NHLBI U01HL092040. Author received support from NIH grants.		
RESULTS (NUMBERS ANALYSED) AND RISK FO BIAS FOR COMPARISON: CCTA VERSUS STANDARD PRACTICE Protocol outcome1: All-cause mortality at 28-day follow-up CCTA 0/501, Standard care group 0/499: Risk of bias: Low; Indirectness of outcome: No indirectness			

Protocol outcome 2: Non-fatal MI at 28-day follow-up CCTA 1/501, Standard care group 4/499: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: PCI at 28-day follow-up CCTA 5/501, Standard care group 3/499: Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: CABG at 28-day follow-up CCTA 1/501, Standard care group 1/499: Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	All-cause mortality at 1-year follow-up, cardiovascular mortality at 30 days and 1 year, hospitalisation at 30-day follow-up for cardiac causes, hospitalisation at 30-day follow-up for non-cardiac causes, quality of life, adverse events related to related to index non-invasive test, adverse events related to treatment: major bleeding.

H.3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

H.3.1 Multi-detector CT

Study	ACRIN PA 2012[430]
Study type	Cohort
Number of studies (number of participants	n=667
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age: 49 Male (%): 49

Study	ACRIN PA 2012[430]
	White (%): 40 Diabetes (%): 14 Smoking (%): 32 Hypertension (%): 51
Patient characteristics	Inclusion criteria: patients presenting with possible acute coronary syndrome Exclusion criteria: symptoms of non-cardiac origin
Index test	64-slice MDCT (≥50% stenosis of the LM, LAD, LF, or artery, or first order branch)
Reference standard	ICA: 5% (≥70% stenosis) MACE at 30-days: 95% (cardiac death, acute MI, ACS)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 28 9 0 640 1.00 0.99

Study	Beigel 2009[125]
Study type	Cohort
Number of studies (number of participants	n=308

Study	Beigel 2009[125]
Country and setting	Israel
Funding	Non-industry funded
Duration of study	Not reported
Age, gender, ethnicity	Mean age (SD): 54 (12) Male (%): 73% White (%): NR Diabetes (%): 24 Smoking (%): NR Hypertension (%): 52
Patient characteristics	Inclusion criteria: patients presenting to ED and subsequently referred to a chest pain unit Exclusion criteria: high risk probability of ACS and increased troponin
Index test	64-slice MDCT (>50% stenosis)
Reference standard	ICA: 7% (NR) MACE at 5 months (repeat cardiac chest pain, ICA, PCI, ACS, death)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 13 13 0 302 1.00 0.99

Study	Chang 2008[203]
Study type	Cohort
Number of studies (number of participants	n=123
Country and setting	Korea
Funding	Non-industry funded
Duration of study	May 2006–February 2007
Age, gender, ethnicity	Mean age (SD): 57 (14) Male (%): 61 White (%): NR Diabetes (%): NR Smoking (%): 17 Hypertension (%): NR Dyslipidaemia (%): 29
Patient characteristics	Inclusion criteria: People over 18 years with acute chest pain Exclusion criteria: NR
Index test	64-slice MDCT (≥50%)
Reference standard	ACC/AHA guideline for ACS: 51%
Target condition	ACS
Results: High risk TP FP FN TN	 99 10 1 17

Study	Chang 2008[203]
Sensitivity%	99
Specificity%	100
Intermediate risk	
TP	20
FP	2
FN	0
TN	33
Sensitivity%	100
Specificity%	94
Low risk	
TP	5
FP	0
FN	0
TN	48
Sensitivity%	100
Specificity%	100

Study	Christiaens 2012[226]
Study type	Cohort
Number of studies (number of participants	n=175
Country and setting	France

Study	Christiaens 2012[226]
Funding	Non-industry funded
Duration of study	October 2007–2009
Age, gender, ethnicity	Mean age (SD): 60 (8) Male (%): 71 White (%): NR Diabetes (%): 22 Smoking (%): 44 Hypertension (%): 546
Patient characteristics	Inclusion criteria: patients with symptoms suggested of ACS Exclusion criteria: elevated troponin, new diagnostic ECG changes
Index test	64-slice MDCT (≥50% stenosis)
Reference standard	ICA: 19% (≥50%) MACE at 6 months: 81% (CVD events)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 28 3 0 136 1.0 0.98

Study	CT-Compare 2014[317]
Study type	Cohort
Number of studies (number of participants	n=322
Country and setting	USA
Funding	Non-industry funded
Duration of study	January 2010–April 2011
Age, gender, ethnicity	Mean age (SD): 52.2 (10.7) Male (%): 59 White (%): NR Diabetes (%): 7 Smoking (%): 24 Hypertension (%): 31 Dyslipidaemia (%): 25
Patient characteristics	Inclusion criteria: male patients older than 30 and females older than 40 years with an intermediate probability of coronary artery disease. No evidence of ischaemia on ECG and normal troponin. Exclusion criteria: not reported.
Index test	Exercise ECG
Reference standard	ACS using case report forms based on Cardiac Society of Australia and New Zealand guidelines
Target condition	ACS
Results: TP FP FN TN	 32 8 0 213

Study	CT-Compare 2014[317]
Sensitivity% Specificity%	100 96

Study	Gallagher 2007[275]
Study type	Cohort
Number of studies (number of participants	n=85
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age: 50 Male (%): 61 White (%): NR Diabetes (%): 4 Smoking (%): 11 Hypertension (%): 15
Patient characteristics	Inclusion criteria: patients presenting to ED with acute chest pain Exclusion criteria: positive for cardiac markers or ECG changes
Index test	64-slice MDCT (>50% stenosis and CAC>400)
Reference standard	ICA: 12% (>70% stenosis) MACE at 30 days: 88% (cardiac death, non-fatal MI or unstable angina)

Study	Gallagher 2007[275]
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 6 6 1 72 1.0 0.92

Study	Goldstein 2007[300]
Study type	Cohort
Number of studies (number of participants	n=99
Country and setting	USA
Funding	Non-industry funded
Duration of study	March–September 2005
Age, gender, ethnicity	Mean age (SD): ACP 50 (14) ACS negative 49 (10) Male (%): ACP 71 ACP negative 51 White (%): NR Diabetes (%): ACP 14 ACP negative 9 Smoking (%): ACP 57 ACP negative 23 Hypertension (%): ACP 57 ACP negative 35 Dyslipidaemia (%): ACP 29 ACP negative 27

Study	Goldstein 2007[300]
Patient characteristics	Inclusion criteria: patients with acute chest pain deemed to be low risk Exclusion criteria: known CAD or ECG changes
Index test	64-slice MDCT (>70% stenosis)
Reference standard	ICA: 14% (NR) MACE at 30 days: 86% (cardiac death, non-fatal MI or unstable angina)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 8 3 0 88 88 86

Study	Hascoët 2012[322]
Study type	Cohort
Number of studies (number of participants	n=123
Country and setting	France
Funding	Non-industry funded
Duration of study	April 2008–September 2009

Study	Hascoët 2012[322]
Age, gender, ethnicity	Mean age (SD): 50.9 (13.8) Male (%): 89 White (%): NR Diabetes (%): 13 Smoking (%): 55.3 Hypertension (%): 33.3
Patient characteristics	Inclusion criteria: low to intermediate risk patients presenting with acute chest pain to ED Exclusion criteria: high risk patients including ECG changes and increased troponin
Index test	64-slice MDCT(≥50%)
Reference standard	ICA: 24% (≥50%) MACE at median (IQR) 15 (7–19) months (CV death, MI, revascularisation): 76%
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 10 19 0 94 1.00 0.83

Study	Hollander 2007[335]

Study	Hollander 2007[335]
Study type	Cohort
Number of studies (number of participants	n=54
Country and setting	USA
Funding	Non-industry funded
Duration of study	January 2005–June2006
Age, gender, ethnicity	Mean age (SD): 46.5 (8.5) Male (%): 71 White: 22 Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: Patients older than 30 years presenting with chest pain and who received an ECG and angiography Exclusion criteria: not reported.
Index test	ICA: 15% (≥50% stenosis) MACE: 85% (cardiac death or non-fatal MI) at 30 days
Reference standard	≤10% Normal or non-specific ECG, negative cardiac biomarkers
Target condition	ACS
Results: TP FP FN TN	 2 4 0 48

Study	Hollander 2007[335]
Sensitivity% Specificity%	100 92

Study	Hollander 2009[334]
Study type	Cohort
Number of studies (number of participants	n=519
Country and setting	USA
Funding	Non-industry funded
Duration of study	Jan 2005–October 2007
Age, gender, ethnicity	Mean age (SD): 47 (8.9) Male (%): 44 White (%): 26 Diabetes (%): 14 Smoking (%): NR Hypertension (%): 44
Patient characteristics	Inclusion criteria: patients presenting to the ED with acute chest pain requiring an ECG Exclusion criteria: chest pain of non-cardiac origin
Index test	64-slice MDCT (≥50% stenosis)
Reference standard	ICA:3% (≥50% stenosis) MACE at 30 days: 97% (cardiac death or non-fatal MI)
Target condition	ACS
Results:	

Study	Hollander 2009[334]
TP	7
FP	47
FN	0
TN	508
Sensitivity%	1.00
Specificity%	0.92

Study	Johnson 2007[360]
Study type	Cohort
Number of studies (number of participants	n=55
Country and setting	Germany
Funding	Non-industry funded
Duration of study	July 2004–March 2005
Age, gender, ethnicity	Mean age (SD): 67 (10) Male (%): 70% Diabetes (%): NR Smoking (%): NR Hypertension (%): NR
Patient characteristics	Inclusion criteria: patients referred to a cardiologist with unclear origin of chest pain Exclusion criteria: NR

Study	Johnson 2007[360]
Index test	64-slice MDCT (>50% stenosis)
Reference standard	ICA:100% (>50% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 16 3 1 35 0.94 0.92

Study	Meijboom 2008[471]
Study type	Cohort
Number of studies (number of participants	n=127
Country and setting	The Netherlands
Funding	Non-industry funded
Duration of study	12 months
Age, gender, ethnicity	Mean age: 59 Male (%): 37 Diabetes (%): 4

Study	Meijboom 2008[471]
	Smoking (%): 20 Hypertension (%): 26
Patient characteristics	Inclusion criteria: unstable angina, negative ECG and troponin; NTEMI, negative ECG raised troponin Exclusion criteria: not reported.
Index test	64-slice MDCT (≥50% stenosis)
Reference standard	ICA:100% (≥50% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 16 4 0 8 100 99

Study	ROMICAT 2009[330]
Study type	Cohort
Number of studies (number of participants	n=368
Country and setting	USA

Study	ROMICAT 2009[330]
Funding	Non-industry funded
Duration of study	May 2005–2007
Age, gender, ethnicity	Mean age (SD): 52.7 (12) Male (%): 61 White (%): 85 Diabetes (%): 11 Smoking (%): 49 Hypertension (%): 39
Patient characteristics	Inclusion criteria: patients with chest pain Exclusion criteria: history of CAD, ECG changes
Index test	64-slice MDCT (>50% stenosis)
Reference standard	ACS Acute MI developed positive troponin during serial testing at 6 hours or 9 hours after presentation UA according to the ACC/ AHA and ESC guidelines
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 24 44 7 293 100 87

Study	ROMICAT 2009[330]

Study	ROMICAT-II 2008[332,333]
Study type	Cohort
Number of studies (number of participants	n=501
Country and setting	USA
Funding	Non-industry funded
Duration of study	April 2010–Janurary 2012
Age, gender, ethnicity	Mean age (SD): 54.2 (8) Male (%): 43.2 White (%): 66 Diabetes (%): No ACS 104 ACS 16.1 Smoking (%): No ACS 26.1 ACS 16.1 Hypertension (%): No ACS 37.1 No ACS 64.5 Dyslipidaemia (%): No ACS 34.7 No ACS 58.1
Patient characteristics	Inclusion criteria: people with at least 5 minutes of chest pain, <75 but older than 40, in sinus rhythm and able to hold their breath for 10 s Exclusion criteria: diagnostic ECG changes, history of coronary artery disease, elevated troponins
Index test	ICA: 6% (>50% stenosis) MACE at 28 days: 4% (CVD events)
Reference standard	≤10% No ischaemic changes on ECG, initial troponin negative
Target condition	ACS

Study	ROMICAT-II 2008[332,333]
Results: TP FP FN TN Sensitivity% Specificity%	 19 1 3 297 0.86 1.0

Study	Rubinstein 2007[584]
Study type	Cohort
Number of studies (number of participants	n=58
Country and setting	Israel
Funding	Non-industry funded
Duration of study	15 months
Age, gender, ethnicity	Mean age (SD): 56 (10) Male (%): 69 White (%): NR Diabetes (%): 21 Smoking (%): 38 Hypertension (%): Dyslipidaemia (%): 57
Patient characteristics	Inclusion criteria: patients with suspected ACS

Study	Rubinstein 2007[584]
	Exclusion criteria: not reported.
Index test	64-slice MDCT (≥50% stenosis)
Reference standard	ICA: 74% (≥50% stenosis) SPECT: 26% (perfusion defects indicative of myocardial ischaemia)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 24 3 0 35 100 92

Study	Ueno 2009[697]
Study type	Cohort
Number of studies (number of participants	n=36
Country and setting	Japan
Funding	Non-industry funded
Duration of study	February 2005–March 2006

Study	Ueno 2009[697]
Age, gender, ethnicity	Mean age: 67 Diabetes (%): 30 Smoking (%): 36 Hypertension (%): 8
Patient characteristics	Inclusion criteria: patients with chest pain suggestive of cardiac Exclusion criteria: presence of ECG changes
Index test	64-slice MDCT (>50% stenosis)
Reference standard	ACC/AHA guideline for ACS: 100%
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 11 4 1 20 92 83

Study	van Velzen 2012[708]
Study type	Cohort
Number of studies (number of participants	n=106

Study	van Velzen 2012[708]
Country and setting	The Netherlands
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): 57 (10) Male (%): 67 White (%): Diabetes (%): 16 Smoking (%): NR Hypertension (%): 52 Dyslipidaemia (%): 39
Patient characteristics	Inclusion criteria: patients with acute chest pain Exclusion criteria: included studies list and previous CABG
Index test	320-slice MDCT (≥50% stenosis)
Reference standard	ICA:100% (≥50% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 55 4 0 26 1.0 1.0

Study	von Ziegler 2014[719]
Study type	Cohort
Number of studies (number of participants	n=134
Country and setting	Germany
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age: 71.2 (6.4) Male (%): NR White (%): NR Diabetes (%): 33 Smoking (%): 33 Hypertension (%): 54
Patient characteristics	Inclusion criteria: patients with acute chest pain of possible cardiac origin Exclusion criteria: ECG changes and abnormal troponin
Index test	64-slice MDCT (>50% stenosis)
Reference standard	ICA:100% (≥50% stenosis)
Target condition	ACS
Results: TP FP FN TN	 81 3 5 45

Study	von Ziegler 2014[719]
Sensitivity% Specificity%	94 94

H.3.2 Dual source CT

Study	Hansen 2010[320]
Study type	Cohort
Number of studies (number of participants	n=89
Country and setting	Australia
Funding	Non-industry funded
Duration of study	October 2007-July 2008
Age, gender, ethnicity	Mean age (SD): 56.3 (8.6) Male (%): 63 White (%): NR Diabetes (%): 8 Smoking (%): 44 Hypertension (%): 39 Dyslipidaemia (%): 42
Patient characteristics	Inclusion criteria: patients presenting to ED with chest pain with an unclear diagnosis and whose ECGs showed no evidence of ischaemia and with normal troponin. Exclusion criteria: not reported.
Index test	DSCT (>50% stenosis)

Study	Hansen 2010[320]
Reference standard	CA: 100% (>70% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 3 1 0 86 99 100

Study	Johnson 2008[359]
Study type	Cohort
Number of studies (number of participants	n=2007
Country and setting	Germany
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Median age (IQR): 64 (59–67) Male (%): NR White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR

Study	Johnson 2008[359]
	Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain Exclusion criteria: included positive ECG and troponin test
Index test	DSCT (>50% stenosis)
Reference standard	ICA: 100% (>50% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 15 4 0 90 100 96

H.3.3 SPECT

Study	Beigel 2009[125]
Study type	Cohort
Number of studies (number of participants	n=322
Country and setting	Israel

Study	Beigel 2009[125]
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): 57 (12) Male (%): 73 White (%): NR Diabetes (%): 24 Smoking (%): 38 Hypertension (%): 52 Dyslipidaemia (%): 65
Patient characteristics	Inclusion criteria: patients with chest pain aged over 20 years Exclusion criteria: high risk probability for acute coronary syndrome, ECG changes and abnormal troponins
Index test	Stress SPECT (ischaemia and angina pain and/or decrease in SBP >10 mmHg)
Reference standard	ICA: 7% (NR) MACE at 5 months (repeat cardiac chest pain, ICA, PCI, ACS, death)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 18 14 12 291 60 95

Study	Beigel 2009[125]

Study	Conti 2001[229]
Study type	Cohort
Number of studies (number of participants	n=80
Country and setting	Italy
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): M 58.2 (8.7), F 71.3 (8.9) Male (%): NR White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain lasting greater than 5 minutes and occurring less than 24 hours before presentation, non-diagnostic ECG, age >30 years, normal troponin and chest X-ray. Exclusion criteria: previous history if angina and documented coronary artery disease.
Index test	SPECT (perfusion)
Reference standard	ICA (≥50% stenosis) and/or acute MI during hospital stay acute MI: 31% MACE at 6 months: 69% (sudden death or ischaemic cardiac events)

Study	Conti 2001[229]
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 16 16 1 47 94 75

Study	Conti 2005[232]
Study type	Cohort
Number of studies (number of participants	n=503
Country and setting	Italy
Funding	Non-industry funded
Duration of study	2000–2002
Age, gender, ethnicity	Mean age (SD): 59.5 (12.3) Male (%): NR White (%): NR Diabetes (%): 7 Smoking (%): 27 Hypertension (%): 30 Dyslipidaemia (%): NR

Study	Conti 2005[232]
Patient characteristics	Inclusion criteria: patients with chest pain with normal ECG and troponins Exclusion criteria: NR
Index test	Stress SPECT (perfusion defects and abnormal wall motion)
Reference standard	ICA: 30% (≥50% stenosis) MACE at 30 days 6 months: 70% (sudden death, non-fatal MI, PCI, CABG readmission for chest pain, significant stenosis [>50%])
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 81 70 13 339 86 83

Study	Conti 2011[229]
Study type	Cohort
Number of studies (number of participants	n=1089
Country and setting	Italy

Study	Conti 2011[229]
Funding	Non-industry funded
Duration of study	2001–2010
Age, gender, ethnicity	Mean age: 64: Male (%): NR White (%): NR Diabetes (%): 13 Smoking (%): 17 Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain Exclusion criteria: patients with normal ECG and troponins
Index test	Stress SPECT (perfusion defects)
Reference standard	ICA (≥50% stenosis) MACE at 6 months: 69% (sudden death or ischaemic cardiac events)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 155 121 23 790 87 87

Study	Forberg 2009[266]
Study type	Cohort
Number of studies (number of participants	n=40
Country and setting	Sweden
Funding	Non-industry funded
Duration of study	2002–2006
Age, gender, ethnicity	Mean age (SD): 55 (2) Male (%): 50 White (%): NR Diabetes (%): 5 Smoking (%): 27 Hypertension (%): 22 Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain suspicious of acute coronary syndrome Exclusion criteria: NR
Index test	Rest SPECT (perfusion defects)
Reference standard	ACS defined from ACC/AHA and ESC guidelines
Target condition	ACS
Results: TP FP	 2 11

Study	Forberg 2009[266]
FN	0
TN	27
Sensitivity%	100
Specificity%	71

Study	Gallagher 2007[275]
Study type	Cohort
Number of studies (number of participants	n=85
Country and setting	
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): ACS 50 (14) ACS negative 49 (10) Male (%): ACS 71 ACS negative 51 White (%): NR Diabetes (%): ACS 14 ACS negative 9 Smoking (%): ACS 57 ACS negative 23 Hypertension (%): ACS 57 ACS negative 35 Dyslipidaemia (%): ACS 29 ACS negative 27
Patient characteristics	Inclusion criteria: people with acute chest pain Exclusion criteria: diagnostic ECG, elevated troponins and known coronary artery disease
Index test	Stress SPECT (perfusion defect)
Reference standard	ICA: 12% (>70% stenosis) MACE at 30 days: 88% (cardiac death, non-fatal MI or unstable angina)

Study	Gallagher 2007[275]
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 5 8 2 70 71 90

Study	Vogel-Claussen 2009[716]
Study type	Cohort
Number of studies (number of participants	n=31
Country and setting	USA
Funding	Non-industry funded
Duration of study	12 months
Age, gender, ethnicity	Mean age (SD): 56.3 (13.2) Male (%): 50 White (%): NR Diabetes (%): 56 Smoking (%): 67

Study	Vogel-Claussen 2009[716]
	Hypertension (%): 78
Patient characteristics	Inclusion criteria: patients with chest pain, negative ECG and cardiac enzymes Exclusion criteria: NR
Index test	Stress SPECT (perfusion defects)
Reference standard	ICA: 12% (≥70% stenosis): 4/31 256-slice MDCT: 1/31(≥70% stenosis) MACE at mean (SD) 14 (4.7) months: 69% (all-cause mortality, MI, stroke)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 2 2 2 23 60 95

H.3.4 ECG

Study	Atar 2000[99]
Study type	Cohort
Number of studies (number of participants	n=54

Study	Atar 2000[99]
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): 64 (10) Male (%): 61 White (%): NR Diabetes (%): 35 Smoking (%): 35 Hypertension (%): 63 Dyslipidaemia (%): 63
Patient characteristics	Inclusion criteria: new onset chest pain, negative troponin and ECG Exclusion criteria: atrial fibrillation
Index test	Pacing stress ECHO (New or worsened WMA)
Reference standard	ICA: 100% (≥75%)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 36 2 2 13 95 87

Study	Bedetti 2008[124]
Study type	Cohort
Number of studies (number of participants	n=546
Country and setting	Italy
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Median age (IQR): NR Male (%): NR White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with acute chest pain Exclusion criteria: NR
Index test	Stress ECHO (New or worsened WMA)
Reference standard	ICA: 8% (≥50% stenosis) MACE at 13 months: 92% (cardiac death, non-fatal MI)
Target condition	ACS
Results:	

Study	Bedetti 2008[124]
TP	44
FP	6
FN	2
TN	494
Sensitivity%	96
Specificity%	99

Study	Bholasingh 2003[145]
Study type	Cohort
Number of studies (number of participants	n=377
Country and setting	Holland
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD) 56 (12) Male (%): 58 White (%): NR Diabetes (%): 10 Smoking (%): 37 Hypertension (%): 38 Dyslipidaemia (%): 35
Patient characteristics	Inclusion criteria: patients with chest pain (maximum 6 hours duration) with a non-diagnostic ECG

Study	Bholasingh 2003[145]
	Exclusion criteria: history of cardiac problems
Index test	Stress ECHO (New WMA)
Reference standard	ICA: 7% (≥50% stenosis) MACE at 30 days: 93% (cardiac death, non-fatal MI, unstable angina, PCI, CABG)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 11 14 15 337 42 96

Study	Buchsbaum 1999
Study type	Cohort
Number of studies (number of participants	n=145
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR

Study	Buchsbaum 1999
Age, gender, ethnicity	Mean age (SD): 47 (9) Male (%): 56 White (%): NR Diabetes (%): 3 Smoking (%): 52 Hypertension (%): 26 Dyslipidaemia (%): 20
Patient characteristics	Inclusion criteria: low risk patients 30 years or older with a normal ECG and no prior history of coronary artery disease Exclusion criteria: NR
Index test	Stress ECHO (New WMA)
Reference standard	ICA:5% (≥50% stenosis) MACE at 6 months: 95%
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 11 14 15 337 42 96

Study	Conti 2005[232]
Study type	Cohort
Number of studies (number of participants	n=503
Country and setting	Italy
Funding	Non-industry funded
Duration of study	2000–2002
Age, gender, ethnicity	Mean age (SD): 59.5 (12.3) Male (%): NR White (%): NR Diabetes (%): 7 Smoking (%): 27 Hypertension (%): 30 Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain with normal ECG and troponins Exclusion criteria: NR
Index test	Stress SPECT (perfusion defects and abnormal wall motion)
Reference standard	ICA: 30% (≥50% stenosis) MACE at 30 days 6 months: 70% (sudden death, non-fatal MI, PCI, CABG readmission for chest pain, significant stenosis [>50%])
Target condition	ACS
Results: TP FP FN	 880 19 14

Study	Conti 2005[232]
TN	390
Sensitivity%	85
Specificity%	95

Study	Conti 2015[228]
Study type	Cohort
Number of studies (number of participants	n=188
Country and setting	Italy
Funding	Non-industry funded
Duration of study	January–December 2013
Age, gender, ethnicity	Mean age (SD): 59.2 (16.4) Male (%): 68 White (%): NR Diabetes (%): 13 Smoking (%): 25 Hypertension (%): 50 Dyslipidaemia (%): 30
Patient characteristics	Inclusion criteria: patients with chest pain consistent with angina with normal ECG and troponins Exclusion criteria: positive ECG and abnormal troponins
Index test	Stress SPECT Stress ECHO (New WMA)

Study	Conti 2015[228]
Reference standard	ICA (≥50% stenosis) MACE at 3 months (ACS, CV death, revascularisation)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 12 6 8 162 60 96

Study	Gaibazzi 2011[270]
Study type	Cohort
Number of studies (number of participants	n=92
Country and setting	Italy
Funding	Non-industry funded
Duration of study	2008
Age, gender, ethnicity	Mean age (SD): 62 (12) Male (%): 62 White (%): NR Diabetes (%): 50

Study	Gaibazzi 2011[270]
	Smoking (%): 18 Hypertension (%): 50 Dyslipidaemia (%): 7
Patient characteristics	Inclusion criteria: patients with chest pain and normal ECG Exclusion criteria: included severe reduced ventricular ejection fraction
Index test	Stress ECHO (New WMA)
Reference standard	ICA: 71% (≥50% stenosis) MACE at 6 months (cardiac death, non-fatal MI, revascularisation)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 15 6 18 8 45 57

Study	Iglesias-Garriz 2005[346]
Study type	Cohort
Number of studies (number of participants	n=78

Study	Iglesias-Garriz 2005[346]
Country and setting	Spain
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): 67 (8) Male (%): 76 White (%): NR Diabetes (%): 35 Smoking (%): 24 Hypertension (%): 55 Dyslipidaemia (%): 55
Patient characteristics	Inclusion criteria: 18 years or older, non-traumatic chest pain of suggested ischaemic nature and no history of coronary artery disease Exclusion criteria: Known history of ischaemic disease
Index test	Stress ECHO (≥2 adjacent segments of WMA)
Reference standard	ICA: 100% (>% stenosis)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 44 7 15 13 75 65

Study	Iglesias-Garriz 2005[346]

Study	Innocenti 2012
Study type	Cohort
Number of studies (number of participants	n=434
Country and setting	2013
Funding	Non-industry funded
Duration of study	June 2008–May 2011
Age, gender, ethnicity	Mean age (SD): 67 (12) Male (%): 58 White (%): NR Diabetes (%): 15 Smoking (%): 62 Hypertension (%): 62 Dyslipidaemia (%): 41
Patient characteristics	Inclusion criteria: spontaneous chest pain, non-cardiac chest painExclusion criteria: NR
Index test	Stress ECHO (New WMA)
Reference standard	ICA:23% (≥50% stenosis) MACE: at 6 months: 77% (cardiac death, non-fatal ACS, revascularisation)
Target condition	ACS
Results: TP FP	 80 26

Study	Innocenti 2012
FN	9
TN	319
Sensitivity%	90
Specificity%	82

Study	Tsutsui 2005[693]
Study type	Cohort
Number of studies (number of participants	n=158
Country and setting	USA
Funding	Non-industry funded
Duration of study	January 2000–May 2003
Age, gender, ethnicity	Mean age (SD): 61 (13) Male (%): 50 White (%): NR Diabetes (%): 11 Smoking (%): 43 Hypertension (%): 73 Dyslipidaemia (%): 59
Patient characteristics	Inclusion criteria: people with chest pain or a possible cardiac origin with normal troponin Exclusion criteria: STEMI
Index test	Stress ECHO (≥2 adjacent segments of WMA)
Reference standard	ICA: 39% (>50% stenosis)

Study	Tsutsui 2005[693]
	MACE at 6 months: 46% (cardiac death, non-fatal MI, UA, revascularisation)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 30 20 18 90 63 82

H.3.5 MRI

Study	Kwong 2003[400]
Study type	Cohort
Number of studies (number of participants	n=161
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): ACS 68 (13) No ACS 57 (14) Male (%): ACS 60 No ACS 57 White (%): NR Diabetes (%): ACS 28 No ACS 10 Smoking (%): ACS 48 No ACS 39

Study	Kwong 2003[400]
	Hypertension (%): ACS 56 No ACS 43 Dyslipidaemia (%): ACS 64 No ACS 47
Patient characteristics	Inclusion criteria: People with chest pain 30 minutes or greater compatible with myocardial infarction Exclusion criteria: STEMI
Index test	MRI (regional wall abnormality or delayed hyper-enhancement)
Reference standard	ACC/AHA guideline for ACS: 14%
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 29 19 3 114 89 86

Study	Miller 2010
Study type	Cohort
Number of studies (number of participants	n=53
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR

Study	Miller 2010
Age, gender, ethnicity	Median age (IQR): 55 (48–61) Male (%): 47 White (%): 66 Diabetes (%): 38 Smoking (%): 34 Hypertension (%): 68 Dyslipidaemia (%): 74
Patient characteristics	Inclusion criteria: people 18 years or older and symptoms of possible acute coronary syndrome Exclusion criteria: increased troponin and STEMI
Index test	Stress MRI (wall motion- perfusion- abnormalities, delayed enhancement)
Reference standard	ACS defined as one of the following: acute MI, ischaemia leading to revascularisation, death likely related to ischaemia, discharge diagnosis of definite/probable UA or inducible ischaemia on stress test
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 1 5 0 43 100 90

Study	Vogel- Claussen 2009[716]

Study	Vogel- Claussen 2009[716]
Study type	Cohort
Number of studies (number of participants	n=31
Country and setting	USA
Funding	Non-industry funded
Duration of study	12 months
Age, gender, ethnicity	Mean age (SD): 56.3 (13.2) Male (%): 56 White (%): NR Diabetes (%): 33 Smoking (%): 67 Hypertension (%): 78 Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: people with chest pain with negative cardiac enzymes Exclusion criteria: NR
Index test	Stress MRI (reversible regional perfusion deficit in a coronary artery territory lasting for >6 heart beats)
Reference standard	ICA: 12% (≥70% stenosis): 4/31 256-slice MDCT: 1/31(≥70% stenosis) MACE at mean (SD) 14 (4.7) months: 69% (all-cause mortality, MI, stroke)
Target condition	ACS
Results: TP FP	 5 1

Study	Vogel- Claussen 2009[716]
FN	0
TN	25
Sensitivity%	100
Specificity%	96

H.3.6 Exercise ECG

Study	Amsterdam2002[72]
Study type	Cohort
Number of studies (number of participants	n=765
Country and setting	USA
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): M 49 (12) W 52 (11) Male (%): 45 White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients who underwent immediate stress testing with non-traumatic chest pain of suspected cardiac origin but low clinical risk

Study	Amsterdam2002[72]
	Exclusion criteria: previous coronary artery disease, abnormal ECG or serum markers
Index test	Exercise ECG (exercise-induced ST-segment alterations)
Reference standard	ICA: 7% (NR) Stress MPS: 9% (NR) Stress ECHO: 3% (NR) MACE at 30 days: 84% (cardiac death, non-fatal MI, non-invasive imaging test showing CAD)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 33 9 2 638 84 87

Study	Bennett 2013[133]
Study type	Cohort
Number of studies (number of participants	n=196
Country and setting	UK
Funding	Non-industry funded
Duration of study	NR

Study	Bennett 2013[133]
Age, gender, ethnicity	Mean age: 56 Male (%): NR White (%): NR Diabetes (%): Nr Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain of suspected cardiac origin without elevated troponins Exclusion criteria: NR
Index test	Exercise ECG
Reference standard	ICA: 18% (NR) Readmission for chest pain at 12 months: 82%
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 16 18 7 168 70 90

Study	CT-Compare 2014[317]
Study type	Cohort
Number of studies (number of participants	N=240
Country and setting	USA
Funding	Non-industry funded
[317]Duration of study	
Age, gender, ethnicity	Mean age (SD): 52.3 (9.8) Male (%): 58 White (%): NR Diabetes (%): 6 Smoking (%): 23 Hypertension (%): 31 Dyslipidaemia (%): 24
Patient characteristics	Inclusion criteria: male patients older than 30 and females older than 40 years with an intermediate probability of coronary artery disease. No evidence of ischaemia on ECG and normal troponin. Exclusion criteria: not reported.
Index test	Exercise ECG
Reference standard	ACS using case report forms based on Cardiac Society of Australia and New Zealand guidelines
Target condition	ACS
Results: TP FP FN TN	 4 22 1 213

Study	CT-Compare 2014[317]
Sensitivity% Specificity%	80 91

Study	Conti 2001[229]
Study type	Cohort
Number of studies (number of participants	n=151 (low) n=80 (intermediate)
Country and setting	Italy
Funding	Non-industry funded
Duration of study	NR
Age, gender, ethnicity	Mean age (SD): M 57.4 (12.1) F 59.9 (10.7) Male (%): NR White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain lasting greater than 5 minutes and occurring less than 24 hours before presentation, non-diagnostic ECG, age >30 years, normal troponin and chest X-ray Exclusion criteria: previous history of angina and documented coronary artery disease

Study	Conti 2001[229]
Index test	SPECT (perfusion)
Reference standard	ICA (≥50% stenosis) and/or acute MI during hospital stay acute MI: 31% MACE at 6 months: 69% (sudden death or ischaemic cardiac events)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 18 22 1 110 95 83

Study	Gaibazzi 2011[270]
Study type	Cohort
Number of studies (number of participants	n=151
Country and setting	Italy
Funding	Non-industry funded
Duration of study	2008
Age, gender, ethnicity	Mean age (SD): NR Male (%): NR

Study	Gaibazzi 2011[270]
	White (%): NR Diabetes (%): NR Smoking (%): NR Hypertension (%): NR Dyslipidaemia (%): NR
Patient characteristics	Inclusion criteria: patients with chest pain and normal ECG Exclusion criteria: included severe reduced ventricular ejection fraction
Index test	Stress ECHO (New WMA)
Reference standard	ICA: 71% (≥50% stenosis) MACE at 6 months (cardiac death, non-fatal MI, revascularisation)
Target condition	ACS
Results: TP FP FN TN Sensitivity% Specificity%	 15 6 8 18 65 75

Appendix I: GRADE tables

I.1 High sensitivity cardiac troponins

None.

I.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Table 7: Clinical evidence profile: MDCT versus standard practice at 30 days follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MDCT versus standard management 30-day	Control	Relative (95% CI)	Absolute		
All-cause mortality												
3	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/845 (0%)	0/842 (0%)	Not pooled	Not pooled	MODERATE	CRITICAL
Cardiovascular mortality												
2	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	0/1193 (0%)	1/853 (0.12%)	RR 0.46 (0.02 to 11.17)	1 fewer per 1000 (from 1 fewer to 12 more)	VERY LOW	CRITICAL
MI												
3	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	11/1694 (0.65%)	12/1252 (0.96%)	RR 0.58 (0.25 to 1.38)	4 fewer per 1000 (from 7 fewer to 4 more)	VERY LOW	CRITICAL

PCI												
3	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	52/845 (6.2%)	31/842 (3.7%)	RR 1.67 (1.08 to 2.58)	25 more per 1000 (from 3 more to 58 more)	LOW	CRITICAL
CABG												
3	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	7/845 (0.83%)	8/842 (0.95%)	RR 0.89 (0.34 to 2.29)	1 fewer per 1000 (from 6 fewer to 12 more)	VERY LOW	CRITICAL
Readmission due to cardiac causes												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	7/285 (2.5%)	11/291 (3.8%)	RR 0.65 (0.25 to 1.64)	13 fewer per 1000 (from 28 fewer to 24 more)	VERY LOW	CRITICAL

[a] *Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[b] *Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs*

Table 8: Clinical evidence profile: MDCT versus SPECT at 30 days follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**MDCT versus SPECT 30-day**	**Control**	**Relative (95% CI)**	**Absolute**		
All-cause mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/361 (0%)	0/338 (0%)	Not pooled	Not pooled	LOW	CRITICAL
MI												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	1/361 (0.28%)	5/338 (1.5%)	RR 0.19 (0.02 to 1.58)	12 fewer per 1000 (from 14 fewer to 9 more)	VERY LOW	CRITICAL
PCI												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	9/361 (2.5%)	8/338 (2.4%)	RR 1.05 (0.41 to 2.66)	1 more per 1000 (from 14 fewer to 39 more)	VERY LOW	CRITICAL
CABG												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	4/361 (1.1%)	0/338 (0%)	RR 8.52 (0.46 to 158.88)	-	VERY LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[2]*Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs*

Table 9: Clinical evidence profile: MDCT versus exercise ECG at 30 days follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MDCT versus Exercise ECG 30-day	Control	Relative (95% CI)	Absolute		
All-cause mortality OR												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/322 (0%)	0/240 (0%)	Not pooled	Not pooled	LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*

Table 10: Clinical evidence profile: MDCT versus exercise ECG at 1 year follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MDCT versus Exercise ECG 1 year	Control	Relative (95% CI)	Absolute		
All-cause mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	2/322 (0.62%)	1/240 (0.42%)	RR 1.49 (0.13 to 15.55)	2 more per 1000 (from 4 fewer to 61 more)	VERY LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[2]*Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs*

Table 11: Clinical evidence profile: SPECT versus standard practice at 30 days follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SPECT versus standard management 30-day	Control	Relative (95% CI)	Absolute		
All-cause mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	4/1215 (0.33%)	2/1260 (0.16%)	OR 2.08 (0.38 to 11.36)	2 more per 1000 (from 1 fewer to 16 more)	VERY LOW	CRITICAL
PCI												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	46/1215 (3.8%)	50/1260 (4%)	RR 0.95 (0.64 to 1.41)	2 fewer per 1000 (from 14 fewer to 16 more)	VERY LOW	CRITICAL
CABG												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	18/1215 (1.5%)	30/1260 (2.4%)	RR 0.63 (0.35 to 1.11)	9 fewer per 1000 (from 15 fewer to 3 more)	VERY LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[2]*Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs*

Table 12: Clinical evidence profile: Stress SPECT versus standard practice at 30 days follow-up

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Stress SPECT versus standard management 30-day	Control	Relative (95% CI)	Absolute		
Cardiac mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/1004 (0%)	0/504 (0%)	Not pooled	Not pooled	LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*

Table 13: Clinical evidence profile: Stress SPECT versus standard practice at 1 year follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Stress SPECT versus standard management 1 year**	**Control**	**Relative (95% CI)**	**Absolute**		
Cardiac mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	3/1004 (0.3%)	0/504 (0%)	RR 3.53 (0.18 to 68.4)	-	VERY LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[2]*Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs*

Table 14: Clinical evidence profile: Stress MRI versus standard practice at 30 days follow-up

Quality assessment							No of patients		Effect		Quality	Importance
No of	**Design**	**Risk of**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Stress MRI versus standard management**	**Control**	**Relative**	**Absolute**		

studies		bias				considerations	30-day		(95% CI)			
All-cause mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/52 (0%)	0/53 (0%)	Not pooled	Not pooled	LOW	CRITICAL
CV mortality												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/57 (0%)	0/53 (0%)	Not pooled	Not pooled	LOW	CRITICAL
MI												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	1/57 (1.8%)	1/53 (1.9%)	RR 1.02 (0.06 to 12.89)	0 more per 1000 (from 18 fewer to 224 more)	VERY LOW	CRITICAL
PCI												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	0/57 (0%)	1/53 (1.9%)	RR 0.33 (0.01 to 7.34)	13 fewer per 1000 (from 19 fewer to 120 more)	VERY LOW	CRITICAL
CABG												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	5/57 (8.8%)	1/53 (1.9%)	RR 5.09 (0.62 to 25.65)	77 more per 1000 (from 7 fewer to 465 more)	VERY LOW	CRITICAL

Stress testing adverse events												
1	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/57 (0%)	0/53 (0%)	Not pooled	Not pooled	LOW	CRITICAL

[1]*Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
[2]*Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs*

I.3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

None.

Appendix J: Forest plots

J.1 High sensitivity cardiac troponins

J.1.1 Coupled sensitivity and specificity forest plots

Figure 4: Low risk 0 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Collinson 2013 14 0h	53	33	14	733	14.0	98.0	62.0	0.79 [0.67, 0.88]	0.96 [0.94, 0.97]
Freund 2011 14 0h	20	36	2	202	14.0	99.0	36.0	0.91 [0.71, 0.99]	0.85 [0.80, 0.89]

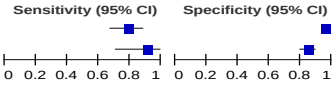


Figure 5: Low risk change 0-1.5 hours

Study	TP	FP	FN	TN	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Collinson 2013 p14 0-1.5h	57	43	11	736	99.0	57.0	0.84 [0.73, 0.92]	0.94 [0.93, 0.96]

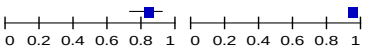


Figure 6: Moderate risk 0 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Hochholzer 2011 11 0h	90	177	3	454	11.0	99.0	34.0	0.97 [0.91, 0.99]	0.72 [0.68, 0.75]
Sebbane 2013 14 0h	19	25	6	142	14.0	96.0	43.0	0.76 [0.55, 0.91]	0.85 [0.79, 0.90]
Sebbane 2013 18 0h	19	17	6	150	18.0	96.0	53.0	0.76 [0.55, 0.91]	0.90 [0.84, 0.94]

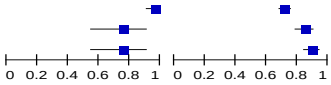


Figure 7: Moderate risk – older adults 0 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Borna 2016	117	198	12	150	14.0	99.0	40.0	0.91 [0.84, 0.95]	0.43 [0.38, 0.48]

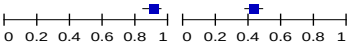


Figure 8: Moderate risk – older adults 3-4 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Borna 2016	129	212	0	136	14.0	99.0	40.0	1.00 [0.97, 1.00]	0.39 [0.34, 0.44]
b Borna 2016	120	143	9	205	20.0	96.0	46.0	0.93 [0.87, 0.97]	0.59 [0.54, 0.64]
c Borna 2016	116	87	13	261	30.0	95.0	57.0	0.90 [0.83, 0.95]	0.75 [0.70, 0.79]

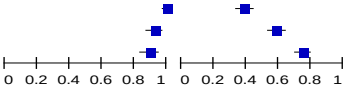


Figure 9: Moderate risk change score 0-3 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	% change	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Irfan 2013 14 17% change 0-1h	65	202	43	520	14.0	17.0	92.0	24.0	0.60 [0.50, 0.69]	0.72 [0.69, 0.75]
Reichlin 2011 14 30% change 0-2h	43	84	24	439	14.0	27.0	95.0	35.0	0.64 [0.52, 0.76]	0.84 [0.81, 0.87]
Irfan 2013 14 27% change 0-1h	68	245	40	477	14.0	30.0	92.0	22.0	0.63 [0.53, 0.72]	0.66 [0.62, 0.70]

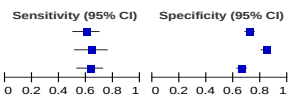


Figure 10: High risk 0 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
e Aldous 2012 3 0h	196	383	9	351	3.0	98.0	34.0	0.96 [0.92, 0.98]	0.48 [0.44, 0.52]
c Aldous 2012 5 0h	192	305	13	429	5.0	97.0	39.0	0.94 [0.89, 0.97]	0.58 [0.55, 0.62]
Kurz 2010 9.5 0h	38	11	8	37	9.5	82.0	78.0	0.83 [0.69, 0.92]	0.77 [0.63, 0.88]
a Aldous 2012 14 0h	181	134	24	600	14.0	96.0	57.0	0.88 [0.83, 0.92]	0.82 [0.79, 0.84]
Eggers 2012 14 0h	101	59	27	173	14.0	87.0	63.0	0.79 [0.71, 0.86]	0.75 [0.68, 0.80]
g Melki 2011 14 0h	112	21	2	98	14.0	98.0	84.0	0.98 [0.94, 1.00]	0.82 [0.74, 0.89]
m Kurz 2010 14 0h	16	7	10	24	14.0	71.0	70.0	0.62 [0.41, 0.80]	0.77 [0.59, 0.90]
Santalo 2013 14 0h	71	80	8	199	14.0	96.0	47.0	0.90 [0.81, 0.96]	0.71 [0.66, 0.77]
Eggers 2012 45.7 0h	65	11	63	221	45.7	77.0	86.0	0.51 [0.42, 0.60]	0.95 [0.92, 0.98]

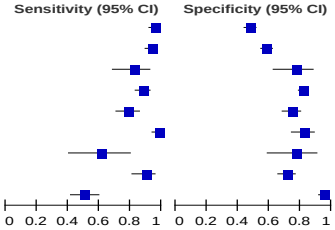


Figure 11: High risk 2 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
b Aldous 2012 14 2h	189	149	16	585	14.0	97.0	56.0	0.92 [0.88, 0.95]	0.80 [0.77, 0.83]
h Melki 2011 14 2h	114	25	0	94	14.0		82.0	1.00 [0.97, 1.00]	0.79 [0.71, 0.86]
d Aldous 2012 5 2h	196	340	9	394	5.0	98.0	37.0	0.96 [0.92, 0.98]	0.54 [0.50, 0.57]
f Aldous 2012 3 2h	201	424	4	310	3.0	99.0	32.0	0.98 [0.95, 0.99]	0.42 [0.39, 0.46]

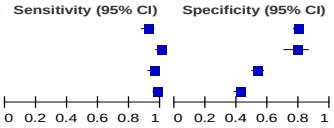


Figure 12: High risk 3 hours

Study	TP	FP	FN	TN	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
n Kurz 2010 14 3h	26	7	0	23		79.0	1.00 [0.87, 1.00]	0.77 [0.58, 0.90]

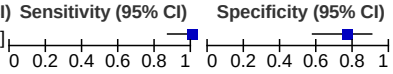


Figure 13: High risk change 0-8 hours

Study	TP	FP	FN	TN	Threshold (ng/L)	% change	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
Aldous 2011 14 and 20% change 0-2h	99	43	101	696	14.0	20.0	87.0	70.0	0.49 [0.42, 0.57]	0.94 [0.92, 0.96]
Aldous 2011 14 or 20% change 0-2h	195	260	5	479	14.0	20.0	99.0	43.0	0.97 [0.94, 0.99]	0.65 [0.61, 0.68]
Kurz 2010 14 20% change 0-3h	11	27	15	3	14.0	20.0	17.0	29.0	0.42 [0.23, 0.63]	0.10 [0.02, 0.27]
Santalo 2013 20% change 0+2+4+6-8h	79	94	0	185	14.0	20.0		46.0	1.00 [0.95, 1.00]	0.66 [0.60, 0.72]

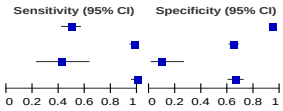
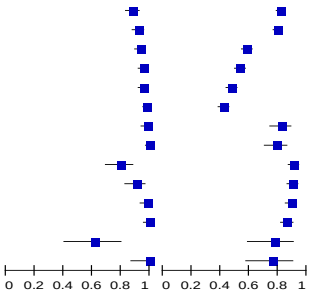


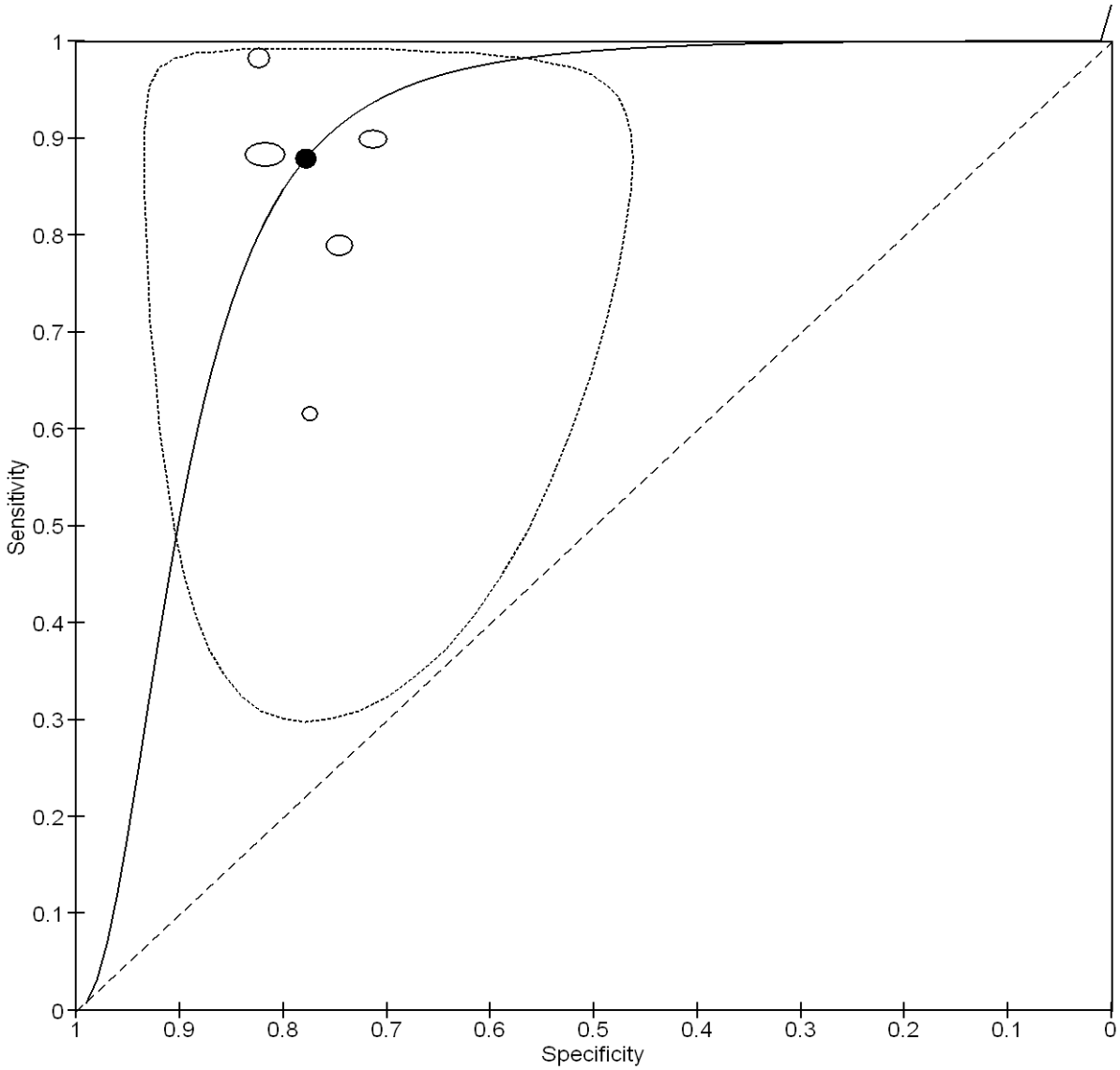
Figure 14: High risk – serial measurements

Study	TP	FP	FN	TN	Threshold (ng/L)	NPV	PPV	Sensitivity (95% CI)	Specificity (95% CI)
a Aldous 2012 14 0h	181	134	24	600	14.0	96.0	57.0	0.88 [0.83, 0.92]	0.82 [0.79, 0.84]
b Aldous 2012 14 2h	189	149	16	585	14.0	97.0	56.0	0.92 [0.88, 0.95]	0.80 [0.77, 0.83]
c Aldous 2012 5 0h	192	305	13	429	5.0	97.0	39.0	0.94 [0.89, 0.97]	0.58 [0.55, 0.62]
d Aldous 2012 5 2h	196	340	9	394	5.0	98.0	37.0	0.96 [0.92, 0.98]	0.54 [0.50, 0.57]
e Aldous 2012 3 0h	196	383	9	351	3.0	98.0	34.0	0.96 [0.92, 0.98]	0.48 [0.44, 0.52]
f Aldous 2012 3 2h	201	424	4	310	3.0	99.0	32.0	0.98 [0.95, 0.99]	0.42 [0.39, 0.46]
g Melki 2011 14 0h	112	21	2	98	14.0	98.0	84.0	0.98 [0.94, 1.00]	0.82 [0.74, 0.89]
h Melki 2011 14 2h	114	25	0	94	14.0		82.0	1.00 [0.97, 1.00]	0.79 [0.71, 0.86]
i Santalo 2013 0h	63	25	16	254	14.0	94.0	72.0	0.80 [0.69, 0.88]	0.91 [0.87, 0.94]
j Santalo 2013 change 20%2h	72	27	7	252		97.0	72.0	0.91 [0.83, 0.96]	0.90 [0.86, 0.94]
k Santalo 2013 change 20% 4h	78	30	1	249		100.0	72.0	0.99 [0.93, 1.00]	0.89 [0.85, 0.93]
l Santalo 2013 change 20% 6-8h	79	38	0	241			68.0	1.00 [0.95, 1.00]	0.86 [0.82, 0.90]
m Kurz 2010 14 0h	16	7	10	24	14.0	71.0	70.0	0.62 [0.41, 0.80]	0.77 [0.59, 0.90]
n Kurz 2010 14 3h	26	7	0	23	14.0		79.0	1.00 [0.87, 1.00]	0.77 [0.58, 0.90]



I.1.2 ROC curves

Figure 15: Imprecision and confidence regions – high risk threshold 14 0 hours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1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Specificity
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

J.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

I.2.1 MDCT versus standard practice at 30 days follow-up

Figure 16: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: all-cause mortality

Figure 17: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: CV mortality

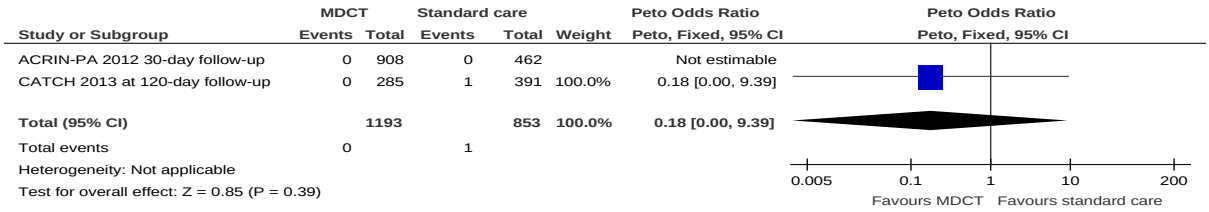


Figure 18: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: non-fatal MI

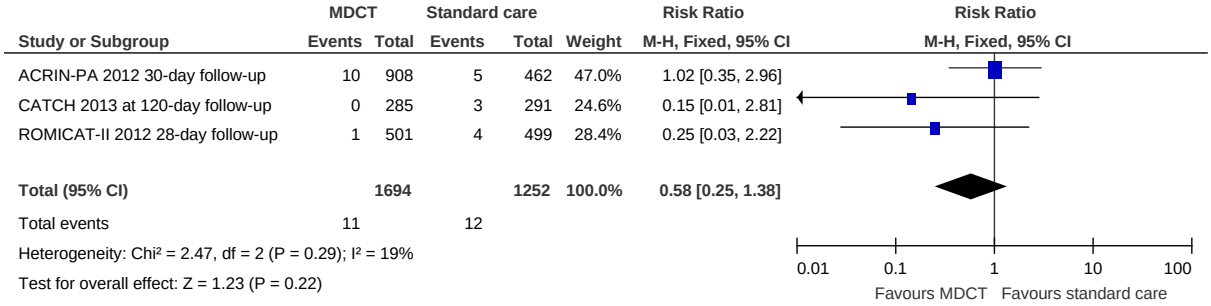


Figure 19: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: PCI

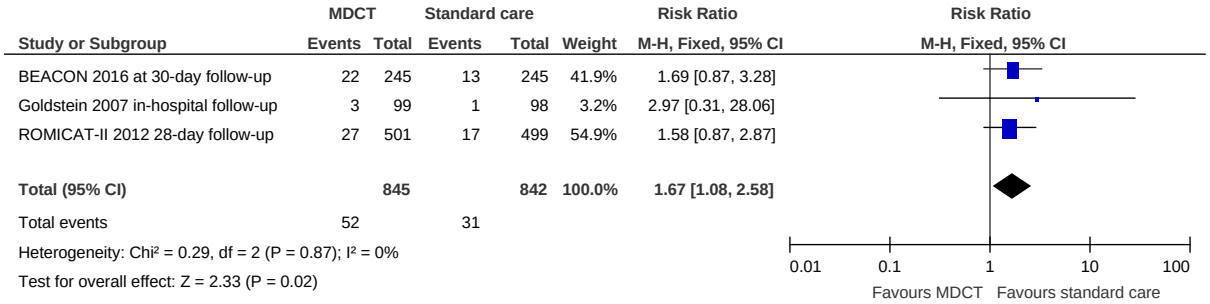


Figure 20: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: CABG

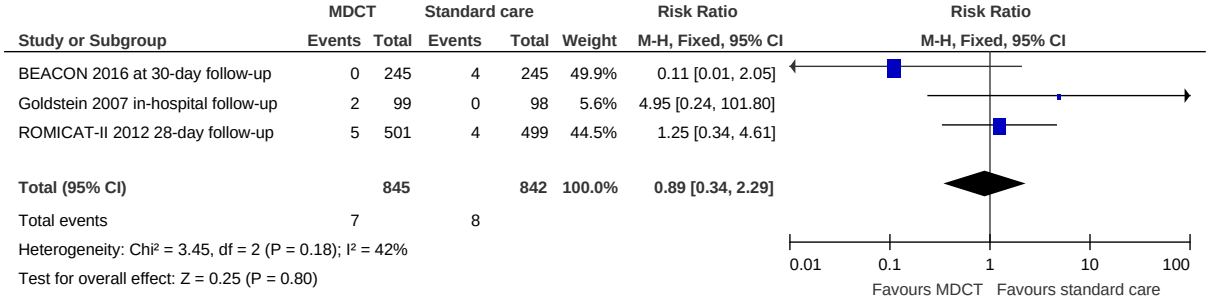
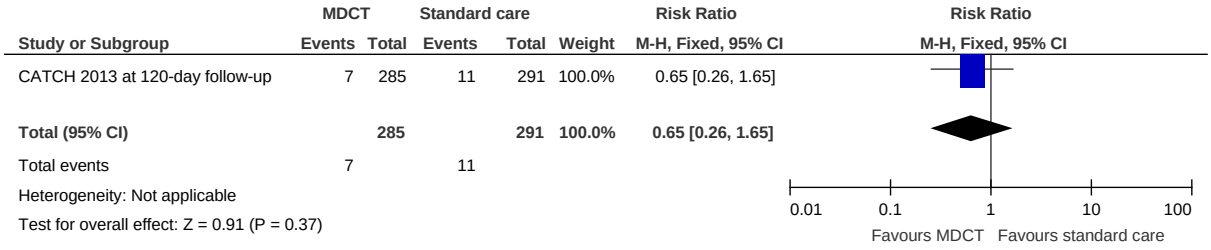


Figure 21: MDCT versus standard practice in people with suspected NSTEMI/unstable angina: Re-admission due to cardiac causes



I.2.2 MDCT versus SPECT at 30 days follow-up

Figure 22: MDCT versus SPECT in people with suspected NSTEMI/unstable angina: all-cause mortality

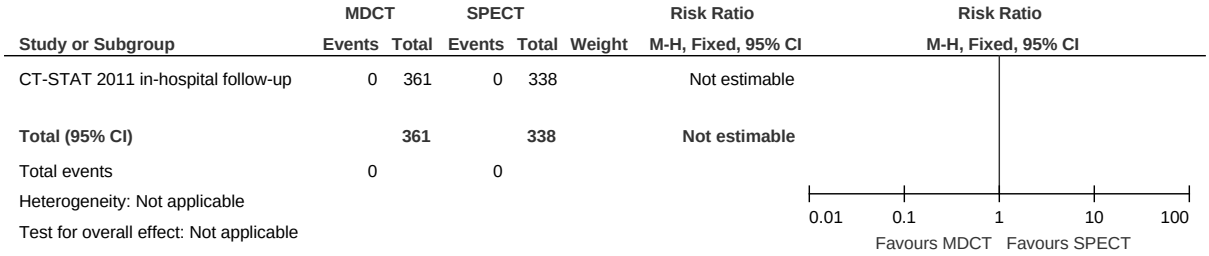


Figure 23: MDCT versus SPECT in people with suspected NSTEMI/unstable angina: non-fatal MI

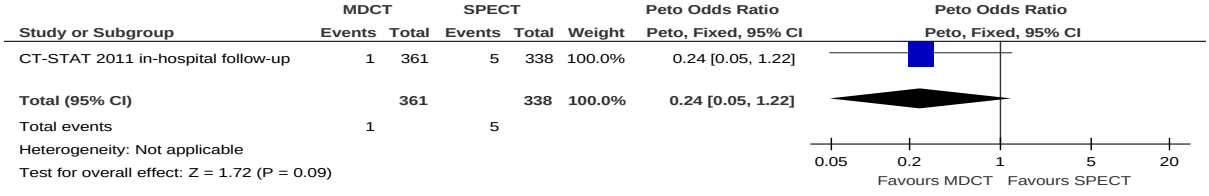


Figure 24: MDCT versus SPECT in people with suspected NSTEMI/unstable angina: PCI

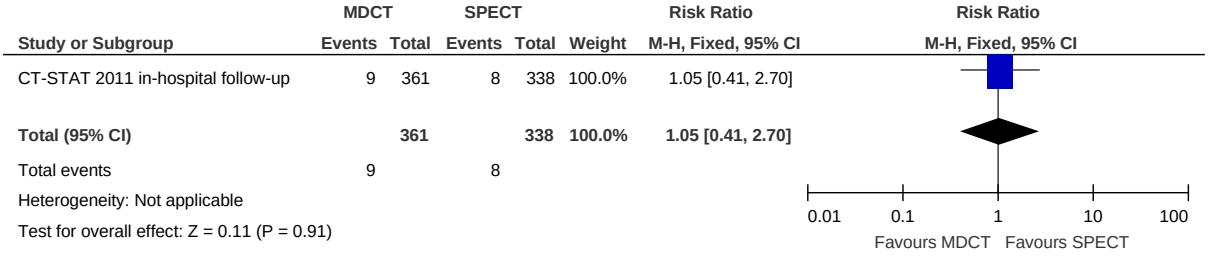
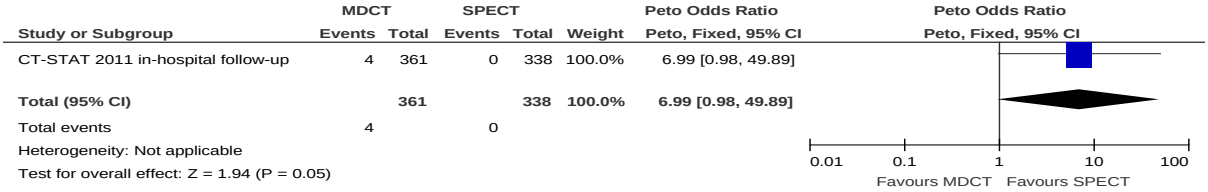
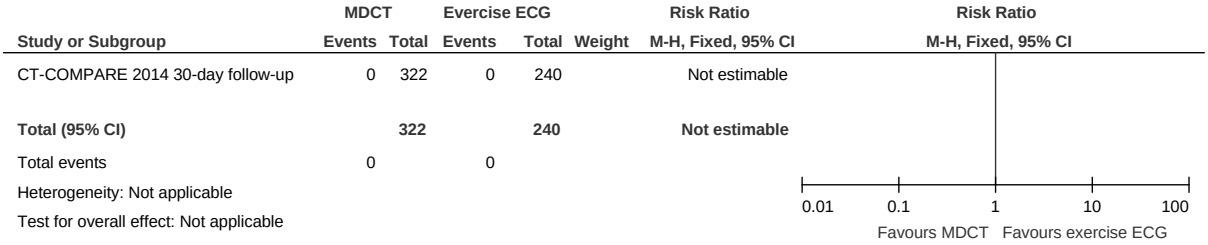


Figure 25: MDCT versus SPECT in people with suspected NSTEMI/unstable angina: CABG



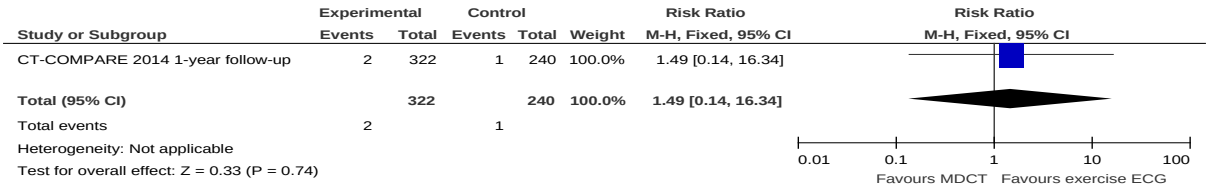
I.2.3 MDCT versus exercise ECG at 30 days follow-up

Figure 26: MDCT versus exercise ECG in people with suspected NSTEMI/unstable angina: all-cause mortality



I.2.4 MDCT versus exercise ECG at 1 year follow-up

Figure 27: MDCT versus exercise ECG in people with suspected NSTEMI/unstable angina: all-cause mortality



I.2.5 Resting SPECT versus standard practice at 30 days follow-up

Figure 28: Resting SPECT versus standard practice in people with suspected NSTEMI/unstable angina: all-cause mortality

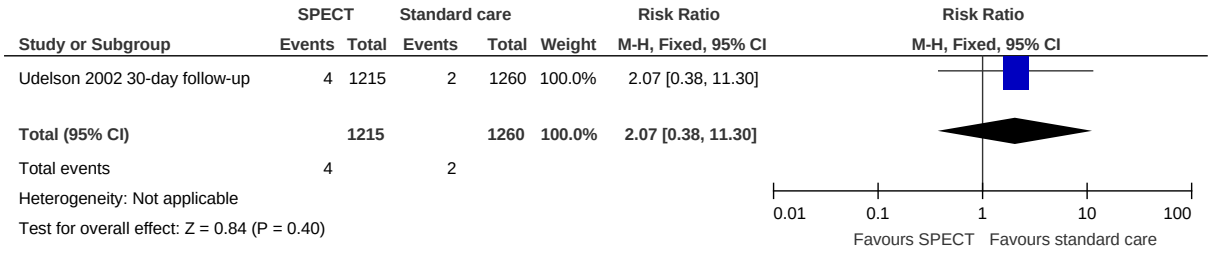


Figure 29: Resting SPECT versus standard practice in people with suspected NSTEMI/unstable angina: PCI

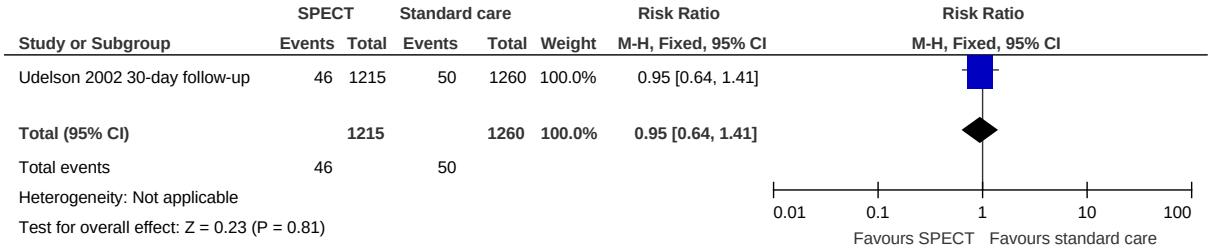
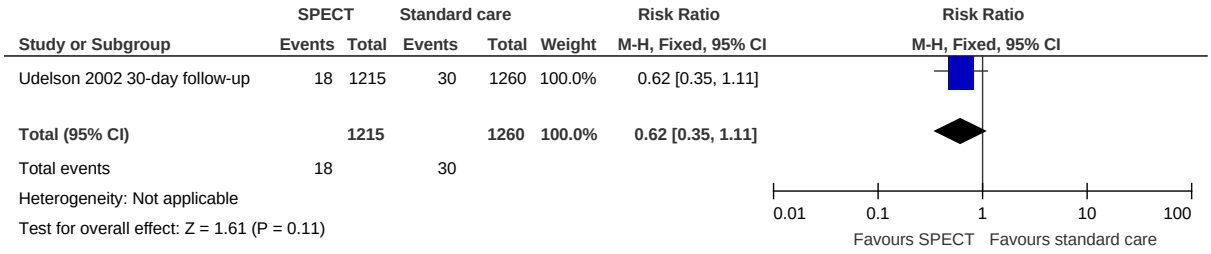
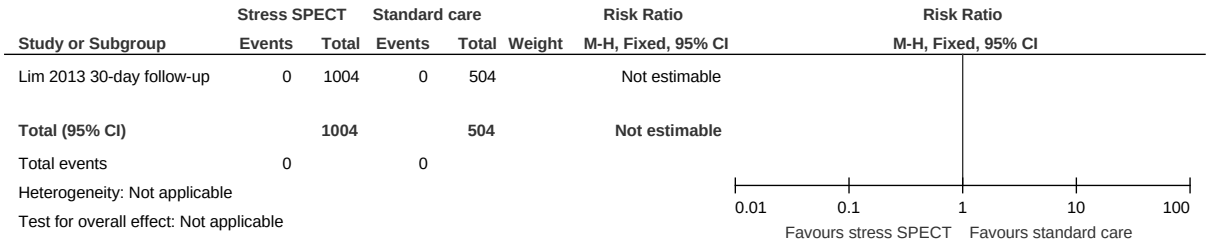


Figure 30: Resting SPECT versus standard practice in people with suspected NSTEMI/unstable angina: CABG



I.2.6 Stress SPECT versus standard practice at 30 days follow-up

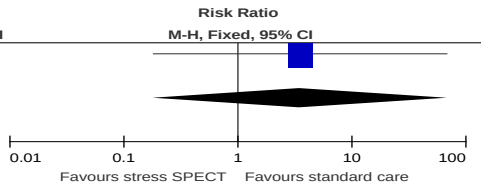
Figure 31: Stress SPECT versus standard practice in people with suspected NSTEMI/unstable angina: cardiac mortality



I.2.7 Stress SPECT versus standard practice at 1 year follow-up

Figure 32: Stress SPECT versus standard practice in people with suspected NSTEMI/unstable angina: cardiac mortality

Study or Subgroup	Stress SPECT Events	Total	Standard care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lim 2013 1-year follow-up	3	1004	0	504	100.0%	3.52 [0.18, 67.96]
Total (95% CI)		**1004**		**504**	**100.0%**	**3.52 [0.18, 67.96]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.41)						



I.2.8 Stress MRI versus standard practice at 30 days follow-up

Figure 33: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: all-cause mortality

Study or Subgroup	Stress MRI Events	Total	Standard care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Miller 2013 90-day follow-up	0	52	0	53		Not estimable
Total (95% CI)		**52**		**53**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

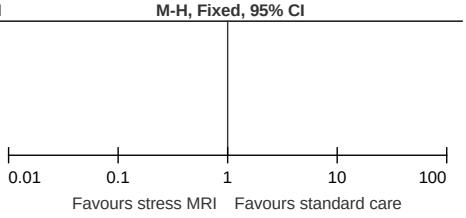


Figure 34: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: cardiac mortality

Study or Subgroup	Stress MRI Events	Total	Standard care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Miller 2010 30-day follow-up	0	53	0	57		Not estimable
Total (95% CI)		**53**		**57**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

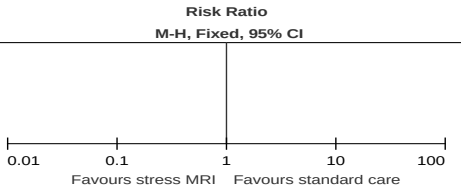


Figure 35: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: non-fatal MI

Study or Subgroup	Stress MRI Events	Total	Standard care Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Miller 2010 30-day follow-up	1	53	1	57	100.0%	1.08 [0.07, 17.46]
Total (95% CI)		**53**		**57**	**100.0%**	**1.08 [0.07, 17.46]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						

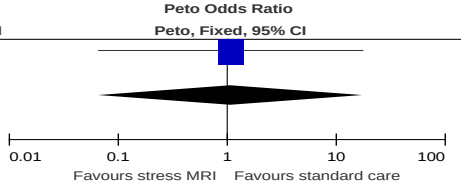


Figure 36: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: PCI

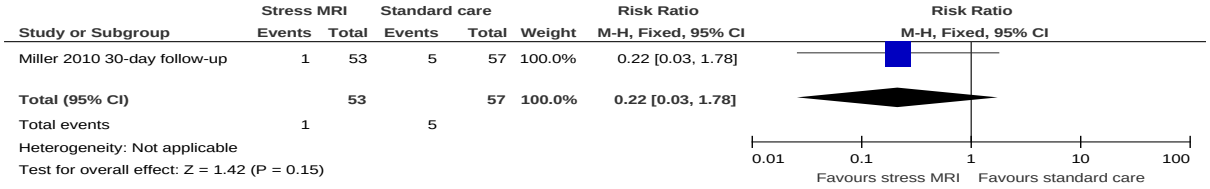


Figure 37: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: CABG

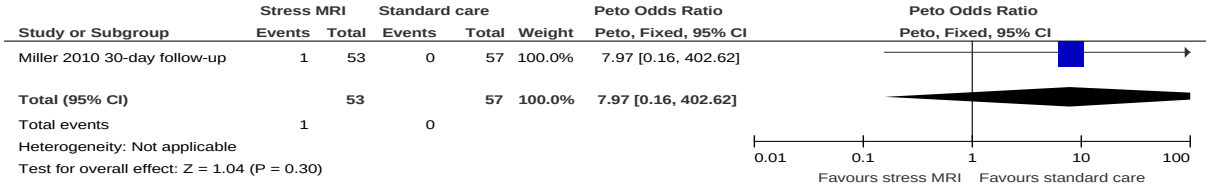
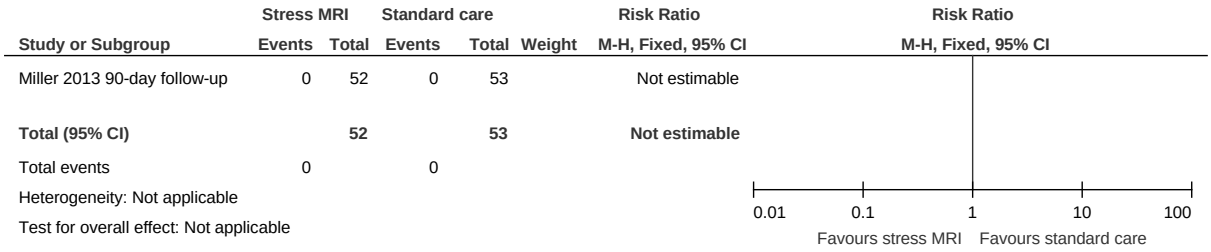


Figure 38: Stress MRI versus standard practice in people with suspected NSTEMI/unstable angina: Stress testing adverse events



J.3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

I.3.1 Coupled sensitivity and specificity forest plots: MDCT

Figure 39: MDCT in populations with prevalence of NSTEMI and/or UA of ≤10%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
ACRIN-PA 2012	28	9	0	640	1.00 [0.88, 1.00]	0.99 [0.97, 0.99]
Beigel 2009	13	13	0	302	1.00 [0.75, 1.00]	0.96 [0.93, 0.98]
Gallagher 2007	6	6	1	72	0.86 [0.42, 1.00]	0.92 [0.84, 0.97]
Goldstein 2007	8	3	0	88	1.00 [0.63, 1.00]	0.97 [0.91, 0.99]
Hascoet 2012	10	19	0	94	1.00 [0.69, 1.00]	0.83 [0.75, 0.90]
Hollander 2007	2	4	0	48	1.00 [0.16, 1.00]	0.92 [0.81, 0.98]
Hollander 2009	7	47	0	508	1.00 [0.59, 1.00]	0.92 [0.89, 0.94]
ROMICAT 2009	24	44	7	293	0.77 [0.59, 0.90]	0.87 [0.83, 0.90]
ROMICAT-II 2012	19	1	3	297	0.86 [0.65, 0.97]	1.00 [0.98, 1.00]

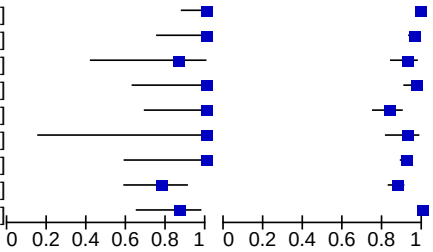


Figure 40: MDCT in populations with prevalence of NSTEMI and/or UA between >10% to 20%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chang 2008	5	0	0	48	1.00 [0.48, 1.00]	1.00 [0.93, 1.00]
Christiaens 2012	28	3	0	136	1.00 [0.88, 1.00]	0.98 [0.94, 1.00]
CT-COMPARE 2014	32	8	0	213	1.00 [0.89, 1.00]	0.96 [0.93, 0.98]

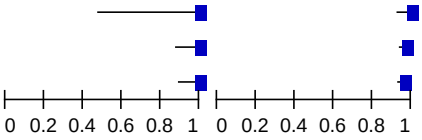


Figure 41: MDCT in populations with prevalence of NSTEMI and/or UA between >20% to 50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chang 2008	20	2	0	33	1.00 [0.83, 1.00]	0.94 [0.81, 0.99]
Johnson 2007	16	3	1	35	0.94 [0.71, 1.00]	0.92 [0.79, 0.98]
Rubinshtein 2007	24	3	0	35	1.00 [0.86, 1.00]	0.92 [0.79, 0.98]
Ueno 2009	11	4	1	20	0.92 [0.62, 1.00]	0.83 [0.63, 0.95]

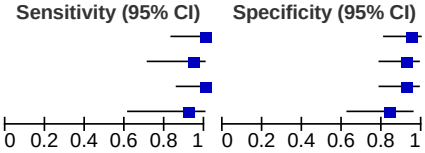
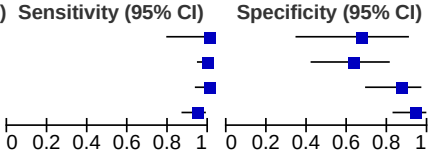


Figure 42: MDCT in populations with prevalence of NSTEMI and/or UA of >50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chang 2008	16	4	0	8	1.00 [0.79, 1.00]	0.67 [0.35, 0.90]
Meijboom 2008	99	10	1	17	0.99 [0.95, 1.00]	0.63 [0.42, 0.81]
van Velzen 2012	55	4	0	26	1.00 [0.94, 1.00]	0.87 [0.69, 0.96]
von Ziegler 2014	81	3	5	45	0.94 [0.87, 0.98]	0.94 [0.83, 0.99]



I.3.2 Coupled sensitivity and specificity forest plots: DSCT

Figure 43: DSCT in populations with prevalence of NSTEMI and/or UA of ≤10%

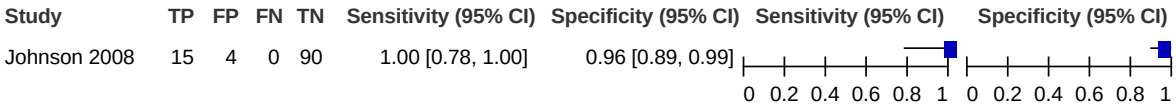
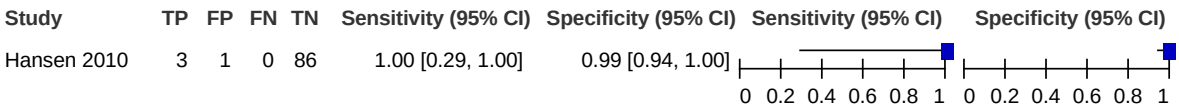


Figure 44: DSCT in populations with prevalence of NSTEMI and/or UA of between >10% and 20%



I.3.3 Coupled sensitivity and specificity forest plots: resting and stress SPECT

Figure 45: Resting SPECT in populations with prevalence of NSTEMI and/or UA of ≤10%

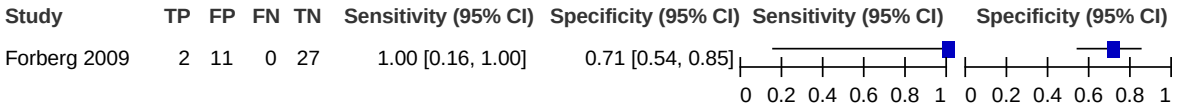


Figure 46: Resting SPECT in populations with prevalence of NSTEMI and/or UA between >20% to 50%

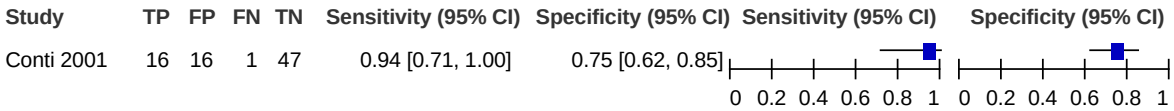


Figure 47: Stress SPECT in populations with prevalence of NSTEMI and/or UA of ≤10%

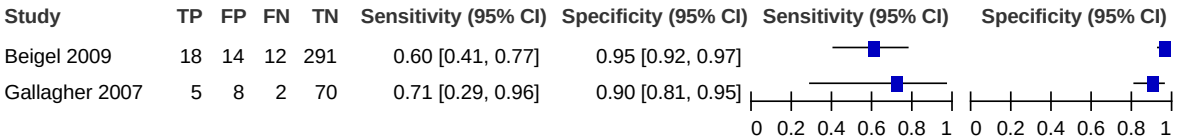
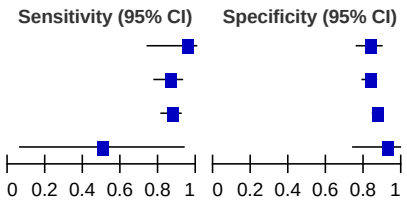


Figure 48: Stress SPECT in in populations with prevalence of NSTEMI and/or UA of >10% to 20%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Conti 2001	18	22	1	110	0.95 [0.74, 1.00]	0.83 [0.76, 0.89]
Conti 2005	81	70	13	339	0.86 [0.78, 0.92]	0.83 [0.79, 0.86]
Conti 2011	155	121	23	790	0.87 [0.81, 0.92]	0.87 [0.84, 0.89]
Vogel-Claussen 2009	2	2	2	23	0.50 [0.07, 0.93]	0.92 [0.74, 0.99]



I.3.4 Coupled sensitivity and specificity forest plots: stress echocardiography

Figure 49: Stress echocardiography in populations with prevalence of NSTEMI and/or UA of ≤10%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bedetti 2005	44	6	2	494	0.96 [0.85, 0.99]	0.99 [0.97, 1.00]
Bholasingh 2003	11	14	15	337	0.42 [0.23, 0.63]	0.96 [0.93, 0.98]
Buchsbaum 2001	3	4	1	137	0.75 [0.19, 0.99]	0.97 [0.93, 0.99]

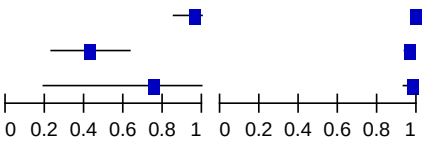


Figure 50: Stress echocardiography in populations with prevalence of NSTEMI and/or UA between >10% to 20%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Conti 2005	80	19	14	390	0.85 [0.76, 0.92]	0.95 [0.93, 0.97]
Conti 2015	12	6	8	162	0.60 [0.36, 0.81]	0.96 [0.92, 0.99]

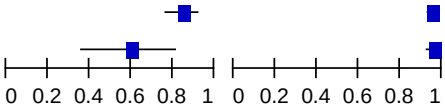


Figure 51: Stress echocardiography in in populations with prevalence of NSTEMI and/or UA between >20% to 50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Innocenti 2013	80	26	9	319	0.90 [0.82, 0.95]	0.92 [0.89, 0.95]
Tsutsui 2005	30	20	18	90	0.63 [0.47, 0.76]	0.82 [0.73, 0.89]

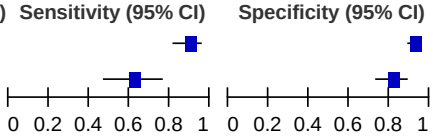
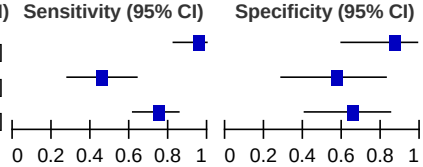


Figure 52: Stress echocardiography in in populations with prevalence of NSTEMI and/or UA of >50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Atar 2000	36	2	2	13	0.95 [0.82, 0.99]	0.87 [0.60, 0.98]
Gaibazzi 2009	15	6	18	8	0.45 [0.28, 0.64]	0.57 [0.29, 0.82]
Iglesias-Garriz 2005	44	7	15	13	0.75 [0.62, 0.85]	0.65 [0.41, 0.85]



I.3.5 Coupled sensitivity and specificity forest plots: rest and stress MRI

Figure 53: Rest MRI in populations with prevalence of NSTEMI and/or UA between >10% to 20%

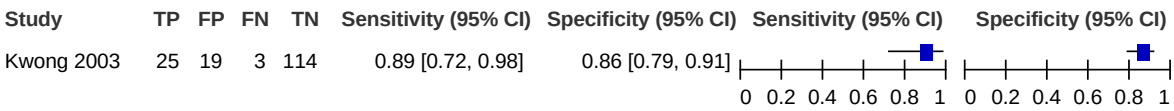


Figure 54: Stress MRI in populations with prevalence of NSTEMI and/or UA of ≤10%

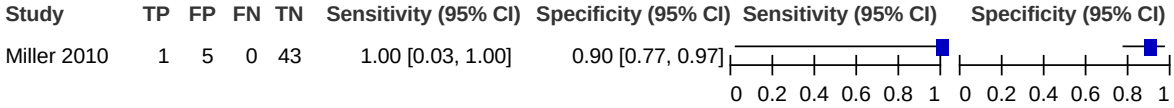
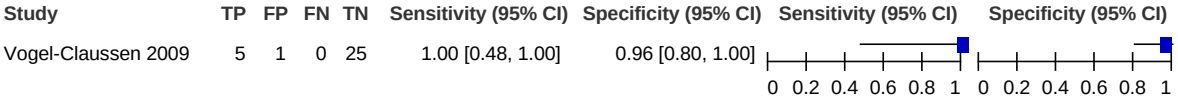


Figure 55: Stress MRI in populations with prevalence of NSTEMI and/or UA between >10% to 20%



I.3.6 Coupled sensitivity and specificity forest plots: Exercise ECG

Figure 56: Exercise ECG in populations with prevalence of NSTEMI and/or UA of ≤10%

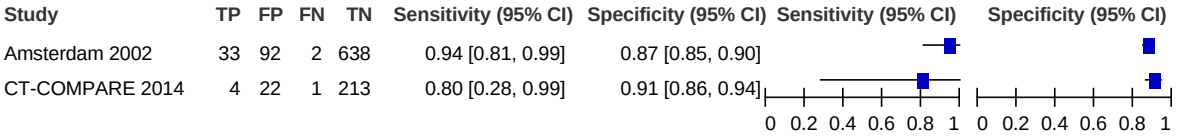


Figure 57: Exercise ECG in populations with prevalence of NSTEMI and/or UA between >10% to 20%

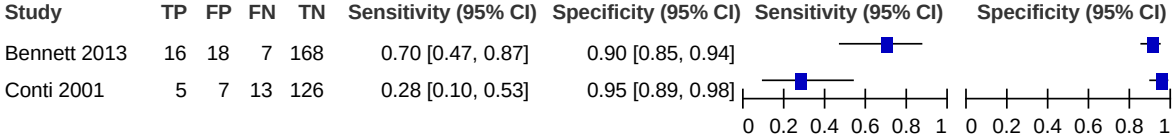
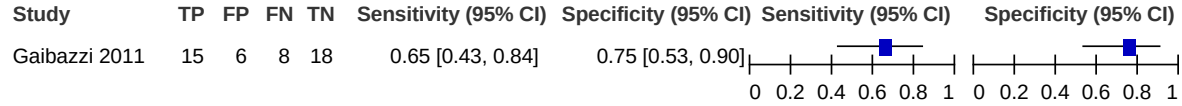


Figure 58: Exercise ECG in populations with prevalence of NSTEMI and/or UA of >50%



I.3.7 ROC curves: MDCT

Figure 59: MDCT in populations with prevalence of NSTEMI or UA of ≤10%

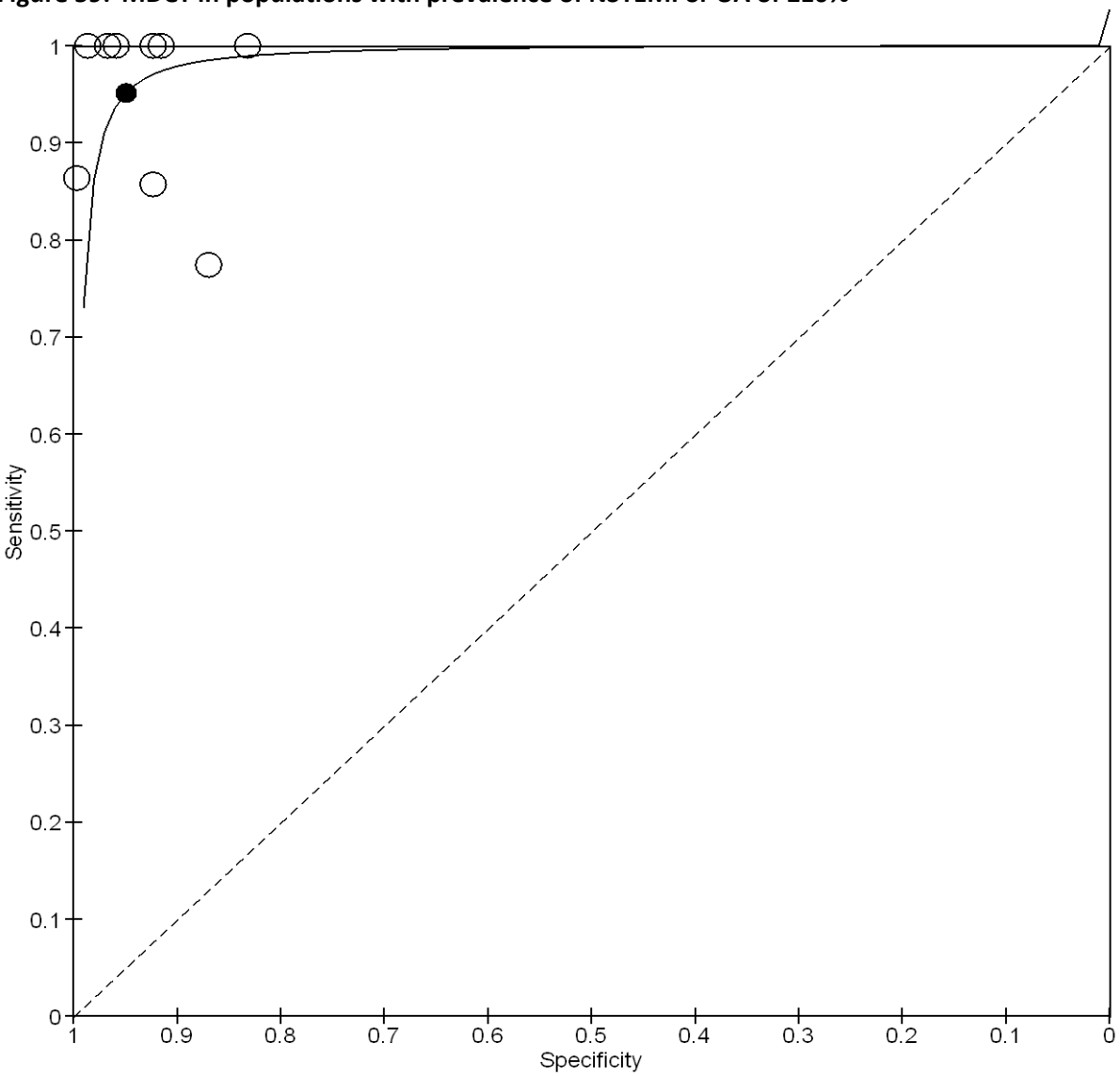


Figure 60: MDCT in populations with prevalence of NSTEMI or UA of >10% to 20%

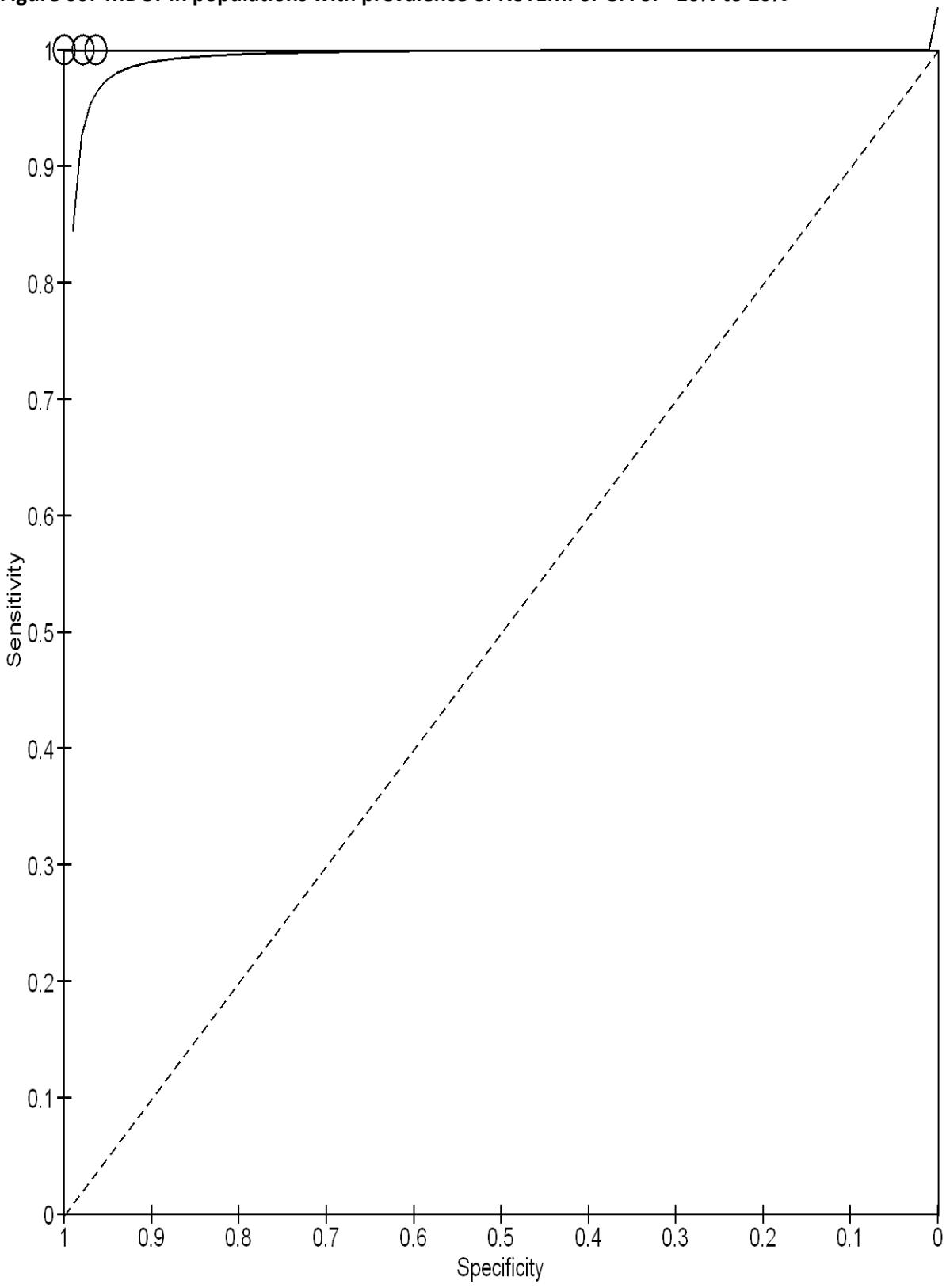


Figure 61: MDCT in populations with prevalence of NSTEMI or UA of between > 20% to 50%

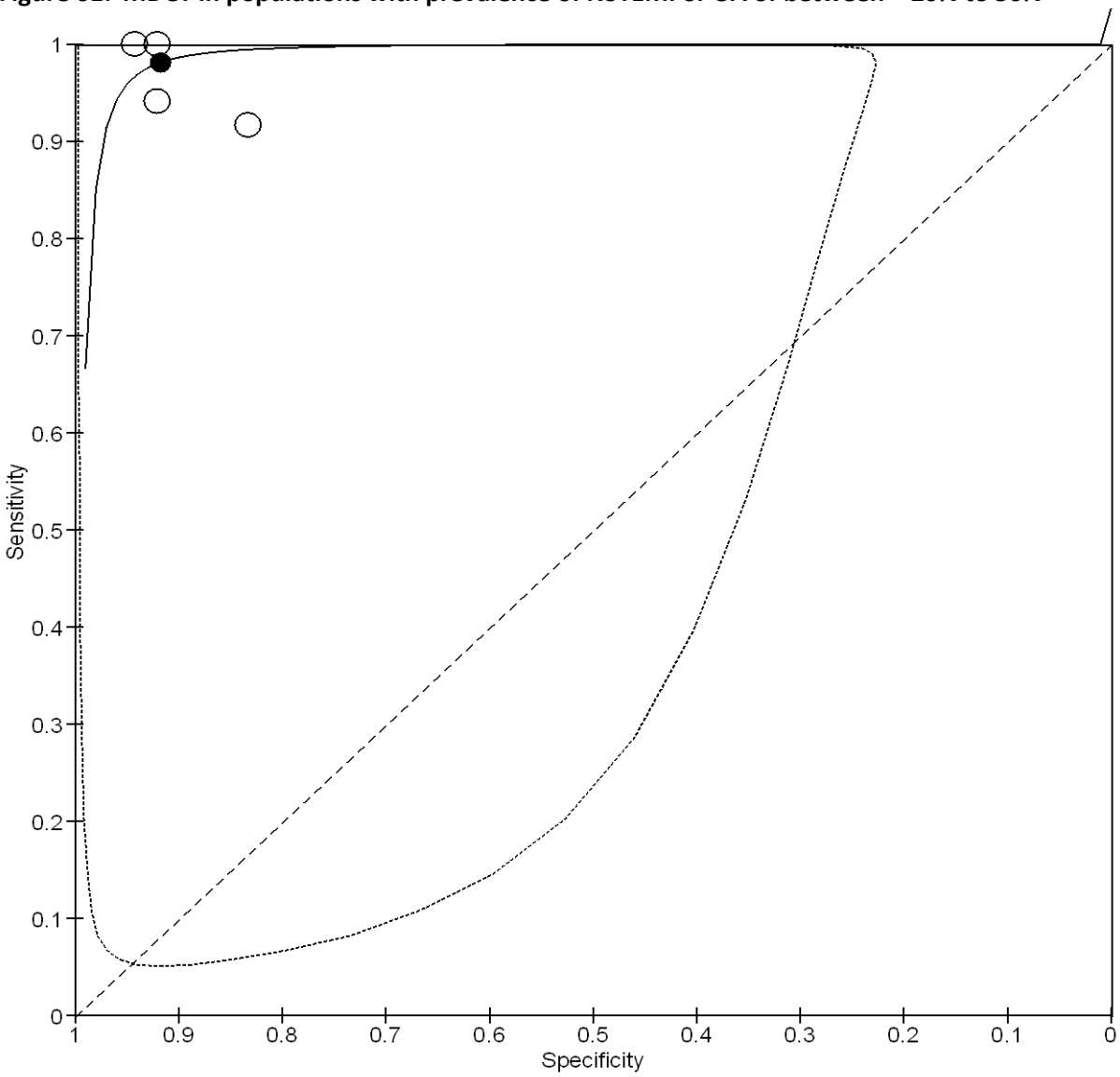
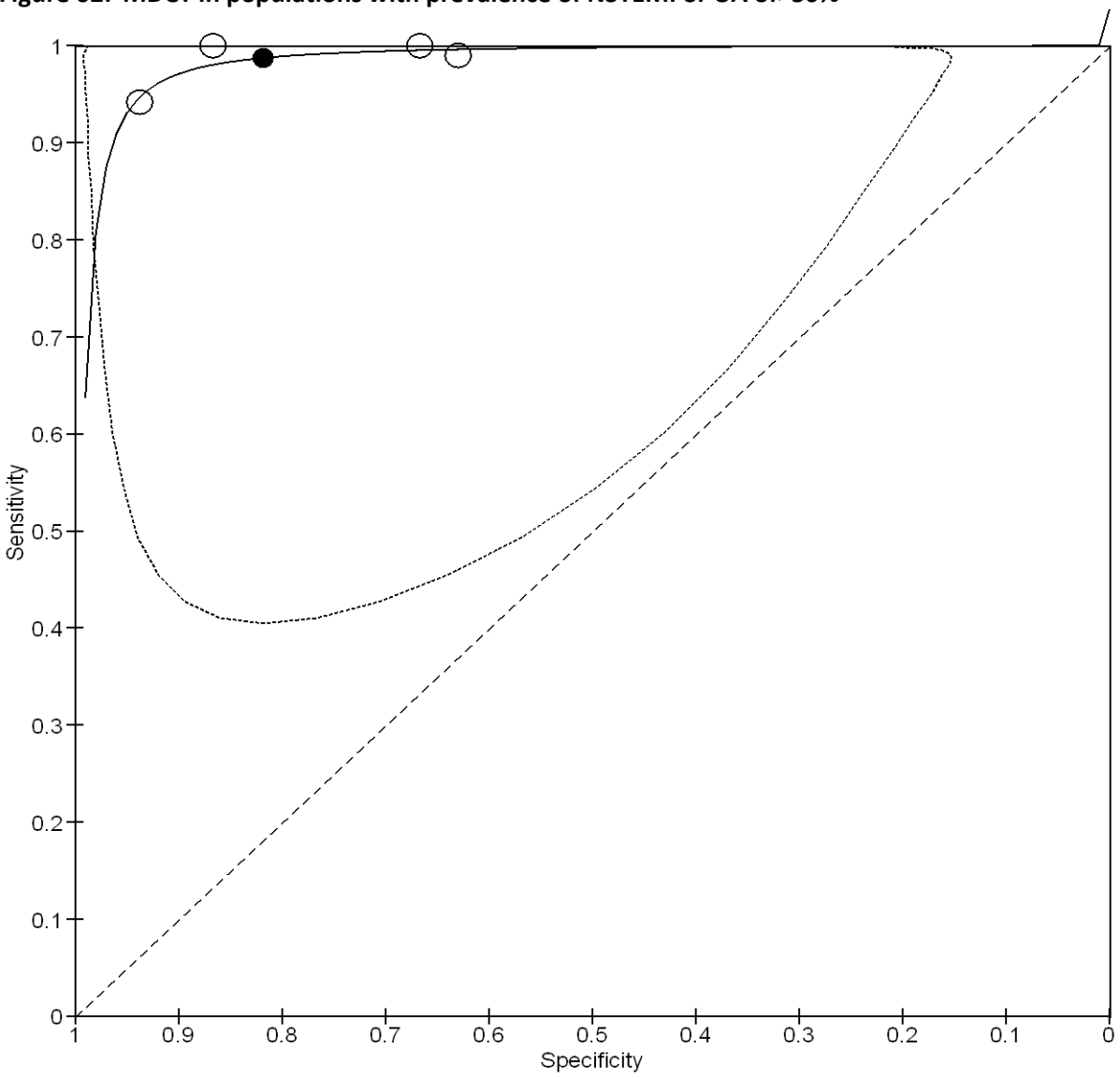
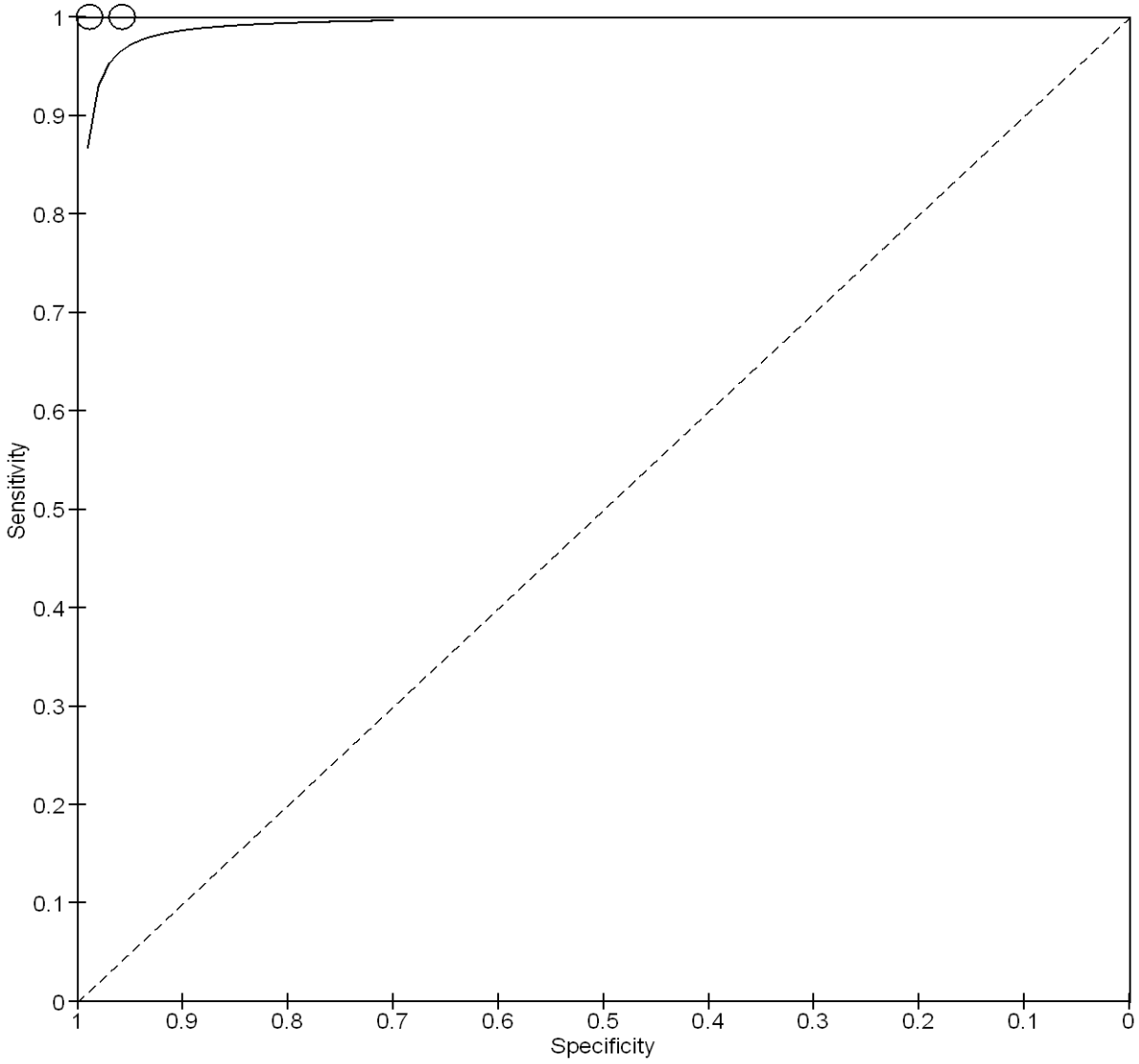


Figure 62: MDCT in populations with prevalence of NSTEMI or UA of>50%



I.3.8 ROC curves: DSCT

Figure 63: DSCT in populations with prevalence of NSTEMI or UA of ≤10%



I.3.9 ROC curves: Resting and stress SPECT

Figure 64: Resting SPECT in populations with prevalence of NSTEMI or UA of ≤10%

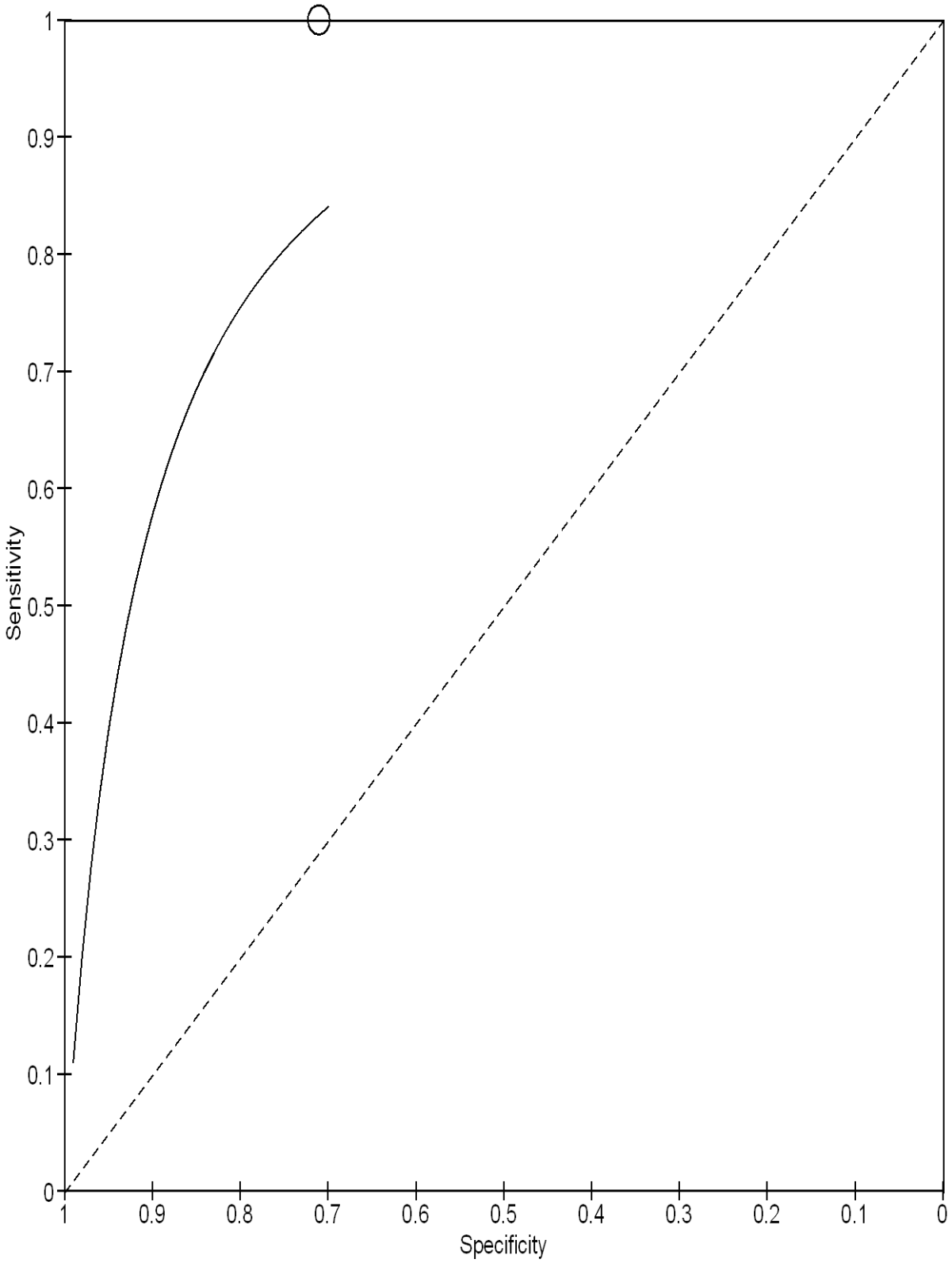


Figure 65: Resting SPECT in populations with prevalence of NSTEMI or UA between >20% and 50%

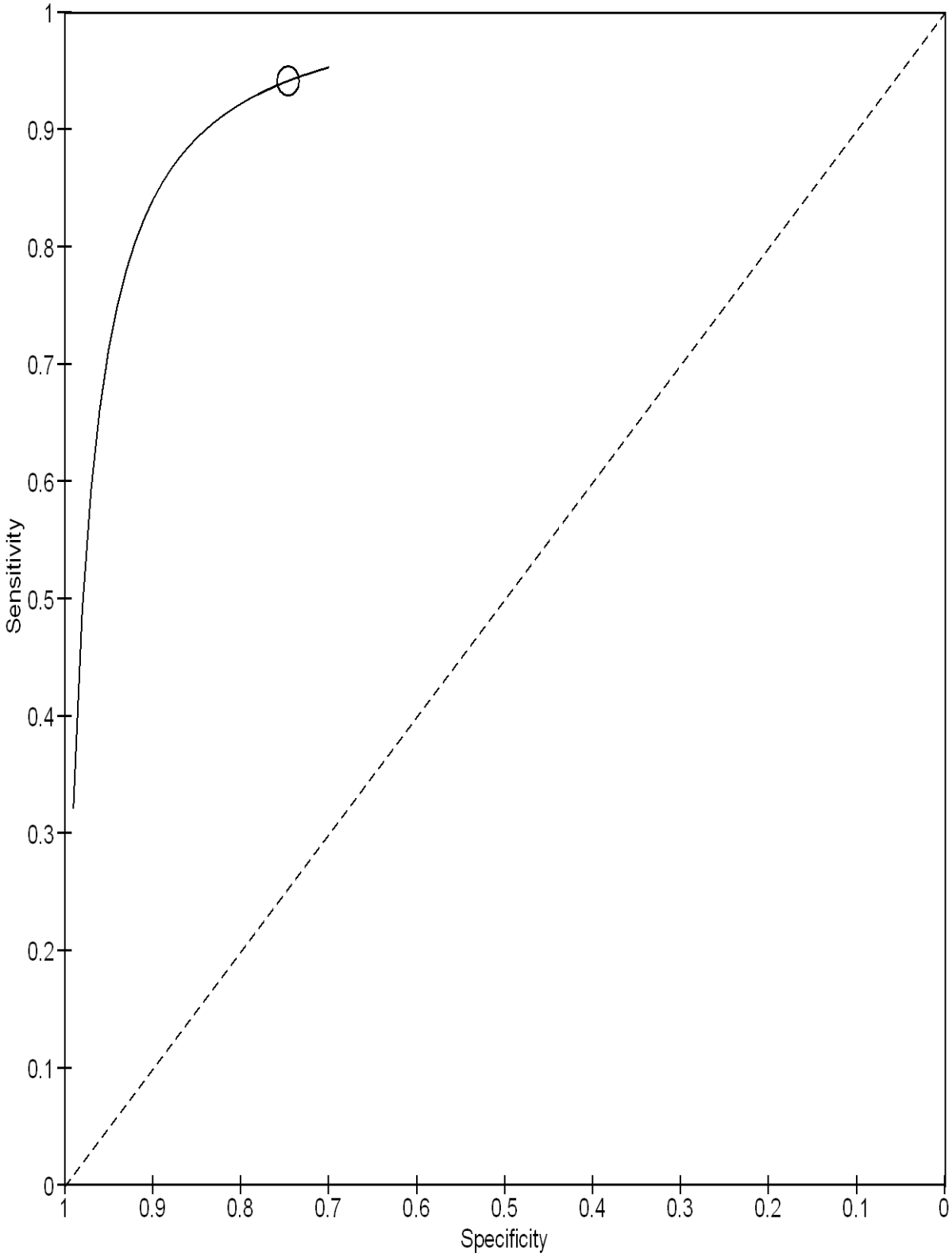


Figure 66: Stress SPECT in populations with prevalence of NSTEMI or UA

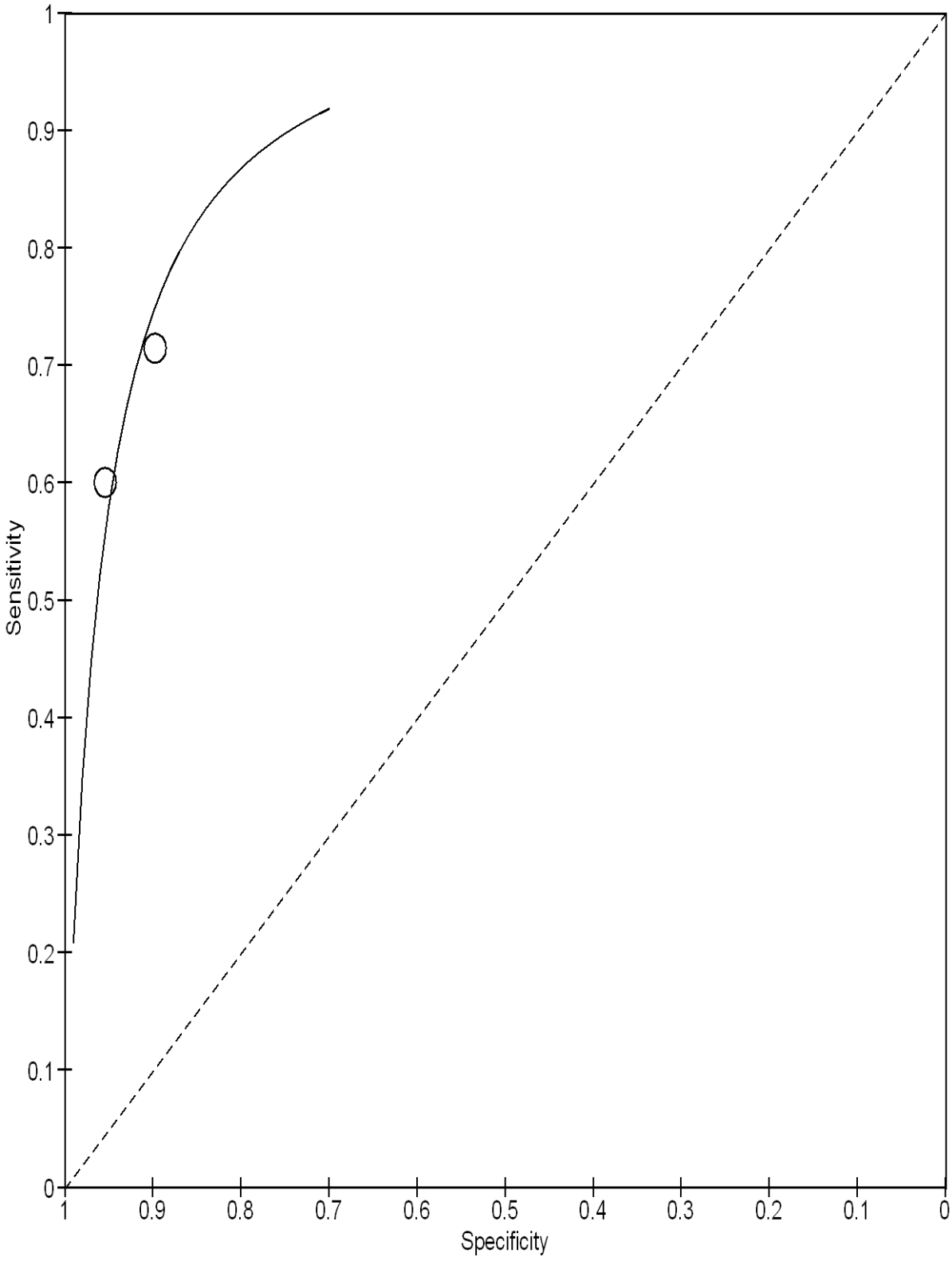
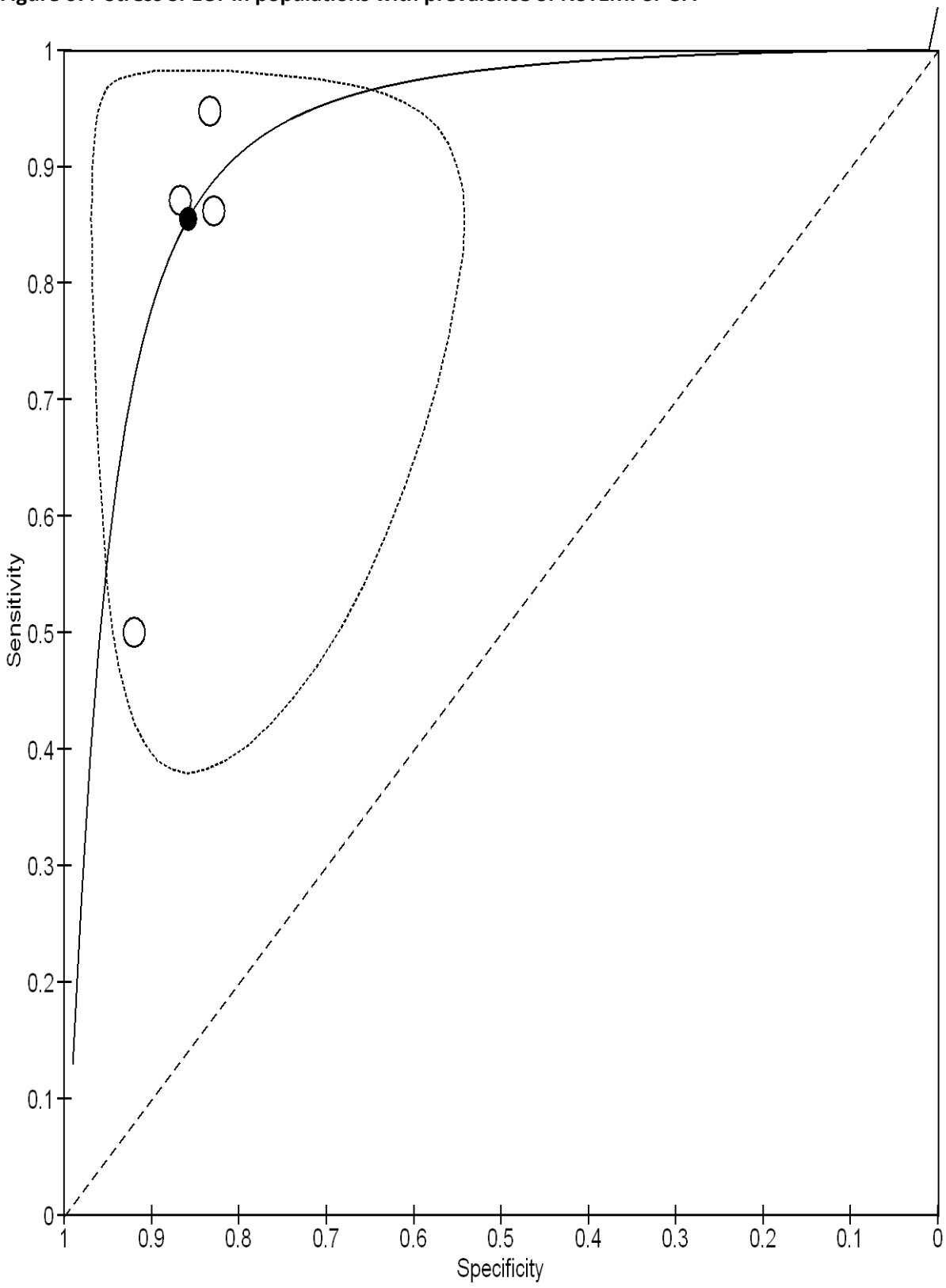


Figure 67: Stress SPECT in populations with prevalence of NSTEMI or UA



I.3.10 ROC curves: Stress echocardiography

Figure 68: Stress echocardiography in populations with prevalence of NSTEMI and/or UA ≤10%

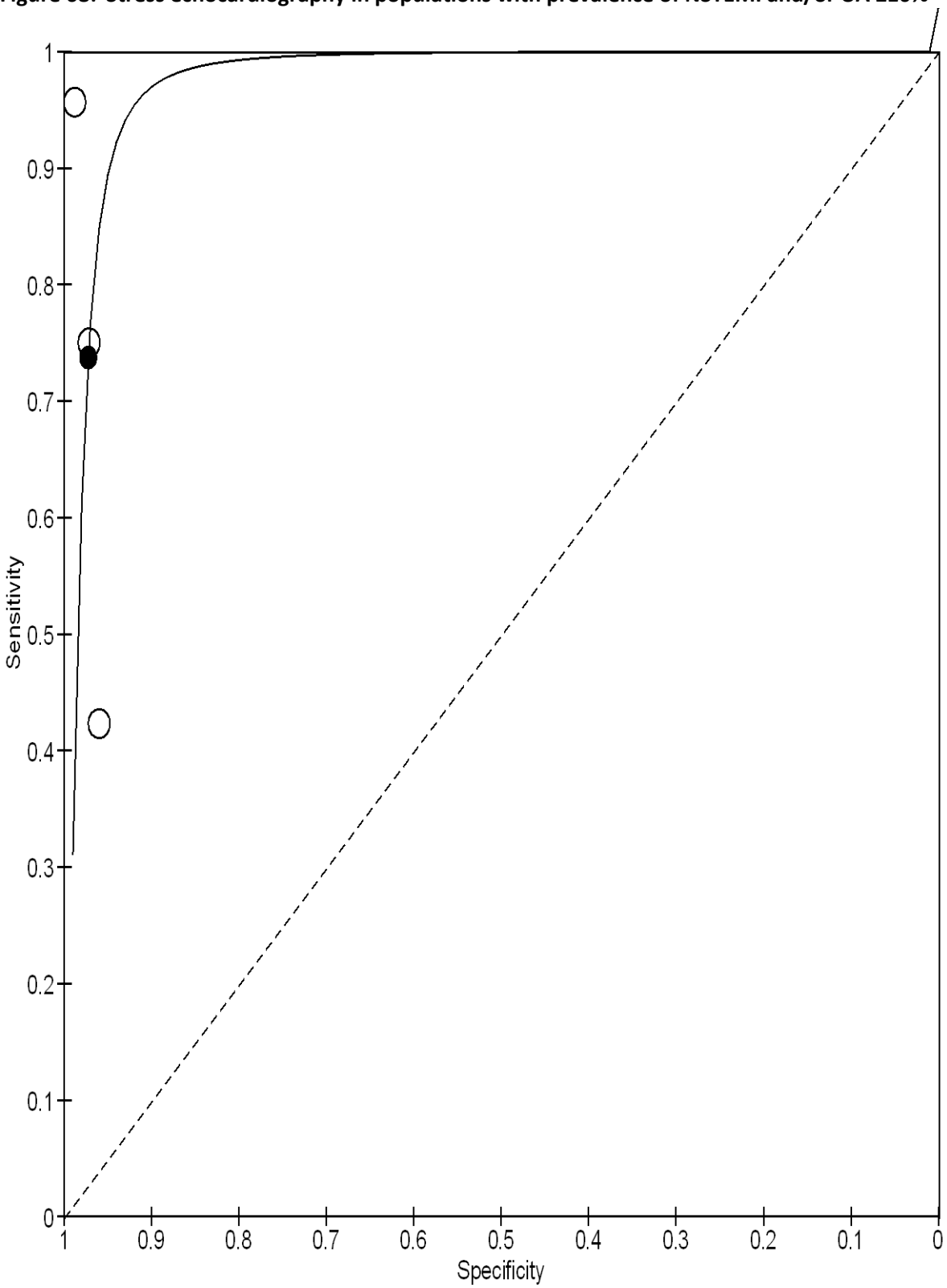


Figure 69: Stress echocardiography in populations with prevalence of NSTEMI and/or UA between >10% to 20%

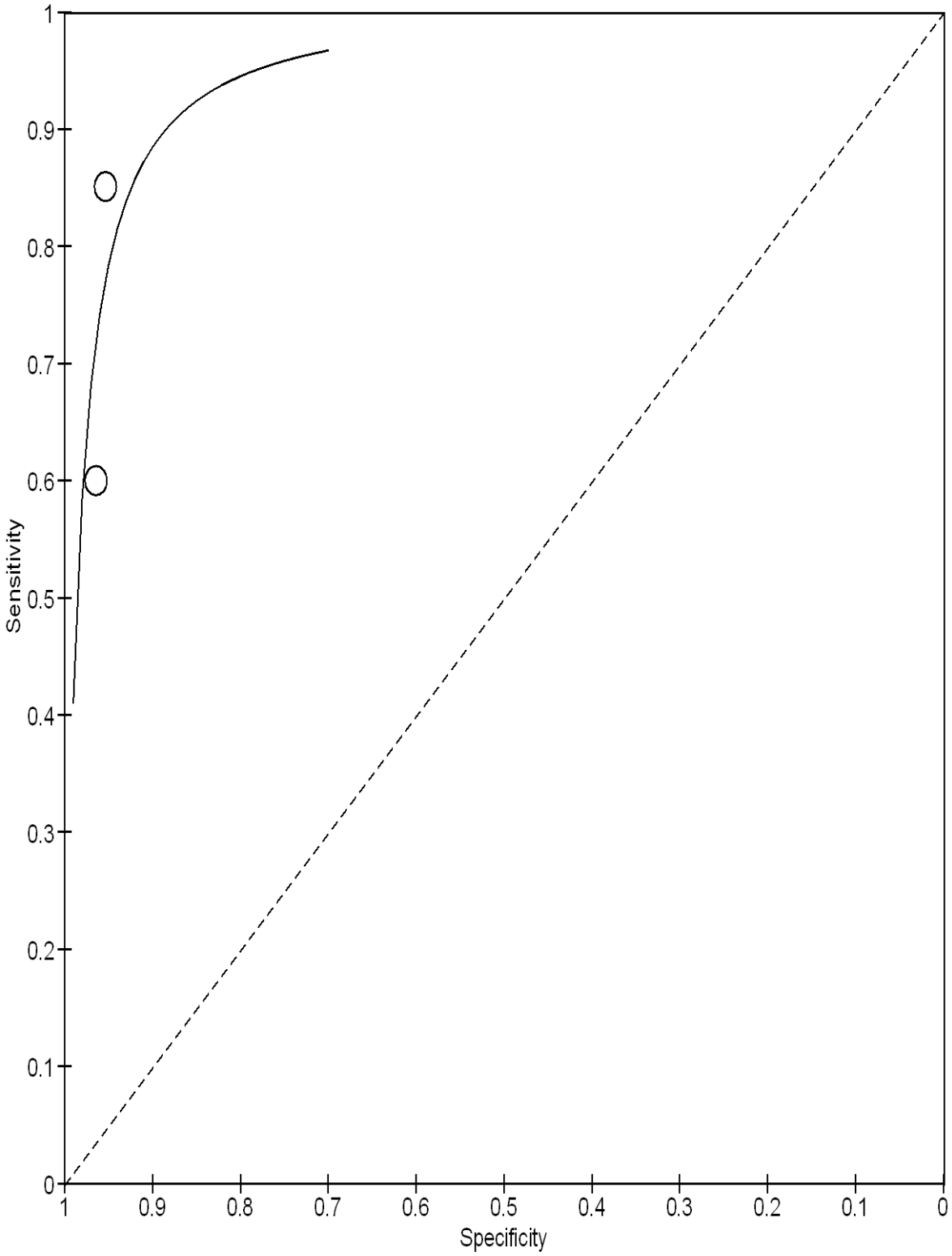


Figure 70: Stress echocardiography in populations with prevalence of NSTEMI and/or UA between >20% to 50%

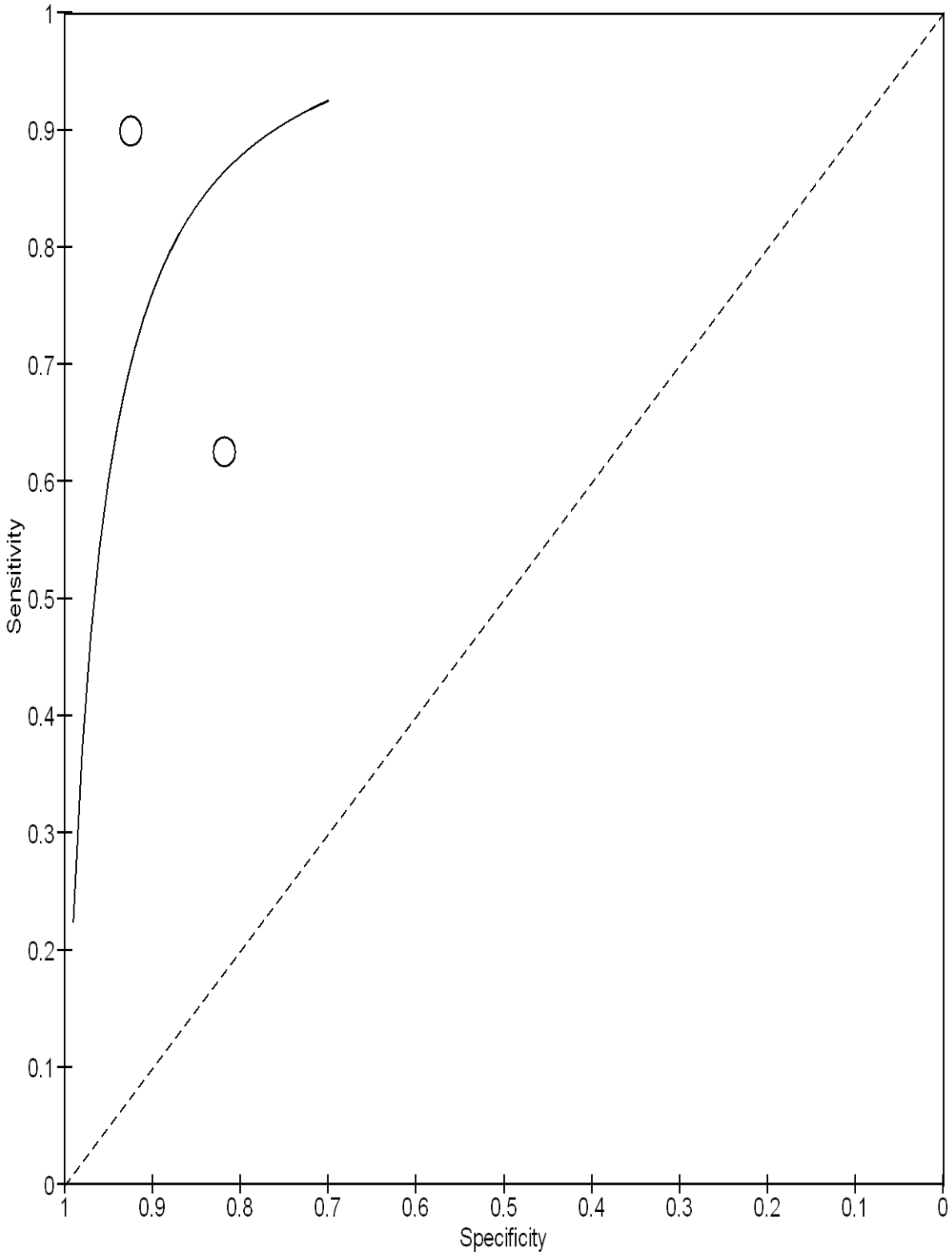
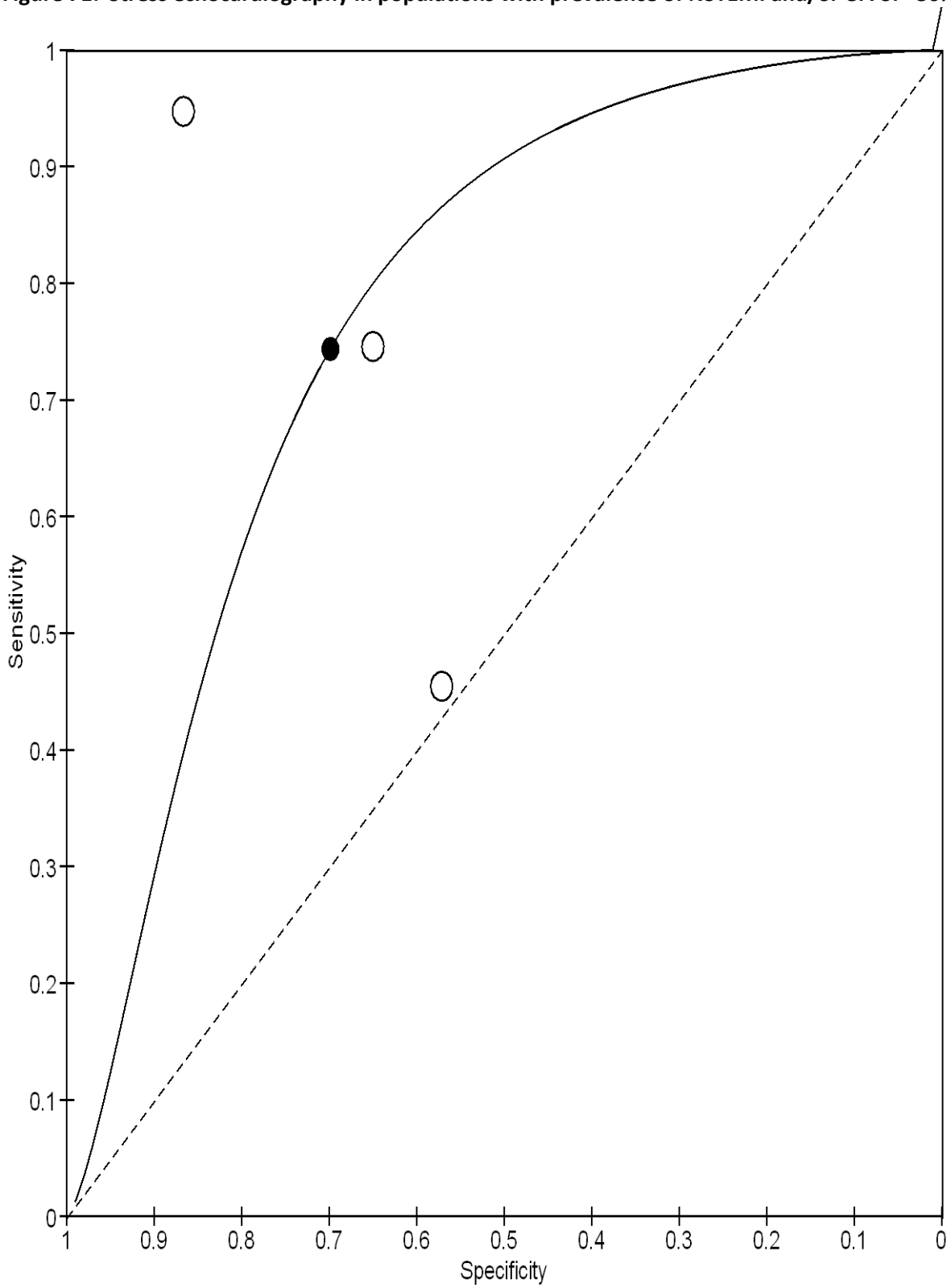


Figure 71: Stress echocardiography in populations with prevalence of NSTEMI and/or UA of >50%



I.3.11 ROC curves: Resting and stress MRI

Figure 72: Rest MRI in populations with prevalence of NSTEMI and/or UA between >10% to 20%

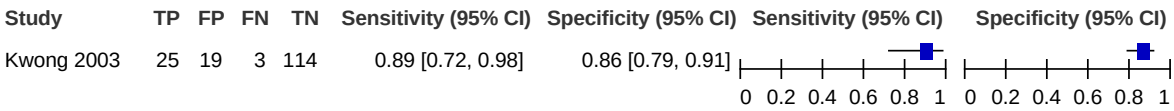


Figure 73: Stress MRI in populations with prevalence of NSTEMI and/or UA of ≤10%

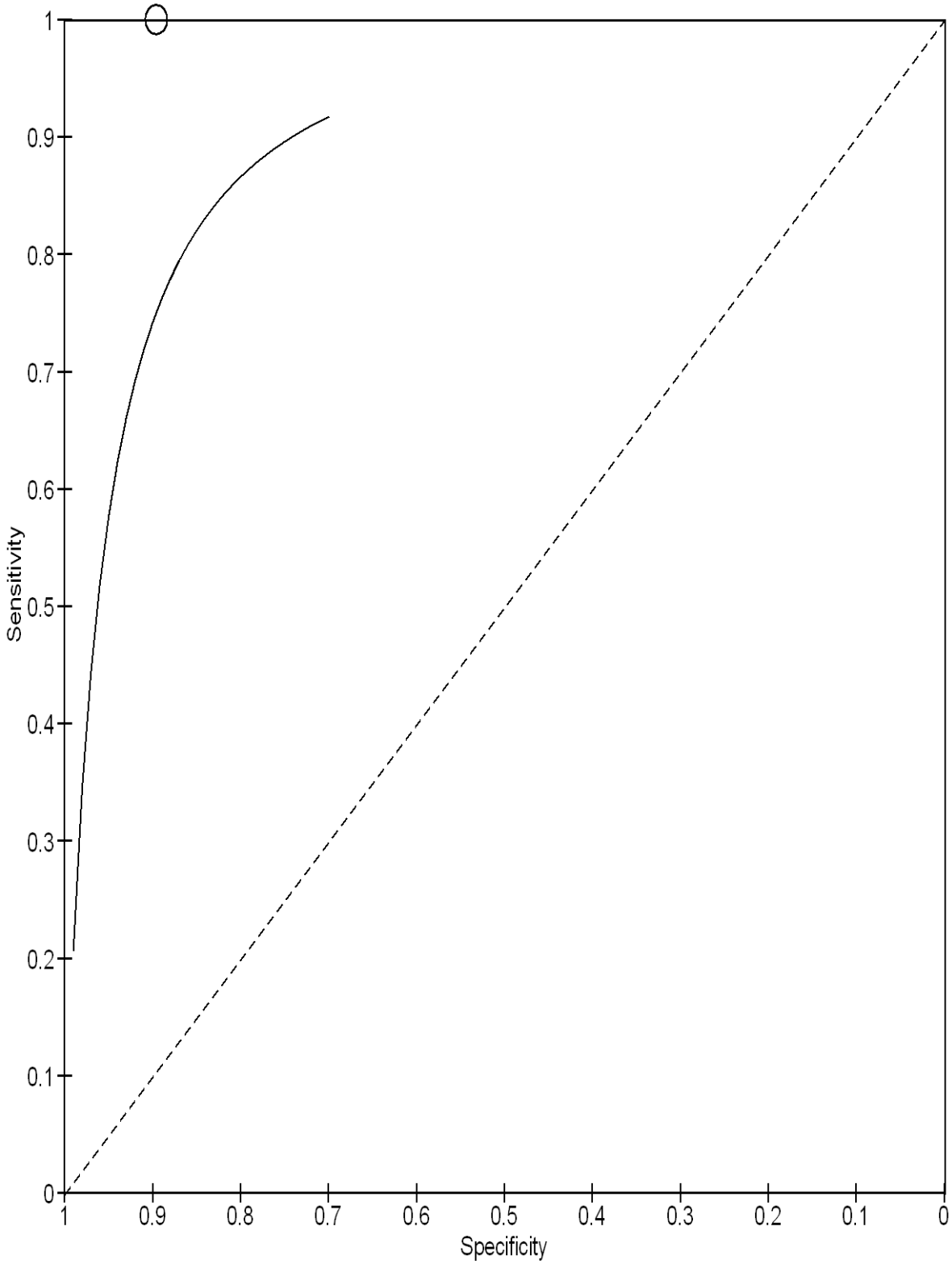
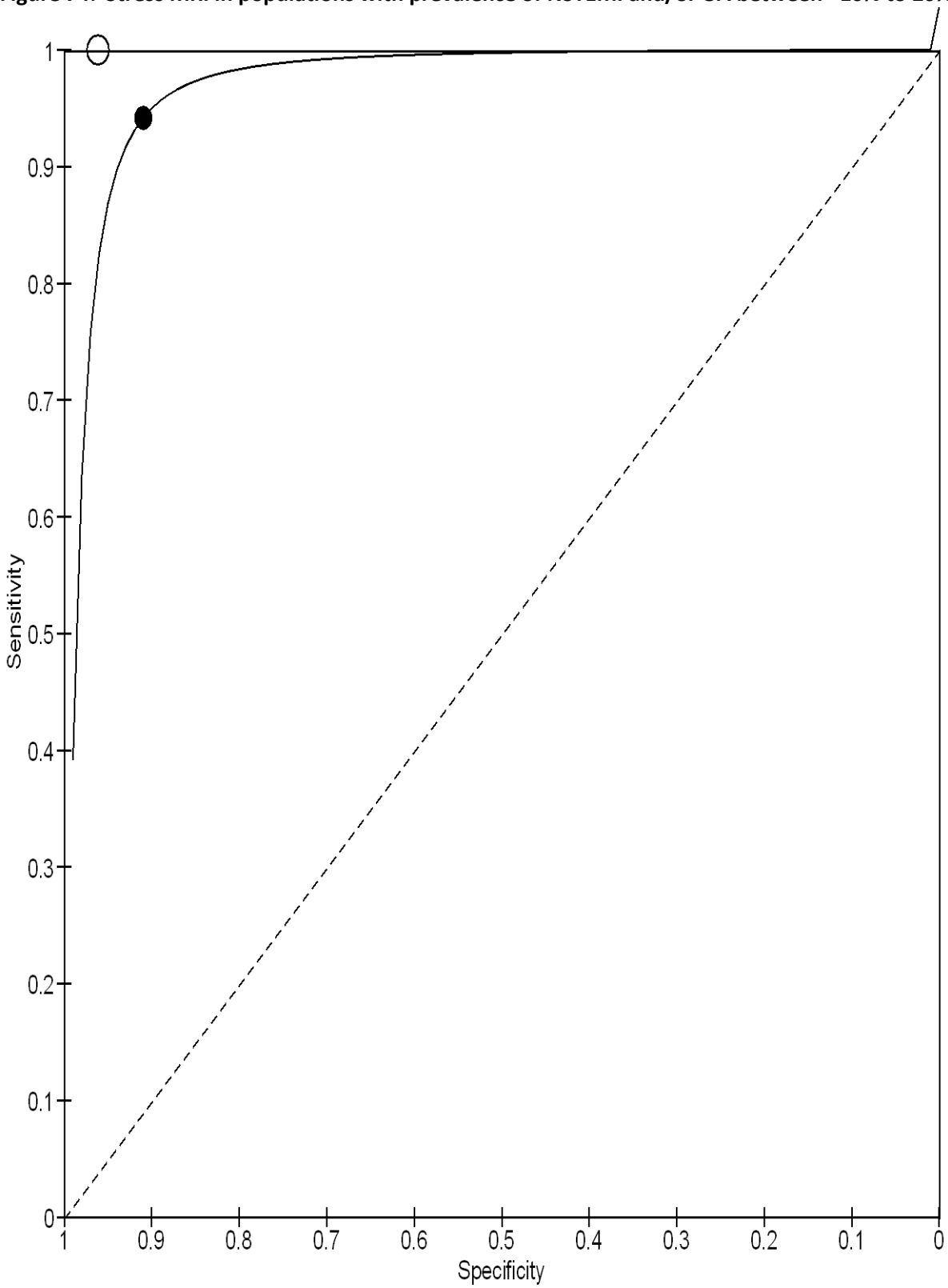


Figure 74: Stress MRI in populations with prevalence of NSTEMI and/or UA between >10% to 20%



I.3.12 ROC curves: Exercise ECG

Figure 75: Exercise ECG in populations with prevalence of NSTEMI and/or UA of ≤10%

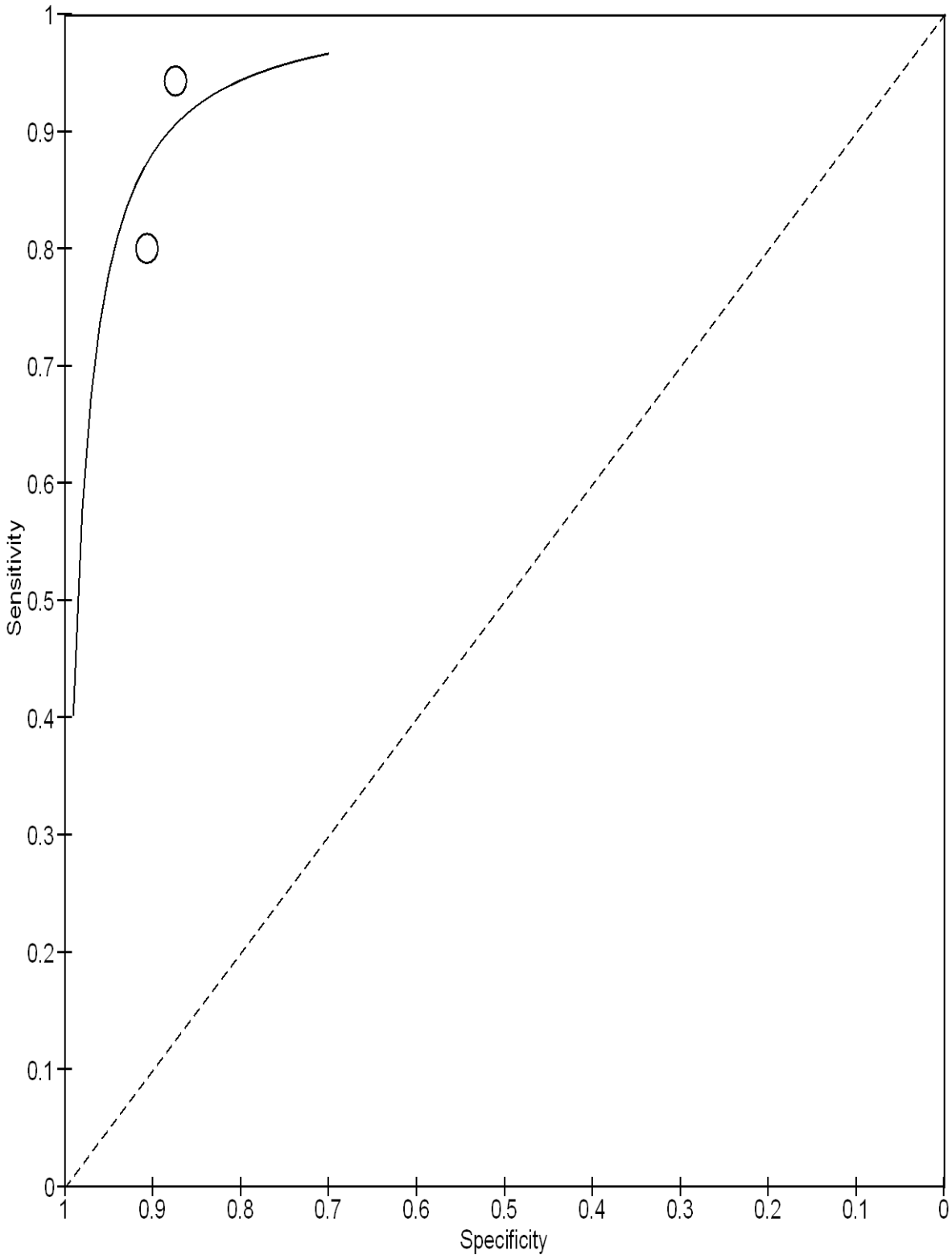


Figure 76: Exercise ECG in populations with prevalence of NSTEMI and/or UA between >10% to 20%

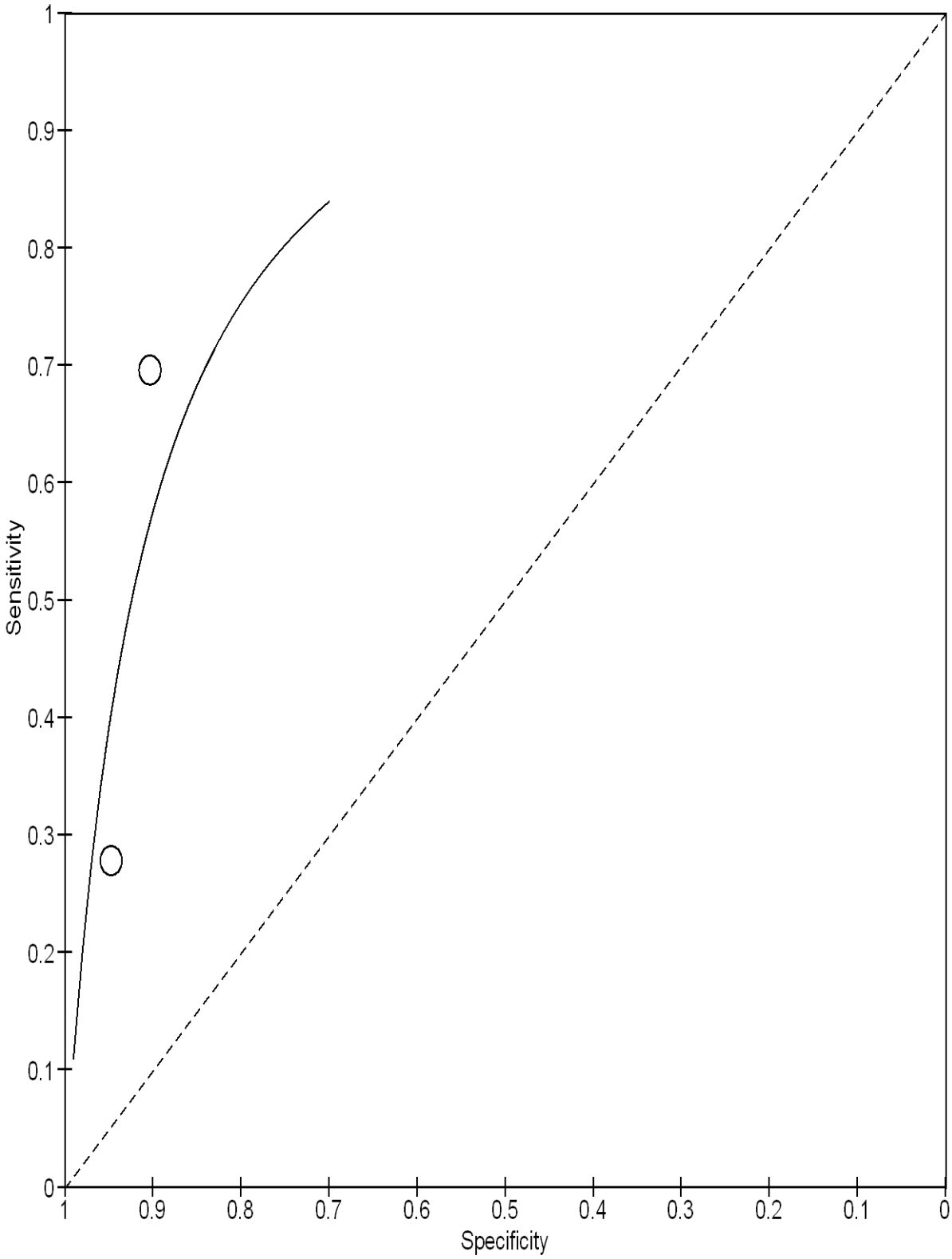
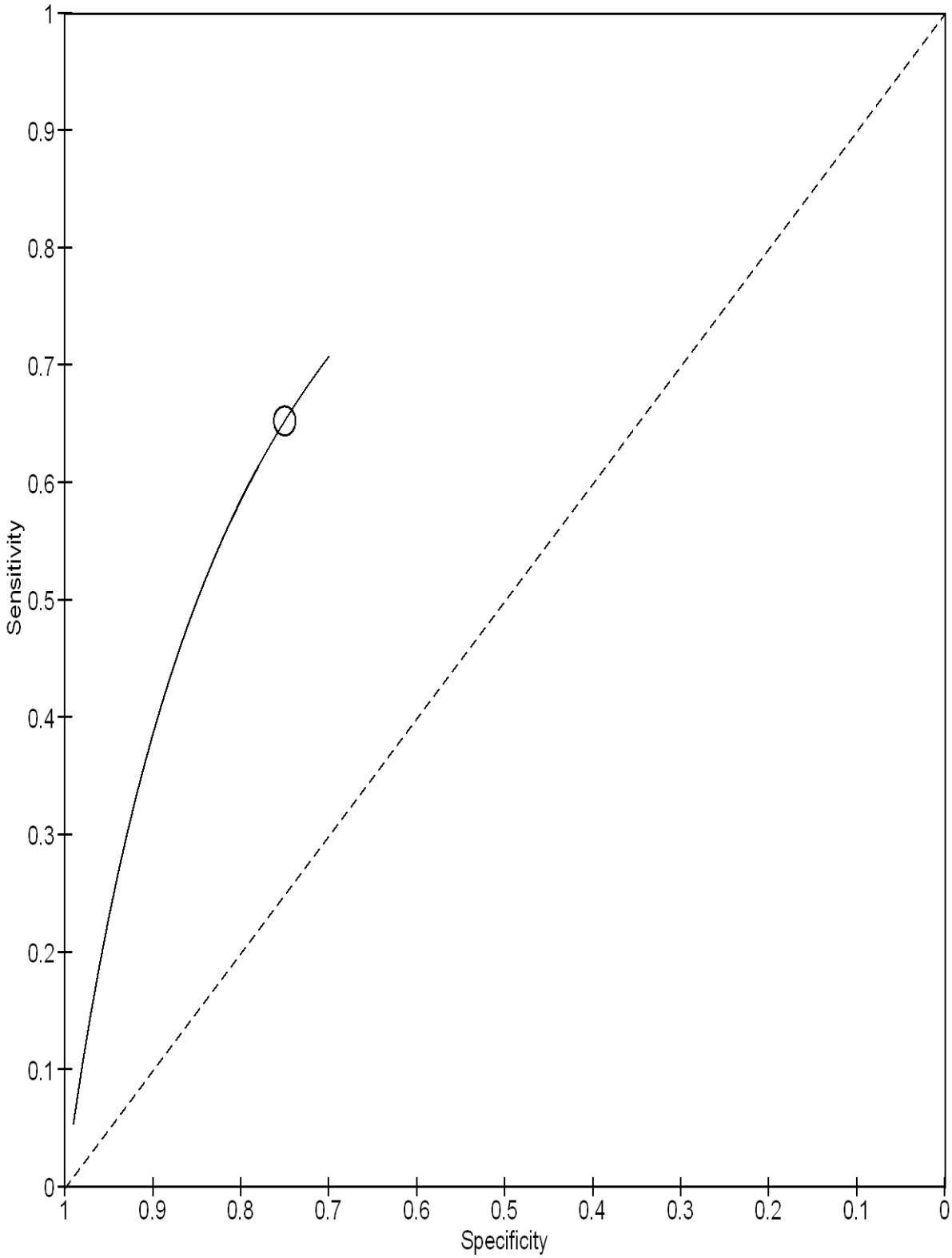


Figure 77: Exercise ECG in populations with prevalence of NSTEMI and/or UA >50%



Appendix K: Excluded clinical studies

K.1 High sensitivity cardiac troponins

Table 15: Studies excluded from the clinical review

Reference	Reason for exclusion
Aldous 2012[45]	STEMI patients not reported separately
Apple 2009[87]	Incorrect biomarker
Bahrmann 2012[102]	Population does not match protocol. Patients 70 years over admitted to the ED but not necessarily with acute chest pain or related symptoms.
Balmelli 2013[104]	Unclear reference standard. AUC data only.
Bhardwaj 2011[143]	Index test does not match protocol
Bialek 2015[147]	Population does not match protocol
Biener 2013[148]	Index test does not match protocol
Body 2011[155]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Bradburn 2011[163]	Post hoc analysis looking at inter-hospital variation in outcomes
Bruins Slot (2008)[173]	Primary care population
Bruins Slot (2010)[175]	Incorrect biomarker
Bruins Slot 2013[174]	Index test does not match protocol
Buccelletti 2012[176]	Reference standard does not match protocol
Carroll 2013[193]	Incorrect biomarker
Ceriani 2012[196]	Editorial
Chenevier-Gobeaux 2013[214]	Not primary study. Primary study included (Freund).
Cheng 2014[216]	Index test does not match protocol
Christ 2010[225]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Cuda 2012[236]	Case control study
Cullen 2013[237]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
De Winter 2000[240]	Incorrect biomarker
Diercks 2011[246]	Incorrect biomarker
Dierecks 2011[248]	Incorrect biomarker
Drexler 2012[315]	No data presented to calculate 2 x 2 table
Duchenne 2014[251]	Index test does not match protocol
Fitzgeral 2011[265]	No clinical data to calculate 2 x 2 table
Giannitis 2010[294]	Population does not match protocol
Giannitsis 2011[295]	Unclear reference standard and index test
Giavarina 2011[296]	Index test does not match protocol
Gimenez 2013[583]	2 x 2 table cannot be calculated
Haaf 2011[315]	NSTEMI patients not reported separately
Hammerer-Lercher 2013[318]	Population does not match protocol
Hoeller 2013[329]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.

Reference	Reason for exclusion
Hjorthshoj 2010[327]	Incorrect reference standard
Inoue 2011[348]	STEMI and NSTEMI patients included. Diagnostic accuracy of NSTEMI reported separately but unclear whether the total number of patients was used to calculated sensitivity and specificity (2 x 2 could not be calculated).
Keller 2009[373]	Incorrect biomarker
Keller 2009[375]	Index test does not match protocol
Keller 2010[373]	Incorrect biomarker
Keller 2011[374]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Khan 2011[376]	Reference standard does not match protocol
Kume 2011[397]	Incorrect biomarker
Kurz 2011[399]	2 x 2 table could not be calculated
Lindahl 2010[425]	No diagnostic accuracy data
Limon 2014[422]	Index test does not match protocol
Lippi 2012[429]	Incorrect biomarker
Lippi 2013[428]	Meta analysis checked for included studies
Lipinski 2014[427]	Index test does not match protocol
Lotze 2011[436]	Reference standard does not match protocol
Normann 2012[539]	Reference standard does not state that the universal definition of myocardial infarction/ACA/ECS criteria was used
Olivieri 2012[542]	Index test does not match protocol
Pyati 2015[566]	Index test does not match protocol
Pracon[563]	Index test does not match protocol
Potocki 2012 [562]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Raskovalova 2013[567]	Index test does not match protocol
Reichlin 2009[570]	Incorrect biomarker
Reichlin 2009[569]	NSTEMI patients not reported separately
Reichlin 2012[572]	Reference standard does not match protocol
Reiter 2011[575]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Reiter 2012[574]	NSTEMI patients not reported separately
Reiter 2012[576]	Incorrect biomarker
Sanchis 2012[597]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Saenger 2010[592]	NSTEMI not presented separately
Shah 2015[627]	Abstract
Shah 2013[626]	Review
Shah 2015[625]	Includes STEMI patients. Results of STEMI and NSTEMI/UA not reported separately.
Shah 2014[627]	No diagnostic accuracy data
Than 2014[673]	RCT comparing a diagnostic protocol with a standard care protocol
Thelin 2013[675]	STEMI and NSTEMI patients included. Diagnostic accuracy of NSTEMI reported separately but unclear whether the total number of patients was used to calculated sensitivity and specificity (2 x 2 could not be

Reference	Reason for exclusion
	calculated).
Tomonga 2011[681]	Primary care population
Truong 2012[683]	Index test does not match protocol
Volz 2012[717]	Incorrect biomarker
Weber 2011[725]	Population does not match protocol
White 2014[733]	No diagnostic accuracy data
Zhang 2015[747]	Index test does not match protocol

K.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

Table 16: Studies excluded from the clinical review

Reference	Reason for exclusion
A, 2013[18]	Wrong diagnostic intervention
Abbasi, 2014[1]	Wrong population
Abbott, 2000[2]	Wrong study type
Abbott, 2003[3]	Wrong study type
Abd, 2015[4]	Wrong study type
Abdelmoneim, 2009[7]	Wrong study type
Abdelmoneim, 2011[8]	Wrong population
Abdelmoneim, 2010[9]	Wrong population
Abdelmoneim, 2010[10]	Wrong population
Abdelmoneim, 2009[11]	Wrong population
Abdelmoneim, 2009[12]	Wrong population
Abdelmoneim, 2015[13]	Wrong diagnostic comparison
Abdel-Rahman, 2015[5]	Wrong population
Abdel-Salam, 2015[6]	Wrong diagnostic intervention
Abdool, 2014[14]	Wrong population
Abdulla, 2007[15]	Wrong population
Abdulla, 2012[16]	Wrong intervention
Abraham, 2010[17]	Wrong study type
Abramson, 2000[19]	Wrong population
Achenbach, 2010[20]	Wrong study type
Achenbach, 2001[21]	Wrong population
Achenbach, 1998[22]	Wrong diagnostic intervention
Achenbach, 2008[23]	Wrong population
Adams, 2007[24]	Wrong population
Adil, 2011[25]	Wrong population
Agarwal, 2012[26]	Wrong population
Aggarwal, 2015[27]	Wrong population
Aggeli, 2011[28]	Wrong population
Aggeli, 2007[29]	Wrong population

Reference	Reason for exclusion
Ahmad, 2001[30]	Wrong population
Ahmadvazir, 2014[31]	Wrong population
Ahn, 2011[32]	Wrong diagnostic intervention
Ahn, 2013[33]	Wrong population
Aidi, 2014[34]	Wrong population
Akbar, 2010[35]	No data of interest
Akram, 2008[36]	Wrong diagnostic intervention
Al Moudi, 2011[42]	Wrong population
Al Moudi, 2014[43]	Wrong diagnostic comparison
Aldweib, 2013[47]	Wrong population
Alessandri, 2009[48]	Wrong population
Alexanderson, 2004[49]	Wrong population
Alexanderson, 2006[50]	Wrong diagnostic intervention
Alexanderson Rosas, 2010[51]	Wrong intervention
Alexopoulos, 2005[52]	Wrong diagnostic intervention
Ali, 2007[53]	Wrong population
AlJaroudi, 2013[54]	Wrong population
Alkadhi, 2008[55]	Wrong population
Alkadhi, 2010[56]	Wrong diagnostic intervention
Al-Kaylani, 2002[37]	Wrong diagnostic evaluation
Allajbeu, 2014[57]	Wrong population
Al-Mallah, 2011[38]	Wrong study type
Al-Mallah, 2014[39]	Wrong population
Almeida, 2002[58]	Wrong population
Almoudi, 2012[59]	Wrong diagnostic intervention
Alqaisi, 2008[60]	Wrong population
al-Saadi, 2002[40]	Wrong population
Al-Saadi, 2000[41]	Wrong population
Altinmakas, 2000[61]	Wrong population
Altiok, 2013[62]	Wrong diagnostic comparison
Altiok, 2012[63]	Wrong diagnostic comparison
Altiok, 2014[64]	Wrong diagnostic comparison
Altun, 2005[65]	Wrong population
Altunkeser, 2002[66]	Wrong population
Alunni, 2015[67]	Wrong diagnostic intervention
Alvarez Tamargo, 2008[68]	Wrong diagnostic intervention
Amanuma, 2015[69]	Wrong population
American College of, 2006[70]	Wrong study type
Amit, 2014[71]	Wrong study type
Anagnostopoulos, 2013[73]	Wrong study type
Anand, 2003[74]	Wrong study type
Anantharam, 2009[75]	No available data
Anders, 2013[76]	Wrong population

Reference	Reason for exclusion
Andrade, 2009[78]	Wrong population
Andrassy, 2011[79]	Wrong population
Andreini, 2016[80]	Wrong study type (report)
Andreini, 2010[81]	Wrong population
Annuar, 2008[82]	Wrong population
Anonymous, 1997[345]	Wrong population
Anonymous, 2009[235]	Wrong study type
Anonymous, 2015[234]	Wrong study type
Antony, 2011[83]	Wrong study type
Anwar, 2013[84]	Wrong population
Aoyagi, 1998[85]	Wrong population
Apostolopoulos, 2012[86]	Wrong population
Arbab-Zadeh, 2015[88]	Wrong population
Arbab-Zadeh, 2011[89]	Wrong intervention
Argulian, 2014[90]	Wrong population
Arnold, 2012[91]	Wrong study type
Arnold, 2010[92]	Wrong population
Arsanjani, 2013[93]	Wrong study type
Arsanjani, 2013[94]	Wrong population
Arsanjani, 2013[95]	Wrong study type
Arumugam, 2013[96]	Wrong study type
Asferg, 2012[97]	Wrong population
Asher, 2015[98]	Wrong intervention
Atar, 2000[99]	Wrong intervention
Athappan, 2010[100]	Different risk categories to protocol and date cut-off May 2008
Babar Imran, 2003[101]	Wrong population
Balaravi, 2006[103]	Wrong analysis and wrong population (prognostic)
Bamberg, 2008[105]	Wrong study type (substudy)
Bamberg, 2014[106]	Wrong population
Bamberg, 2009[107]	Wrong study type (ROMICAT substudy)
Banerjee, 2012[108]	Wrong study type
Bangalore, 2007[109]	Wrong population
Bangalore, 2005[110]	Wrong population
Barbirato, 2009[111]	Not English language
Barletta, 1999[112]	Wrong population
Barmeyer, 2008[113]	Wrong population
Barraclough, 2015[114]	Wrong study type
Baszko, 2001[115]	Wrong population
Bateman, 2009[116]	Wrong population
Bateman, 2006[117]	Wrong population
Bauer, 2010[118]	Wrong population
Bauernfeind, 2011[119]	Not topic of interest – prognostic
Beck, 2002[120]	Wrong population

Reference	Reason for exclusion
Becker, 2007[121]	Wrong population
Becker, 2001[122]	Wrong population
Becker, 2012[123]	Wrong study type
Bekler, 2014[126]	No available data
Belardinelli, 2014[127]	Wrong diagnostic comparison
Ben Bouallegue, 2015[128]	Wrong population
Benchimol, 2000[129]	Wrong population
Benedek, 2013[130]	Wrong population and wrong study type
Benedek, 2014[131]	Wrong study type
Benkiran, 2015[132]	Wrong population
Berdahl, 2013[134]	Wrong study type
Bergeron, 2004[135]	Wrong population
Beslic, 2011[136]	Wrong population
Bettencourt, 2013[137]	Wrong population
Bettencourt, 2013[138]	Wrong population
Bettencourt, 2013[139]	Wrong population and setting
Bettencourt, 2013[140]	Wrong population
Better, 2012[141]	Developing countries
Beule, 2010[142]	Wrong study type
Bholasingh, 2003[144]	Wrong study type
Biagini, 2006[146]	Wrong population
Biglands, 2015[149]	Wrong study type
Bischoff, 2012[150]	Wrong population
Blankstein, 2012[151]	Wrong study type
Blinder, 2005[152]	No DTA data available
Blomstrand, 2004[153]	Wrong population
BlueCross BlueShield Association, 2011[154]	Wrong study type
Bogaert, 2015[156]	Wrong study type
Boglioli, 2001[157]	Wrong study type
Boiten, 2012[158]	Wrong population
Bom, 2015[159]	Wrong population
Boussel, 2008[161]	Wrong population
Bouzas-Mosquera, 2015[162]	Wrong population
Branch, 2012[164]	Wrong study type
Branch, 2013[165]	Wrong diagnostic intervention
Branch, 2013[166]	Wrong population
Brodoefel, 2008[167]	Wrong population
Brodoefel, 2008[168]	Wrong population
Brodoefel, 2008[169]	Wrong population
Brodov, 2015[170]	Wrong population
Brogsitter, 2005[171]	Wrong study type
Brown, 2008[172]	MACE events only

Reference	Reason for exclusion
Bucerius, 2007[177]	Wrong population
Buckert, 2013[178]	Wrong population
Budge, 2011[179]	Wrong study type
Budoff, 2003[180]	Wrong population
Budoff, 2013[181]	Wrong population
Budoff, 2007[182]	Wrong population
Burris, 2015[183]	Wrong diagnostic intervention
Busch, 2011[184]	Wrong population
Cabeda, 2015[185]	Wrong population
Cademartiri, 2008[186]	Wrong population
Cademartiri, 2007[187]	Wrong population
Candell-Riera, 2007[189]	Wrong population
Candell-Riera, 2004[190]	Wrong population
Carlsson, 2013[191]	Wrong population
Carrinho, 2004[192]	Wrong population
Caymaz, 2000[194]	Wrong population
Celik, 2011[195]	Wrong study type
Chammas, 2002[197]	Wrong population
Chan, 2003[198]	Wrong population
Chandra, 2001[199]	Wrong study type
Chandraratna, 2012[200]	Wrong population
Chandraratna, 2012[201]	Wrong diagnostic interventions
Chang, 2008[202]	Wrong study type
Chang, 2008[203]	Wrong population
Chao, 2010[204]	Wrong population
Chaosuwannakit, 2012[205]	Wrong population
Cheezum, 2014[206]	Wrong study type
Chen, 2013[207]	Wrong population
Chen, 1999[208]	Wrong population
Chen, 2014[209]	Wrong population
Chen, 2001[210]	Wrong population
Chen, 2012[211]	Wrong population
Chen, 2011[212]	Wrong diagnostic intervention
Chen, 2010[213]	Wrong diagnostic intervention
Cheng, 2007[215]	Wrong population and study type; no usable data
Cheng, 2013[217]	Wrong study type; no usable data
Cheng, 2013[218]	Developing country
Cheng, 2000[219]	Wrong population
Cheng, 2010[220]	Wrong population
Chiou, 2004[221]	Wrong population
Chiu, 2003[222]	Wrong diagnostic intervention
Choo, 2013[223]	Wrong population
Chow, 2007[224]	Wrong population

Reference	Reason for exclusion
Conti, 2010[230]	Wrong study type
Conti, 2010[231]	Wrong study type
Conti, 2008[233]	Wrong population
Cury, 2013[238]	Wrong diagnostic intervention
Dall Armellina, 2011[239]	Wrong study type
Dedic, 2013[241]	Insufficient method details (systematic review)
Dedic, 2014[242]	Wrong population
Dedic, 2013[244]	Wrong diagnostic intervention
Department of Science and Technology - Brazilian Health Technology Assessment General Coordination (DECIT-CGATS), 2008[245]	Wrong study type
Diercks, 2013[247]	Wrong diagnostic intervention
Dodd, 2008[249]	Wrong study type Wrong study type
Dorgelo, 2005[250]	Wrong diagnostic intervention
Durand, 2009[252]	Wrong study type
Duvall, 2014[253]	Wrong intervention
Edmond, 2002[254]	Wrong study type
Einstein, 2015[256]	Wrong population
Estrada, 2006[257]	Wrong diagnostic intervention
Fanaroff, 2015[258]	Not diagnostic intervention
Ferencik, 2012[259]	Secondary analysis - ROMICAT
Ferencik, 2012[260]	Wrong study type
Fernandez-Friera, 2011[261]	Wrong diagnostic intervention
Fesmire, 2012[262]	Wrong diagnostic intervention
Fesmire, 2002[263]	Wrong intervention
Fesmire, 2001[264]	Wrong reference standard
Gaemperli, 2009[268]	Wrong population
Gaemperli, 2007[269]	Wrong population
Gaibazzi, 2009[271]	Wrong population
Gaibazzi, 2010[272]	Wrong population
Gaibazzi, 2010[273]	Wrong population
Galassi, 2000[274]	Wrong population
Gao, 2011[276]	Wrong population
Gargiulo, 2013[277]	Wrong study type
Gargiulo, 2011[278]	Wrong population
Garrido, 2005[279]	Wrong study type
Gaudio, 2005[280]	Wrong population
Gayed, 2010[281]	Wrong population
Gebker, 2012[282]	Wrong population
Gebker, 2008[283]	Wrong population
Geleijnse, 2000[284]	Wrong study type
Genders, 2013[285]	Wrong population
Gentile, 2001[286]	Wrong population

Reference	Reason for exclusion
George, 2009[287]	Wrong population
George, 2012[288]	Wrong population
George, 2014[289]	Wrong population
Gerbaud, 2012[290]	Wrong population
Gerber, 2005[291]	Wrong population
Ghoshhajra, 2012[292]	Wrong population
Ghostine, 2006[293]	Wrong population
Girzadas, 2009[297]	Wrong diagnostic intervention
Goldenberg, 2012[298]	Wrong diagnostic intervention
Gonzalez, 2013[301]	Not English language
Gonzalez, 2005[302]	Wrong population
Goodacre, 2005[303]	Wrong intervention
Gouya, 2009[305]	Wrong population
Graf, 2007[306]	Wrong population
Greenslade, 2015[307]	Mixed population (MI and ACS)
Greenwood, 2014[308]	Wrong population
Greif, 2013[309]	Wrong population
Greulich, 2012[310]	Wrong population
Greupner, 2012[311]	Wrong population
Groothuis, 2012[312]	Wrong population
Guo, 2011[313]	Wrong population (CAD)
Gupta, 2013[314]	Wrong population
Haberl, 2005[316]	Wrong population
Han, 2013[319]	Developing country
Hansen, 2010[320]	Wrong study type
Hartlage, 2012[321]	Wrong study type
Heitner, 2014[323]	Wrong population
Hermann, 2009[324]	No discernible data
Heuschmid, 2007[325]	Wrong population
Heydari, 2011[326]	Wrong diagnostic intervention
Hoffmann, 2006[331]	Wrong diagnostic intervention
Holubkov, 2002[336]	Wrong population
Hou, 2014[337]	Wrong population
Hsu, 2008[338]	Developing country
Hulten, 2013[339]	Wrong population
Husmann, 2008[340]	Wrong population
Husmann, 2009[341]	Wrong population
Husmann, 2008[342]	Wrong population
Husmann, 2008[343]	Wrong population (CAD)
Hwang, 2014[344]	Wrong population
Imran, 2006[347]	Wrong population
investigators, 2015[349]	Wrong population
Isoda, 1999[351]	Wrong population

Reference	Reason for exclusion
Iyengar, 2016[352]	Wrong population
Jahnke, 2007[353]	Wrong study type
Jahnke, 2004[354]	Wrong population
Jang, 2011[355]	Wrong population
Januzzi, 2010[356]	Wrong intervention
Jeetley, 2006[357]	Wrong study type
Jimenez-Hoyuela Garcia, 2006[358]	Wrong reference standard
Jug, 2012[361]	Wrong study type
Kadokami, 2012[362]	Wrong population
Kajander, 2010[363]	Wrong population
Kaminek, 2001[364]	Wrong population
Kamiya, 2014[365]	Wrong population
Kang, 2005[366]	Wrong intervention
Kang, 1999[367]	Wrong population
Karacavus, 2015[368]	Unclear follow-up
Kaul, 2004[369]	Wrong study type
Kawai, 2004[370]	Wrong population
Kawecki, 2015[371]	Wrong population
Keijer, 2000[372]	Wrong population
Kim, 2008[377]	Wrong population
Kim, 2014[378]	Wrong population
Kim, 2001[379]	Wrong population
Kim, 1999[380]	Wrong population
Kim, 2006[381]	Wrong population
Kirisli, 2014[382]	Wrong population
Kitagawa, 2008[383]	Wrong population
Klem, 2008[384]	Wrong population
Klumpp, 2015[385]	Wrong intervention
Klumpp, 2010[386]	Wrong population
Ko, 2012[387]	Wrong population
Ko, 2012[388]	Wrong population
Ko, 2014[389]	Wrong population
Ko, 2014[390]	Wrong population
Koide, 2001[391]	Wrong population
Kontos, 2008[392]	Wrong study type
Kontos, 1999[393]	Wrong population
Kontos, 2002[394]	Wrong population
Koo, 2011[395]	Wrong population
Krittayaphong, 2003[396]	Wrong population
Kunimasa, 2009[398]	Wrong population
Langdorf, 2010[401]	No data of relevance
Langer, 2009[402]	Wrong population
Laudon, 2010[403]	Wrong diagnostic intervention

Reference	Reason for exclusion
Laudon, 1999[404]	Wrong diagnostic intervention
Layritz, 2014[405]	Wrong population
Lazoura, 2011[406]	Wrong population
Leber, 2007[407]	Wrong population
Leber, 2004[408]	Wrong population
Leber, 2003[409]	Wrong diagnostic intervention
Lee, 2012[410]	Wrong study type
Lee, 2001[411]	Wrong population
Lehmkuhl, 2011[412]	Wrong population
Lei, 2013[413]	Wrong population
Lemos, 2014[414]	Wrong population
Leschka, 2005[415]	Wrong population
Leschka, 2009[416]	Wrong population
Leurent, 2011[417]	Wrong population
Li, 2011[418]	Wrong population
Li, 2012[419]	Wrong population
Li, 2014[420]	Wrong population
Lin, 2010[423]	Wrong study type
Lin, 2008[424]	Wrong study type
Litt, 2012[430]	Wrong study type
Litt, 2015[431]	Wrong population
Lo, 2011[432]	Wrong study type
Lockie, 2011[433]	Wrong population
Loimaala, 1999[434]	Wrong population
Loimaala, 1999[435]	Wrong study type
Lowenstein, 2003[437]	Wrong study type
Lu, 2011[438]	Wrong population
Machida, 2015[439]	Wrong study type
Macor, 2003[440]	Wrong population
Maffei, 2012[441]	Wrong population
Maffei, 2011[442]	Wrong population
Maffei, 2012[443]	Wrong population
Maffei, 2011[444]	Wrong population
Maffei, 2010[445]	Wrong population
Maffei, 2010[446]	Wrong population
Maffei, 2010[447]	Wrong population
Magalhaes, 2011[448]	Wrong population
Magalhaes, 2015[449]	Wrong population
Mahajan, 2010[450]	Wrong population
Maintz, 2007[451]	Wrong diagnostic intervention
Majstorov, 2005[452]	Wrong population
Makaryus, 2014[453]	Wrong population
Malago, 2010[454]	Wrong population

Reference	Reason for exclusion
Malago, 2012[455]	Wrong population
Malago, 2013[456]	Wrong population
Maltagliati, 2000[457]	Wrong population
Manini, 2009[458]	Wrong diagnostic intervention
Manka, 2012[459]	Wrong diagnostic intervention
Manka, 2015[460]	Wrong population
Mannan, 2014[461]	Wrong population
Maret, 2008[462]	Wrong diagnostic intervention
Markman Filho, 2006[463]	Wrong diagnostic intervention; prognostic only
Martuscelli, 2004[464]	Wrong diagnostic intervention
Mas-Stachurska, 2015[465]	Wrong population
Mastrobuoni, 2009[466]	Wrong population
Matsuda, 2015[467]	Wrong diagnostic intervention
Matsumoto, 2006[468]	Wrong population
Matsunari, 2005[469]	Wrong population
Mc Ardle, 2012[470]	Wrong diagnostic intervention
Meijboom, 2007[472]	Wrong population
Meijs, 2010[473]	Wrong study type
Meinel, 2014[474]	Wrong diagnostic intervention
Meintjes, 2016[475]	Wrong study intervention
Mendoza-Rodriguez, 2009[477]	Wrong population
Meng, 2009[478]	Wrong diagnostic intervention
Menon, 2009[479]	Wrong population
Merkle, 2010[480]	Wrong population
Meurin, 2015[481]	Wrong population
Meyer, 2012[482]	Wrong population
Meyer, 2013[483]	Wrong diagnostic intervention
Midiri, 2015[484]	Wrong study type
Mieres, 2007[485]	Wrong population
Miller, 2008[488]	Wrong population
Miller, 2009[489]	Wrong study type
Miller, 2010[490]	Wrong population
Miller, 2002[491]	Wrong population
Miszalski-Jamka, 2006[492]	Wrong population
Mohammadzadeh, 2012[493]	Wrong population
Moir, 2004[494]	Wrong population
Mollet, 2011[495]	Wrong population
Mollet, 2005[496]	Wrong population
Moon, 2011[497]	Wrong population
Moon, 2013[498]	Wrong population
Moon, 2005[499]	Wrong population
Moralidis, 2007[500]	Wrong diagnostic intervention
Moralidis, 2010[501]	Wrong study type

Reference	Reason for exclusion
Mordi, 2014[502]	Wrong population
Mordini, 2014[503]	Wrong population
Morise, 2000[504]	Wrong population
Morton, 2012[505]	Wrong population
Moscariello, 2012[506]	Wrong population
Motevalli, 2014[507]	Developing country
Motoyama, 2013[508]	Wrong population
Motoyasu, 2003[509]	Wrong population
Muhlenbruch, 2007[512]	Wrong population
Muscholl, 2002[513]	Wrong reference standard
Musto, 2007[514]	Wrong population
Nabi, 2010[515]	Wrong diagnostic intervention
Nagao, 2009[516]	Wrong population
Nagao, 2009[517]	Wrong population
Nagori, 2014[518]	Developing country
Nair, 2012[519]	Wrong population
Nakazato, 2012[520]	Wrong population
Nakazato, 2015[521]	Wrong population
Nakazato, 2010[522]	Wrong population
Nasis, 2013[523]	Wrong population
Nasis, 2010[524]	Wrong population
National Horizon Scanning Centre (NHSC), 2007[526]	Wrong study type
National Horizon Scanning Centre (NHSC), 2007[525]	Wrong study type
Nedeljkovic, 2006[529]	Wrong population
Neefjes, 2013[530]	Wrong population
Neglia, 2015[531]	Wrong population
NHSC, 2006[533]	Wrong study type
Nicol, 2008[534]	Wrong population
Nicol, 2008[535]	Wrong population
Nieman, 2009[536]	Wrong population
Nieman, 2002[537]	Wrong population
Nikolaou, 2006[538]	Wrong population
Ogino, 2015[540]	Wrong population
Olivetti, 2006[541]	Wrong diagnostic intervention
Olszowska, 2003[543]	Wrong population
Oncel, 2007[544]	Wrong population
Oncel, 2007[545]	Wrong population
Ovrehus, 2010[546]	Wrong population
Palagi, 2003[547]	Wrong study type
Palumbo, 2009[548]	Wrong population
Parato, 2010[549]	Wrong population
Park, 2007[550]	Wrong population

Reference	Reason for exclusion
Parker, 2015[551]	Wrong population
Parker, 2012[552]	Wrong population
Patsilinakos, 1999[553]	Wrong population
Pavlovic, 2010[554]	Wrong population
Pelliccia, 2013[555]	Wrong population
Pereira, 2013[556]	Wrong population
Pilz, 2010[557]	Wrong population
Plein, 2004[558]	Wrong population
Ponte, 2014[559]	Wrong population
Pontone, 2009[560]	Wrong population
Pontone, 2007[561]	Wrong population
Previtali, 1999[564]	Wrong population
Pursnani, 2015[565]	Wrong population
Rastgou, 2012[568]	Wrong population and developing country
Reinsch, 2012[573]	Wrong population
Rieber, 2006[577]	Wrong population
Rieber, 2004[578]	Wrong population
Rispler, 2011[579]	Wrong population
Rispler, 2007[580]	Wrong population
Rollan, 2002[581]	Wrong population
Ronderos, 2002[582]	Wrong diagnostic intervention
Rubinshtein, 2007[585]	Wrong population
Rubinshtein, 2009[586]	Wrong population
Ruzsics, 2008[587]	Wrong population
Ruzsics, 2009[588]	Wrong population
Saad, 2011[589]	Wrong population
Saba, 2015[590]	Wrong population
Sabharwal, 2007[591]	Wrong population
Sajjadieh, 2013[593]	Wrong population
Sakakura, 2006[594]	Wrong population
Sakuma, 2005[595]	Wrong population
Sampson, 2007[596]	Wrong population
Santana, 2009[599]	Wrong population
Santana, 2000[600]	Wrong population
Santos, 2013[601]	Wrong population
Sara, 2014[602]	Wrong population
Sardanelli, 2000[603]	Wrong population
Sato, 2005[604]	Wrong reference standard
Sato, 2003[605]	Wrong population
Schaap, 2013[606]	Wrong population
Scheffel, 2008[607]	Wrong population
Scheffel, 2010[608]	Wrong population
Schepis, 2007[609]	Wrong population

Reference	Reason for exclusion
Schertler, 2009[610]	Wrong diagnostic intervention
Schlosser, 2004[611]	Wrong diagnostic intervention
Schroeder, 2005[612]	Wrong population
Schuijf, 2005[613]	Wrong diagnostic test
Schuijf, 2006[614]	Wrong population
Schwartz, 2003[615]	Wrong population
Schwitter, 2001[616]	Wrong population
Schwitter, 2008[617]	Wrong population
Schwitter, 2012[618]	Wrong population
Schwitter, 2013[619]	Wrong population
Scotland, 2005[532]	Wrong study type
Sehovic, 2013[621]	Wrong population
Selcoki, 2010[622]	Wrong population
Senior, 2004[623]	Wrong population
Shabestari, 2007[624]	Wrong population
Shaheen, 1998[628]	Wrong population
Shariat, 2014[629]	Wrong population
Sharma, 2012[630]	Wrong population
Sharma, 2015[631]	Wrong population
Shavelle, 2000[632]	Wrong population
Sheikh, 2009[633]	Wrong population
Sheth, 2008[634]	Wrong population
Shi, 2004[635]	Wrong population
Shin, 2009[636]	Wrong population
Shivalkar, 2007[637]	Wrong population
Shouker, 2012[638]	Wrong population
Shuman, 2008[639]	Wrong population
Shuman, 2009[640]	Wrong diagnostic intervention
Shuman, 2010[641]	Wrong population
Siriapisith, 2008[642]	Wrong diagnostic test comparison
Sirol, 2009[643]	Wrong population
Slim, 2012[644]	Wrong population
Smart, 2000[645]	Wrong population
Smart, 2000[646]	Wrong population
So, 2005[647]	Wrong population
Sommer, 2005[648]	Wrong population
Soon, 2007[649]	Wrong diagnostic intervention
Staniak, 2013[650]	Wrong diagnostic intervention
Stolzmann, 2011[651]	Wrong population
Stolzmann, 2011[652]	Wrong population
Sun, 2013[653]	Wrong population
Sun, 2015[654]	Wrong population
Sun, 2010[655]	Wrong population

Reference	Reason for exclusion
Suratkal, 2003[656]	Wrong population
Takahashi, 2004[657]	Wrong diagnostic intervention
Takakuwa, 2008[658]	Wrong study type
Takakuwa, 2011[659]	No diagnostic data
Takase, 2004[660]	Wrong population
Takeuchi, 1999[661]	Wrong population
Takx, 2015[662]	Wrong population
Tan, 2007[663]	Insufficient data
Tanaka, 2008[664]	Wrong assessment (plaque rupture)
Tanaka, 2008[665]	Wrong diagnostic intervention
Tanaka, 2007[666]	Wrong diagnostic intervention
Tanami, 2014[667]	Wrong population
Tandogan, 2001[668]	Wrong population
Tandogan, 2001[669]	Wrong population
Tardif, 2002[670]	Wrong population
Tas, 2013[671]	Wrong population
Ten Kate, 2013[672]	Wrong population
The Swedish Council on Health Technology Assessment, 2011[674]	Wrong study type
Thilo, 2011[676]	Wrong population
Thompson, 2015[678]	Wrong diagnostic intervention
Tomizawa, 2014[680]	Wrong diagnostic intervention
Treuth, 2001[682]	Wrong population
Truong, 2013[684]	No data of interest
Truong, 2015[685]	Wrong study type
Trzaska, 2013[686]	Wrong study type
Tsai, 2007[687]	Wrong diagnostic intervention
Tsai, 2014[688]	Wrong setting
Tsai, 2002[689]	Wrong population
Tsang, 2012[690]	Wrong population
Tsougos, 2008[691]	Wrong population
Tsougos, 2012[692]	Wrong population
Turkvatan, 2008[694]	Wrong diagnostic intervention
Turnipseed, 2009[695]	Wrong study type
Uebleis, 2012[696]	Wrong population
Ueno, 2003[698]	Wrong population
Ulimoen, 2008[699]	Wrong population
Underwood, 1999[700]	Wrong study type
Underwood, 2004[701]	Wrong study type
Utsunomiya, 2015[702]	Wrong population
Valenta, 2014[704]	Wrong population
van der Wall, 2015[705]	Wrong study type
Van Geuns, 1999[706]	Wrong population

Reference	Reason for exclusion
Van Mieghem, 2007[707]	Wrong population
van Velzen, 2011[709]	Wrong population
van Werkhoven, 2010[710]	Wrong population
Vashist, 2007[711]	Wrong population
Vavere, 2011[712]	Wrong diagnostic intervention
Verna, 2000[713]	Wrong population
Vigna, 2001[714]	Wrong population
Vijayakrishnan, 2012[715]	Unclear population
von Ziegler, 2012[718]	Wrong population
Wagdi, 2010[720]	Wrong population
Walker, 2013[721]	Wrong study type
Wang, 2011[722]	Wrong population
Wang, 2011[723]	Wrong population
Watkins, 2007[724]	Wrong diagnostic intervention
Wehrschuetz, 2010[726]	Wrong population
Weinsaft, 2007[727]	Wrong population
Weustink, 2007[729]	Wrong population
Weustink, 2010[730]	Wrong study type
Weustink, 2012[731]	Wrong population
White, 2005[732]	Wrong diagnostic intervention
Wierzbowska-Drabik, 2014[734]	Wrong population
Wilson, 2011[735]	Wrong study type
Winchester, 2015[736]	Unclear analysis
Winchester, 2013[737]	Wrong study type
Winchester, 2012[738]	Wrong population
Xu, 2010[739]	Wrong population
Yamada, 2004[740]	Wrong population
Yang, 2015[741]	Wrong population
Yerramasu, 2014[742]	Wrong population
Zaag-Loonen, 2006[743]	Wrong population
Zancaner, 2012[744]	Wrong study type
Zeb, 2014[745]	Wrong study type
Zeb, 2012[746]	Wrong study type
Zhang, 2010[748]	Wrong population
Zhang, 2004[749]	Developing country
Zhao, 2011[750]	Wrong study type
Zorga, 2012[751]	Wrong study type
Zwank, 2015[752]	Wrong study type

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Reference	Reason for exclusion
A, 2013[18]	Wrong diagnostic intervention
Abbasi, 2014[1]	Wrong population
Abbott, 2000[2]	Wrong study type
Abbott, 2003[3]	Wrong study type
Abd, 2015[4]	Wrong study type
Abdelmoneim, 2009[7]	Wrong study type
Abdelmoneim, 2011[8]	Wrong population
Abdelmoneim, 2010[9]	Wrong population
Abdelmoneim, 2010[10]	Wrong population
Abdelmoneim, 2009[11]	Wrong population
Abdelmoneim, 2009[12]	Wrong population
Abdelmoneim, 2015[13]	Wrong diagnostic comparison
Abdel-Rahman, 2015[5]	Wrong population
Abdel-Salam, 2015[6]	Wrong diagnostic intervention
Abdool, 2014[14]	Wrong population
Abdulla, 2007[15]	Wrong population
Abdulla, 2012[16]	Wrong intervention
Abraham, 2010[17]	Wrong study type
Abramson, 2000[19]	Wrong population
Achenbach, 2010[20]	Wrong study type
Achenbach, 2001[21]	Wrong population
Achenbach, 1998[22]	Wrong diagnostic intervention
Achenbach, 2008[23]	Wrong population
Adams, 2007[24]	Wrong population
Adil, 2011[25]	Wrong population
Agarwal, 2012[26]	Wrong population
Aggarwal, 2015[27]	Wrong population
Aggeli, 2011[28]	Wrong population
Aggeli, 2007[29]	Wrong population
Ahmad, 2001[30]	Wrong population
Ahmadvazir, 2014[31]	Wrong population
Ahn, 2011[32]	Wrong diagnostic intervention
Ahn, 2013[33]	Wrong population
Aidi, 2014[34]	Wrong population
Akbar, 2010[35]	No data of interest
Akram, 2008[36]	Wrong diagnostic intervention
Al Moudi, 2011[42]	Wrong population
Al Moudi, 2014[43]	Wrong diagnostic comparison
Aldweib, 2013[47]	Wrong population
Alessandri, 2009[48]	Wrong population
Alexanderson, 2004[49]	Wrong population

Reference	Reason for exclusion
Alexanderson, 2006[50]	Wrong diagnostic intervention
Alexanderson Rosas, 2010[51]	Wrong intervention
Alexopoulos, 2005[52]	Wrong diagnostic intervention
Ali, 2007[53]	Wrong population
AlJaroudi, 2013[54]	Wrong population
Alkadhi, 2008[55]	Wrong population
Alkadhi, 2010[56]	Wrong diagnostic intervention
Al-Kaylani, 2002[37]	Wrong diagnostic evaluation
Allajbeu, 2014[57]	Wrong population
Al-Mallah, 2011[38]	Wrong study type
Al-Mallah, 2014[39]	Wrong population
Almeida, 2002[58]	Wrong population
Almoudi, 2012[59]	Wrong diagnostic intervention
Alqaisi, 2008[60]	Wrong population
al-Saadi, 2002[40]	Wrong population
Al-Saadi, 2000[41]	Wrong population
Altinmakas, 2000[61]	Wrong population
Altiok, 2013[62]	Wrong diagnostic comparison
Altiok, 2012[63]	Wrong diagnostic comparison
Altiok, 2014[64]	Wrong diagnostic comparison
Altun, 2005[65]	Wrong population
Altunkeser, 2002[66]	Wrong population
Alunni, 2015[67]	Wrong diagnostic intervention
Alvarez Tamargo, 2008[68]	Wrong diagnostic intervention
Amanuma, 2015[69]	Wrong population
American College of, 2006[70]	Wrong study type
Amit, 2014[71]	Wrong study type
Anagnostopoulos, 2013[73]	Wrong study type
Anand, 2003[74]	Wrong study type
Anantharam, 2009[75]	No available data
Anders, 2013[76]	Wrong population
Andrade, 2009[78]	Wrong population
Andrassy, 2011[79]	Wrong population
Andreini, 2016[80]	Wrong study type (report)
Andreini, 2010[81]	Wrong population
Annuar, 2008[82]	Wrong population
Anonymous, 1997[345]	Wrong population
Anonymous, 2009[235]	Wrong study type
Anonymous, 2015[234]	Wrong study type
Antony, 2011[83]	Wrong study type
Anwar, 2013[84]	Wrong population
Aoyagi, 1998[85]	Wrong population
Apostolopoulos, 2012[86]	Wrong population

Reference	Reason for exclusion
Arbab-Zadeh, 2015[88]	Wrong population
Arbab-Zadeh, 2011[89]	Wrong intervention
Argulian, 2014[90]	Wrong population
Arnold, 2012[91]	Wrong study type
Arnold, 2010[92]	Wrong population
Arsanjani, 2013[93]	Wrong study type
Arsanjani, 2013[94]	Wrong population
Arsanjani, 2013[95]	Wrong study type
Arumugam, 2013[96]	Wrong study type
Asferg, 2012[97]	Wrong population
Asher, 2015[98]	Wrong intervention
Atar, 2000[99]	Wrong intervention
Athappan, 2010[100]	Different risk categories to protocol and date cut-off May 2008
Babar Imran, 2003[101]	Wrong population
Balaravi, 2006[103]	Wrong analysis and wrong population (prognostic)
Bamberg, 2008[105]	Wrong study type (substudy)
Bamberg, 2014[106]	Wrong population
Bamberg, 2009[107]	Wrong study type (ROMICAT substudy)
Banerjee, 2012[108]	Wrong study type
Bangalore, 2007[109]	Wrong population
Bangalore, 2005[110]	Wrong population
Barbirato, 2009[111]	Not English language
Barletta, 1999[112]	Wrong population
Barmeyer, 2008[113]	Wrong population
Barraclough, 2015[114]	Wrong study type
Baszko, 2001[115]	Wrong population
Bateman, 2009[116]	Wrong population
Bateman, 2006[117]	Wrong population
Bauer, 2010[118]	Wrong population
Bauernfeind, 2011[119]	Not topic of interest – prognostic
Beck, 2002[120]	Wrong population
Becker, 2007[121]	Wrong population
Becker, 2001[122]	Wrong population
Becker, 2012[123]	Wrong study type
Bekler, 2014[126]	No available data
Belardinelli, 2014[127]	Wrong diagnostic comparison
Ben Bouallegue, 2015[128]	Wrong population
Benchimol, 2000[129]	Wrong population
Benedek, 2013[130]	Wrong population and wrong study type
Benedek, 2014[131]	Wrong study type
Benkiran, 2015[132]	Wrong population
Berdahl, 2013[134]	Wrong study type
Bergeron, 2004[135]	Wrong population

Reference	Reason for exclusion
Beslic, 2011[136]	Wrong population
Bettencourt, 2013[137]	Wrong population
Bettencourt, 2013[138]	Wrong population
Bettencourt, 2013[139]	Wrong population and setting
Bettencourt, 2013[140]	Wrong population
Better, 2012[141]	Developing countries
Beule, 2010[142]	Wrong study type
Bholasingh, 2003[144]	Wrong study type
Biagini, 2006[146]	Wrong population
Biglands, 2015[149]	Wrong study type
Bischoff, 2012[150]	Wrong population
Blankstein, 2012[151]	Wrong study type
Blinder, 2005[152]	No DTA data available
Blomstrand, 2004[153]	Wrong population
BlueCross BlueShield Association, 2011[154]	Wrong study type
Bogaert, 2015[156]	Wrong study type
Boglioli, 2001[157]	Wrong study type
Boiten, 2012[158]	Wrong population
Bom, 2015[159]	Wrong population
Boussel, 2008[161]	Wrong population
Bouzas-Mosquera, 2015[162]	Wrong population
Branch, 2012[164]	Wrong study type
Branch, 2013[165]	Wrong diagnostic intervention
Branch, 2013[166]	Wrong population
Brodoefel, 2008[167]	Wrong population
Brodoefel, 2008[168]	Wrong population
Brodoefel, 2008[169]	Wrong population
Brodov, 2015[170]	Wrong population
Brogsitter, 2005[171]	Wrong study type
Brown, 2008[172]	MACE events only
Bucerius, 2007[177]	Wrong population
Buckert, 2013[178]	Wrong population
Budge, 2011[179]	Wrong study type
Budoff, 2003[180]	Wrong population
Budoff, 2013[181]	Wrong population
Budoff, 2007[182]	Wrong population
Burris, 2015[183]	Wrong diagnostic intervention
Busch, 2011[184]	Wrong population
Cabeda, 2015[185]	Wrong population
Cademartiri, 2008[186]	Wrong population
Cademartiri, 2007[187]	Wrong population
Candell-Riera, 2007[189]	Wrong population

Reference	Reason for exclusion
Candell-Riera, 2004[190]	Wrong population
Carlsson, 2013[191]	Wrong population
Carrinho, 2004[192]	Wrong population
Caymaz, 2000[194]	Wrong population
Celik, 2011[195]	Wrong study type
Chammas, 2002[197]	Wrong population
Chan, 2003[198]	Wrong population
Chandra, 2001[199]	Wrong study type
Chandraratna, 2012[200]	Wrong population
Chandraratna, 2012[201]	Wrong diagnostic interventions
Chang, 2008[202]	Wrong study type
Chang, 2008[203]	Wrong population
Chao, 2010[204]	Wrong population
Chaosuwannakit, 2012[205]	Wrong population
Cheezum, 2014[206]	Wrong study type
Chen, 2013[207]	Wrong population
Chen, 1999[208]	Wrong population
Chen, 2014[209]	Wrong population
Chen, 2001[210]	Wrong population
Chen, 2012[211]	Wrong population
Chen, 2011[212]	Wrong diagnostic intervention
Chen, 2010[213]	Wrong diagnostic intervention
Cheng, 2007[215]	Wrong population and study type; no usable data
Cheng, 2013[217]	Wrong study type; no usable data
Cheng, 2013[218]	Developing country
Cheng, 2000[219]	Wrong population
Cheng, 2010[220]	Wrong population
Chiou, 2004[221]	Wrong population
Chiu, 2003[222]	Wrong diagnostic intervention
Choo, 2013[223]	Wrong population
Chow, 2007[224]	Wrong population
Conti, 2010[230]	Wrong study type
Conti, 2010[231]	Wrong study type
Conti, 2008[233]	Wrong population
Cury, 2013[238]	Wrong diagnostic intervention
Dall Armellina, 2011[239]	Wrong study type
Dedic, 2013[241]	Insufficient method details (systematic review)
Dedic, 2014[242]	Wrong population
Dedic, 2013[244]	Wrong diagnostic intervention
Department of Science and Technology - Brazilian Health Technology Assessment General Coordination (DECIT-CGATS), 2008[245]	Wrong study type
Diercks, 2013[247]	Wrong diagnostic intervention

Reference	Reason for exclusion
Dodd, 2008[249]	Wrong study type Wrong study type
Dorgelo, 2005[250]	Wrong diagnostic intervention
Durand, 2009[252]	Wrong study type
Duvall, 2014[253]	Wrong intervention
Edmond, 2002[254]	Wrong study type
Einstein, 2015[256]	Wrong population
Estrada, 2006[257]	Wrong diagnostic intervention
Fanaroff, 2015[258]	Not diagnostic intervention
Ferencik, 2012[259]	Secondary analysis - ROMICAT
Ferencik, 2012[260]	Wrong study type
Fernandez-Friera, 2011[261]	Wrong diagnostic intervention
Fesmire, 2012[262]	Wrong diagnostic intervention
Fesmire, 2002[263]	Wrong intervention
Fesmire, 2001[264]	Wrong reference standard
Gaemperli, 2009[268]	Wrong population
Gaemperli, 2007[269]	Wrong population
Gaibazzi, 2009[271]	Wrong population
Gaibazzi, 2010[272]	Wrong population
Gaibazzi, 2010[273]	Wrong population
Galassi, 2000[274]	Wrong population
Gao, 2011[276]	Wrong population
Gargiulo, 2013[277]	Wrong study type
Gargiulo, 2011[278]	Wrong population
Garrido, 2005[279]	Wrong study type
Gaudio, 2005[280]	Wrong population
Gayed, 2010[281]	Wrong population
Gebker, 2012[282]	Wrong population
Gebker, 2008[283]	Wrong population
Geleijnse, 2000[284]	Wrong study type
Genders, 2013[285]	Wrong population
Gentile, 2001[286]	Wrong population
George, 2009[287]	Wrong population
George, 2012[288]	Wrong population
George, 2014[289]	Wrong population
Gerbaud, 2012[290]	Wrong population
Gerber, 2005[291]	Wrong population
Ghoshhajra, 2012[292]	Wrong population
Ghostine, 2006[293]	Wrong population
Girzadas, 2009[297]	Wrong diagnostic intervention
Goldenberg, 2012[298]	Wrong diagnostic intervention
Gonzalez, 2013[301]	Not English language
Gonzalez, 2005[302]	Wrong population
Goodacre, 2005[303]	Wrong intervention

Reference	Reason for exclusion
Gouya, 2009[305]	Wrong population
Graf, 2007[306]	Wrong population
Greenslade, 2015[307]	Mixed population (MI and ACS)
Greenwood, 2014[308]	Wrong population
Greif, 2013[309]	Wrong population
Greulich, 2012[310]	Wrong population
Greupner, 2012[311]	Wrong population
Groothuis, 2012[312]	Wrong population
Guo, 2011[313]	Wrong population (CAD)
Gupta, 2013[314]	Wrong population
Haberl, 2005[316]	Wrong population
Han, 2013[319]	Developing country
Hansen, 2010[320]	Wrong study type
Hartlage, 2012[321]	Wrong study type
Heitner, 2014[323]	Wrong population
Hermann, 2009[324]	No discernible data
Heuschmid, 2007[325]	Wrong population
Heydari, 2011[326]	Wrong diagnostic intervention
Hoffmann, 2006[331]	Wrong diagnostic intervention
Holubkov, 2002[336]	Wrong population
Hou, 2014[337]	Wrong population
Hsu, 2008[338]	Developing country
Hulten, 2013[339]	Wrong population
Husmann, 2008[340]	Wrong population
Husmann, 2009[341]	Wrong population
Husmann, 2008[342]	Wrong population
Husmann, 2008[343]	Wrong population (CAD)
Hwang, 2014[344]	Wrong population
Imran, 2006[347]	Wrong population
investigators, 2015[349]	Wrong population
Isoda, 1999[351]	Wrong population
Iyengar, 2016[352]	Wrong population
Jahnke, 2007[353]	Wrong study type
Jahnke, 2004[354]	Wrong population
Jang, 2011[355]	Wrong population
Januzzi, 2010[356]	Wrong intervention
Jeetley, 2006[357]	Wrong study type
Jimenez-Hoyuela Garcia, 2006[358]	Wrong reference standard
Jug, 2012[361]	Wrong study type
Kadokami, 2012[362]	Wrong population
Kajander, 2010[363]	Wrong population
Kaminek, 2001[364]	Wrong population
Kamiya, 2014[365]	Wrong population

Reference	Reason for exclusion
Kang, 2005[366]	Wrong intervention
Kang, 1999[367]	Wrong population
Karacavus, 2015[368]	Unclear follow-up
Kaul, 2004[369]	Wrong study type
Kawai, 2004[370]	Wrong population
Kawecki, 2015[371]	Wrong population
Keijer, 2000[372]	Wrong population
Kim, 2008[377]	Wrong population
Kim, 2014[378]	Wrong population
Kim, 2001[379]	Wrong population
Kim, 1999[380]	Wrong population
Kim, 2006[381]	Wrong population
Kirisli, 2014[382]	Wrong population
Kitagawa, 2008[383]	Wrong population
Klem, 2008[384]	Wrong population
Klumpp, 2015[385]	Wrong intervention
Klumpp, 2010[386]	Wrong population
Ko, 2012[387]	Wrong population
Ko, 2012[388]	Wrong population
Ko, 2014[389]	Wrong population
Ko, 2014[390]	Wrong population
Koide, 2001[391]	Wrong population
Kontos, 2008[392]	Wrong study type
Kontos, 1999[393]	Wrong population
Kontos, 2002[394]	Wrong population
Koo, 2011[395]	Wrong population
Krittayaphong, 2003[396]	Wrong population
Kunimasa, 2009[398]	Wrong population
Langdorf, 2010[401]	No data of relevance
Langer, 2009[402]	Wrong population
Laudon, 2010[403]	Wrong diagnostic intervention
Laudon, 1999[404]	Wrong diagnostic intervention
Layritz, 2014[405]	Wrong population
Lazoura, 2011[406]	Wrong population
Leber, 2007[407]	Wrong population
Leber, 2004[408]	Wrong population
Leber, 2003[409]	Wrong diagnostic intervention
Lee, 2012[410]	Wrong study type
Lee, 2001[411]	Wrong population
Lehmkuhl, 2011[412]	Wrong population
Lei, 2013[413]	Wrong population
Lemos, 2014[414]	Wrong population
Leschka, 2005[415]	Wrong population

Reference	Reason for exclusion
Leschka, 2009[416]	Wrong population
Leurent, 2011[417]	Wrong population
Li, 2011[418]	Wrong population
Li, 2012[419]	Wrong population
Li, 2014[420]	Wrong population
Lin, 2010[423]	Wrong study type
Lin, 2008[424]	Wrong study type
Litt, 2012[430]	Wrong study type
Litt, 2015[431]	Wrong population
Lo, 2011[432]	Wrong study type
Lockie, 2011[433]	Wrong population
Loimaala, 1999[434]	Wrong population
Loimaala, 1999[435]	Wrong study type
Lowenstein, 2003[437]	Wrong study type
Lu, 2011[438]	Wrong population
Machida, 2015[439]	Wrong study type
Macor, 2003[440]	Wrong population
Maffei, 2012[441]	Wrong population
Maffei, 2011[442]	Wrong population
Maffei, 2012[443]	Wrong population
Maffei, 2011[444]	Wrong population
Maffei, 2010[445]	Wrong population
Maffei, 2010[446]	Wrong population
Maffei, 2010[447]	Wrong population
Magalhaes, 2011[448]	Wrong population
Magalhaes, 2015[449]	Wrong population
Mahajan, 2010[450]	Wrong population
Maintz, 2007[451]	Wrong diagnostic intervention
Majstorov, 2005[452]	Wrong population
Makaryus, 2014[453]	Wrong population
Malago, 2010[454]	Wrong population
Malago, 2012[455]	Wrong population
Malago, 2013[456]	Wrong population
Maltagliati, 2000[457]	Wrong population
Manini, 2009[458]	Wrong diagnostic intervention
Manka, 2012[459]	Wrong diagnostic intervention
Manka, 2015[460]	Wrong population
Mannan, 2014[461]	Wrong population
Maret, 2008[462]	Wrong diagnostic intervention
Markman Filho, 2006[463]	Wrong diagnostic intervention; prognostic only
Martuscelli, 2004[464]	Wrong diagnostic intervention
Mas-Stachurska, 2015[465]	Wrong population
Mastrobuoni, 2009[466]	Wrong population

Reference	Reason for exclusion
Matsuda, 2015[467]	Wrong diagnostic intervention
Matsumoto, 2006[468]	Wrong population
Matsunari, 2005[469]	Wrong population
Mc Ardle, 2012[470]	Wrong diagnostic intervention
Meijboom, 2007[472]	Wrong population
Meijs, 2010[473]	Wrong study type
Meinel, 2014[474]	Wrong diagnostic intervention
Meintjes, 2016[475]	Wrong study intervention
Mendoza-Rodriguez, 2009[477]	Wrong population
Meng, 2009[478]	Wrong diagnostic intervention
Menon, 2009[479]	Wrong population
Merkle, 2010[480]	Wrong population
Meurin, 2015[481]	Wrong population
Meyer, 2012[482]	Wrong population
Meyer, 2013[483]	Wrong diagnostic intervention
Midiri, 2015[484]	Wrong study type
Mieres, 2007[485]	Wrong population
Miller, 2008[488]	Wrong population
Miller, 2009[489]	Wrong study type
Miller, 2010[490]	Wrong population
Miller, 2002[491]	Wrong population
Miszalski-Jamka, 2006[492]	Wrong population
Mohammadzadeh, 2012[493]	Wrong population
Moir, 2004[494]	Wrong population
Mollet, 2011[495]	Wrong population
Mollet, 2005[496]	Wrong population
Moon, 2011[497]	Wrong population
Moon, 2013[498]	Wrong population
Moon, 2005[499]	Wrong population
Moralidis, 2007[500]	Wrong diagnostic intervention
Moralidis, 2010[501]	Wrong study type
Mordi, 2014[502]	Wrong population
Mordini, 2014[503]	Wrong population
Morise, 2000[504]	Wrong population
Morton, 2012[505]	Wrong population
Moscariello, 2012[506]	Wrong population
Motevalli, 2014[507]	Developing country
Motoyama, 2013[508]	Wrong population
Motoyasu, 2003[509]	Wrong population
Muhlenbruch, 2007[512]	Wrong population
Muscholl, 2002[513]	Wrong reference standard
Musto, 2007[514]	Wrong population
Nabi, 2010[515]	Wrong diagnostic intervention

Reference	Reason for exclusion
Nagao, 2009[516]	Wrong population
Nagao, 2009[517]	Wrong population
Nagori, 2014[518]	Developing country
Nair, 2012[519]	Wrong population
Nakazato, 2012[520]	Wrong population
Nakazato, 2015[521]	Wrong population
Nakazato, 2010[522]	Wrong population
Nasis, 2013[523]	Wrong population
Nasis, 2010[524]	Wrong population
National Horizon Scanning Centre (NHSC), 2007[526]	Wrong study type
National Horizon Scanning Centre (NHSC), 2007[525]	Wrong study type
Nedeljkovic, 2006[529]	Wrong population
Neefjes, 2013[530]	Wrong population
Neglia, 2015[531]	Wrong population
NHSC, 2006[533]	Wrong study type
Nicol, 2008[534]	Wrong population
Nicol, 2008[535]	Wrong population
Nieman, 2009[536]	Wrong population
Nieman, 2002[537]	Wrong population
Nikolaou, 2006[538]	Wrong population
Ogino, 2015[540]	Wrong population
Olivetti, 2006[541]	Wrong diagnostic intervention
Olszowska, 2003[543]	Wrong population
Oncel, 2007[544]	Wrong population
Oncel, 2007[545]	Wrong population
Ovrehus, 2010[546]	Wrong population
Palagi, 2003[547]	Wrong study type
Palumbo, 2009[548]	Wrong population
Parato, 2010[549]	Wrong population
Park, 2007[550]	Wrong population
Parker, 2015[551]	Wrong population
Parker, 2012[552]	Wrong population
Patsilinakos, 1999[553]	Wrong population
Pavlovic, 2010[554]	Wrong population
Pelliccia, 2013[555]	Wrong population
Pereira, 2013[556]	Wrong population
Pilz, 2010[557]	Wrong population
Plein, 2004[558]	Wrong population
Ponte, 2014[559]	Wrong population
Pontone, 2009[560]	Wrong population
Pontone, 2007[561]	Wrong population
Previtali, 1999[564]	Wrong population

Reference	Reason for exclusion
Pursnani, 2015[565]	Wrong population
Rastgou, 2012[568]	Wrong population and developing country
Reinsch, 2012[573]	Wrong population
Rieber, 2006[577]	Wrong population
Rieber, 2004[578]	Wrong population
Rispler, 2011[579]	Wrong population
Rispler, 2007[580]	Wrong population
Rollan, 2002[581]	Wrong population
Ronderos, 2002[582]	Wrong diagnostic intervention
Rubinshtein, 2007[585]	Wrong population
Rubinshtein, 2009[586]	Wrong population
Ruzsics, 2008[587]	Wrong population
Ruzsics, 2009[588]	Wrong population
Saad, 2011[589]	Wrong population
Saba, 2015[590]	Wrong population
Sabharwal, 2007[591]	Wrong population
Sajjadieh, 2013[593]	Wrong population
Sakakura, 2006[594]	Wrong population
Sakuma, 2005[595]	Wrong population
Sampson, 2007[596]	Wrong population
Santana, 2009[599]	Wrong population
Santana, 2000[600]	Wrong population
Santos, 2013[601]	Wrong population
Sara, 2014[602]	Wrong population
Sardanelli, 2000[603]	Wrong population
Sato, 2005[604]	Wrong reference standard
Sato, 2003[605]	Wrong population
Schaap, 2013[606]	Wrong population
Scheffel, 2008[607]	Wrong population
Scheffel, 2010[608]	Wrong population
Schepis, 2007[609]	Wrong population
Schertler, 2009[610]	Wrong diagnostic intervention
Schlosser, 2004[611]	Wrong diagnostic intervention
Schroeder, 2005[612]	Wrong population
Schuijf, 2005[613]	Wrong diagnostic test
Schuijf, 2006[614]	Wrong population
Schwartz, 2003[615]	Wrong population
Schwitter, 2001[616]	Wrong population
Schwitter, 2008[617]	Wrong population
Schwitter, 2012[618]	Wrong population
Schwitter, 2013[619]	Wrong population
Scotland, 2005[532]	Wrong study type
Sehovic, 2013[621]	Wrong population

Reference	Reason for exclusion
Selcoki, 2010[622]	Wrong population
Senior, 2004[623]	Wrong population
Shabestari, 2007[624]	Wrong population
Shaheen, 1998[628]	Wrong population
Shariat, 2014[629]	Wrong population
Sharma, 2012[630]	Wrong population
Sharma, 2015[631]	Wrong population
Shavelle, 2000[632]	Wrong population
Sheikh, 2009[633]	Wrong population
Sheth, 2008[634]	Wrong population
Shi, 2004[635]	Wrong population
Shin, 2009[636]	Wrong population
Shivalkar, 2007[637]	Wrong population
Shouker, 2012[638]	Wrong population
Shuman, 2008[639]	Wrong population
Shuman, 2009[640]	Wrong diagnostic intervention
Shuman, 2010[641]	Wrong population
Siriapisith, 2008[642]	Wrong diagnostic test comparison
Sirol, 2009[643]	Wrong population
Slim, 2012[644]	Wrong population
Smart, 2000[645]	Wrong population
Smart, 2000[646]	Wrong population
So, 2005[647]	Wrong population
Sommer, 2005[648]	Wrong population
Soon, 2007[649]	Wrong diagnostic intervention
Staniak, 2013[650]	Wrong diagnostic intervention
Stolzmann, 2011[651]	Wrong population
Stolzmann, 2011[652]	Wrong population
Sun, 2013[653]	Wrong population
Sun, 2015[654]	Wrong population
Sun, 2010[655]	Wrong population
Suratkal, 2003[656]	Wrong population
Takahashi, 2004[657]	Wrong diagnostic intervention
Takakuwa, 2008[658]	Wrong study type
Takakuwa, 2011[659]	No diagnostic data
Takase, 2004[660]	Wrong population
Takeuchi, 1999[661]	Wrong population
Takx, 2015[662]	Wrong population
Tan, 2007[663]	Insufficient data
Tanaka, 2008[664]	Wrong assessment (plaque rupture)
Tanaka, 2008[665]	Wrong diagnostic intervention
Tanaka, 2007[666]	Wrong diagnostic intervention
Tanami, 2014[667]	Wrong population

Reference	Reason for exclusion
Tandogan, 2001[668]	Wrong population
Tandogan, 2001[669]	Wrong population
Tardif, 2002[670]	Wrong population
Tas, 2013[671]	Wrong population
Ten Kate, 2013[672]	Wrong population
The Swedish Council on Health Technology Assessment, 2011[674]	Wrong study type
Thilo, 2011[676]	Wrong population
Thompson, 2015[678]	Wrong diagnostic intervention
Tomizawa, 2014[680]	Wrong diagnostic intervention
Treuth, 2001[682]	Wrong population
Truong, 2013[684]	No data of interest
Truong, 2015[685]	Wrong study type
Trzaska, 2013[686]	Wrong study type
Tsai, 2007[687]	Wrong diagnostic intervention
Tsai, 2014[688]	Wrong setting
Tsai, 2002[689]	Wrong population
Tsang, 2012[690]	Wrong population
Tsougos, 2008[691]	Wrong population
Tsougos, 2012[692]	Wrong population
Turkvatan, 2008[694]	Wrong diagnostic intervention
Turnipseed, 2009[695]	Wrong study type
Uebleis, 2012[696]	Wrong population
Ueno, 2003[698]	Wrong population
Ulimoen, 2008[699]	Wrong population
Underwood, 1999[700]	Wrong study type
Underwood, 2004[701]	Wrong study type
Utsunomiya, 2015[702]	Wrong population
Valenta, 2014[704]	Wrong population
van der Wall, 2015[705]	Wrong study type
Van Geuns, 1999[706]	Wrong population
Van Mieghem, 2007[707]	Wrong population
van Velzen, 2011[709]	Wrong population
van Werkhoven, 2010[710]	Wrong population
Vashist, 2007[711]	Wrong population
Vavere, 2011[712]	Wrong diagnostic intervention
Verna, 2000[713]	Wrong population
Vigna, 2001[714]	Wrong population
Vijayakrishnan, 2012[715]	Unclear population
von Ziegler, 2012[718]	Wrong population
Wagdi, 2010[720]	Wrong population
Walker, 2013[721]	Wrong study type
Wang, 2011[722]	Wrong population

Reference	Reason for exclusion
Wang, 2011[723]	Wrong population
Watkins, 2007[724]	Wrong diagnostic intervention
Wehrschuetz, 2010[726]	Wrong population
Weinsaft, 2007[727]	Wrong population
Weustink, 2007[729]	Wrong population
Weustink, 2010[730]	Wrong study type
Weustink, 2012[731]	Wrong population
White, 2005[732]	Wrong diagnostic intervention
Wierzbowska-Drabik, 2014[734]	Wrong population
Wilson, 2011[735]	Wrong study type
Winchester, 2015[736]	Unclear analysis
Winchester, 2013[737]	Wrong study type
Winchester, 2012[738]	Wrong population
Xu, 2010[739]	Wrong population
Yamada, 2004[740]	Wrong population
Yang, 2015[741]	Wrong population
Yerramasu, 2014[742]	Wrong population
Zaag-Loonen, 2006[743]	Wrong population
Zancaner, 2012[744]	Wrong study type
Zeb, 2014[745]	Wrong study type
Zeb, 2012[746]	Wrong study type
Zhang, 2010[748]	Wrong population
Zhang, 2004[749]	Developing country
Zhao, 2011[750]	Wrong study type
Zorga, 2012[751]	Wrong study type
Zwank, 2015[752]	Wrong study type

Appendix L: Excluded health economic studies

L.1 High sensitivity cardiac troponins

Table 17: Studies excluded from the health economic review

Reference	Reason for exclusion
Vaidya, 2014[703]	This study was assessed as not applicable as the population was not stratified into low, medium and high risk groups therefore the results would not aid the guideline committee in deciding how to recommend high-sensitivity troponin for different risk groups.
Thokala, 2012[677]	This study was assessed as not applicable as the population was not stratified into low, medium and high risk groups therefore the results would not aid the guideline committee in deciding how to recommend high-sensitivity troponin for different risk groups.
CADTH, 2012[188]	This study was assessed as not applicable as the population was not stratified into low, medium and high risk groups therefore the results would not aid the guideline committee in deciding how to recommend high-sensitivity troponin for different risk groups.
Westwood, 2015[728]	This study was assessed as not applicable as the population was not stratified into low, medium and high risk groups therefore the results would not aid the guideline committee in deciding how to recommend high-sensitivity troponin for different risk groups.
Goodacre, 2013[304]	This study was assessed as not applicable as the population was not stratified into low, medium and high risk groups therefore the results would not aid the guideline committee in deciding how to recommend high-sensitivity troponin for different risk groups.

L.2 Non-invasive imaging for the identification of people with NSTEMI/unstable angina

None.

L.3 Diagnostic test accuracy of non-invasive imaging for the identification of people with NSTEMI/unstable angina

None.

Appendix M: Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

The sections below detail the costs borne by the NHS for introducing routine non-invasive coronary computerised tomographic angiography (CCTA) scanning at emergency department index visits into the diagnostic pathway of acute coronary syndrome for low risk people presenting with acute chest pain.

Evidence from the diagnostic review showed that CCTA has the highest diagnostic accuracy compared to the other non-invasive tests listed in the guideline protocol (apart from rest SPECT, however there is large uncertainty around the rest SPECT result). The costs in Table 18 show that CCTA also has the lowest unit cost per test, implying that it dominates the other tests in terms of cost-effectiveness (that is, it is more effective and less costly). The guideline committee therefore decided to focus the economic analysis on routine CCTA testing versus standard of care (SOC). Current standard of care after initial triage can include any of the non-invasive tests listed in the guideline protocol.

Table 18: Unit costs of tests

Item	Description	Source	Cost
CCTA	RD28Z, complex computerised tomography scan	NHS Reference Costs 2014-15	£122.11
Rest SPECT	RN20Z, myocardial perfusion scan	NHS Reference Costs 2014-15	£300.00
Stress SPECT	RN21Z, myocardial perfusion scan, stress only	NHS Reference Costs 2014-15	£367.29
ECHO	EY50Z, complex echocardiogram	NHS Reference Costs 2014-15	£271.31
CMR	RA67Z, cardiac magnetic resonance imaging scan, pre- and post-contrast	Enhanced Tariff Option 2015-16	£515.00
Exercise ECG	EY51Z, electrocardiogram monitoring or stress testing	NHS Reference Costs 2014-15	£153.00

The introduction of highly sensitive troponin assays has dramatically changed how people with acute chest pain are managed in UK emergency departments. Test results can be analysed a lot earlier than with the standard troponin assays, as they reach peak diagnostic accuracy in a significantly shorter time frame (4 hours compared to 12 hours). This allows for a more rapid discharge than was previously possible. For this reason, any studies conducted prior to the high-sensitivity troponin era were considered not applicable to current NHS practice. The clinical review found one test-and-treat study on CCTA that was relevant to the population, [243] which had been conducted after the introduction of high-sensitivity troponin assays.

The study was conducted in the Netherlands and compared 30-day outcomes of routine CCTA testing at ED index visits versus standard of care for low risk people presenting to the emergency department with acute chest pain or symptoms suggestive of acute coronary syndrome warranting

further diagnostic investigation. [243] Standard care consisted of some CCTA testing, however this was not routine. People in this group were more likely to receive an exercise ECG test. Some people in the routine CCTA group did not receive a CCTA as for some people the test could not be performed, for example for people with insufficient ability to hold their breath. The results found that CCTA and SOC clinical outcomes were equivalent. The study also gave a detailed breakdown of the resource use over 30 days for each arm of the trial which is given below. It concluded that the average cost per patient was lower in the CCTA group than the SOC group (£284 versus €431).[a]

Resource use breakdown: [243]

*Average cost per patient in the CCTA group = [cost of initial ED evaluation] + [cost CCTA] + 0.13 * [cost XECG] + 0.01 * [cost SPECT] + 0.004 * [cost CMR] + 0.17 * [cost ICA] + 0.09 [cost PCI] + 0 * [cost CABG] + 0.05 [cost repeat ED evaluation] + 0.03 [repeat hospital admission] =* ***£284***

*Average cost per patient in the SOC group = [cost of initial ED evaluation] + 0.58 * [cost XECG] + 0.07 * [cost SPECT] + 0.01 * [cost CMR] + 0.13 * [cost ICA] + 0.05 [cost PCI] + 0.02 * [cost CABG] + 0.08 [cost repeat ED evaluation] + 0.06 [repeat hospital admission] =* ***£431***

Cost minimisation analysis comparing CCTA to SOC

As results from the clinical review and the Netherlands study both reported that clinical outcomes are equivalent between CCTA and SOC, routine CCTA can only be considered cost-effective if it has equal or lower average costs per patient compared to SOC. To determine the cost-effectiveness of CCTA, a de novo cost minimisation analysis was conducted that was based on the resource use reported in the Netherlands study however unit costs from the UK NHS were applied. The unit costs that were included in the analysis are listed in Table 19.

Table 19: UK unit costs

Item	Code and Description	Source	Cost
CCTA	RD28Z, complex computerised tomography scan	NHS Reference Costs 2014-15	£122.11
Stress SPECT	RN21Z, myocardial perfusion scan, stress only	NHS Reference Costs 2014-15	£367.29
CMR	RA67Z, cardiac magnetic resonance imaging scan, pre- and post-contrast	Enhanced Tariff Option 2015-16	£515.00
Exercise ECG	EY51Z, electrocardiogram monitoring or stress testing	NHS Reference Costs 2014-15	£153.00
ICA	EY43A to EY43F, standard cardiac catheterisation with CC score 0-13+	NHS Reference Costs 2014-15, weighted average	£1,141.26
PCI	EY40A to EY41D, standard or complex percutaneous transluminal coronary angioplasty with CC	NHS Reference Costs 2014-15, weighted average	£2,242

[a] Converted from Euros using OECD purchasing power parities (PPPs).

Item	Code and Description	Source	Cost
	score 0-12+		
CABG	ED28A to ED28B, standard coronary artery bypass graft with CC score 0-10+	NHS Reference Costs 2014-15, weighted average	£7,303.00
ED visit (admitted)	VB09Z, emergency medicine, category 1 investigation with category 1-2 treatment	NHS Reference Costs 2014-15	£132.00
ED visit (non-admitted)	VB09Z, emergency medicine, category 1 investigation with category 1-2 treatment	NHS Reference Costs 2014-15	£107.00
Repeat hospital admission	EB10A to EB10E, actual or suspected myocardial infarction, with CC score 0-13+	NHS Reference Costs 2014-15, weighted average	£280.00

The analysis was split into 3 sections: cost of tests during index visit, cost of tests after index visit, and treatment and repeat admission costs. This was done in order to gain a better understanding of where costs are likely to occur.

Cost of tests during index visit

Table 20 gives details on the average costs of each test at the index visit per patient for both the CCTA and SOC groups. There were 245 people followed up in each group of the study, therefore the probabilities were estimated by dividing the number of tests reported to have been carried out during index visits by 245.

Table 20: Cost of tests during index visit per patient

Test	Unit cost	Proportion[b] (n/total n)		Average cost per patient (unit cost * proportion)	
		CCTA	SOC	CCTA	SOC
ExECG	£153.00	0.09 (23/245)	0.53 (130/245)	£13.77	£81.09
CCTA	£122.11	0.971 (238/245)	0.004 (1/245)	£118.62	£0.49
SPECT	£367.29	0.008 (2/245)	0.03 (7/245)	£2.94	£11.02
CMR	£515.00	0.004 (1/245)	0.004 (1/245)	£2.06	£2.06
ICA (no PCI)	£1141.26	0.088 (21.52/245)(a)	0.059 (14.52/245) (a)	£100.43	£67.62
			Total	£237.82	£162.28

(a) The NHS reference cost for a PCI is likely to include the cost of an ICA. The probability of requiring an ICA in each group was adjusted to only include those that received an ICA with no PCI, to ensure the cost of an ICA was not double counted.[c]

Cost of tests after index visit

Table 21 gives details on the estimated average cost of each test after the index visit per person for both groups.

[b] Proportions were sourced from the Netherlands study 243. Dedic A, Lubbers MM, Schaap J, Lammers J, Lamfers EJ, Rensing BJ et al. Coronary CT Angiography for Suspected ACS in the Era of High-Sensitivity Troponins: Randomized Multicenter Study. Journal of the American College of Cardiology. 2016; 67(1):16-26.

[c] Invasive coronary angiography (ICA), percutaneous coronary intervention (PCI).

Table 21: Costs of tests after index visit

Test	Unit cost	Proportion (n/total n)		Average cost per patient (unit cost * proportion)	
		CCTA	SOC	CCTA	SOC
ExECG	£153.00	0.036 (9/245)	0.052 (13/245)	£5.51	£7.96
CCTA	£122.11	0.004 (1/245)	0.008 (2/245)	£0.49	£0.98
SPECT	£367.29	0 (0/245)	0.036 (9/245)	0	£13.22
CMR	£515.00	0 (0/245)	0.008 (2/245)	0	£4.12
ICA (no PCI)	£1141.26	0.018 (4.41/245)(a)	0.014 (3.48/245)(a)	£20.54	£16.23
			Total	£26.54	£42.50

(a) The NHS reference cost for a PCI is likely to include the cost of an ICA. The probability of requiring an ICA in each group was adjusted to only include those that received an ICA with no PCI, to ensure the cost of an ICA was not double counted.

ICA (no PCI)

It is common for PCI treatment to happen directly after an ICA and within the same procedure, therefore the NHS reference cost for a PCI is likely to include the cost of an ICA within it. For this analysis, it was assumed that all the people that receive a PCI also receive an ICA within the same procedure, with the cost of both included in the PCI cost. However not everyone goes on to receive a PCI after an ICA. For this analysis the probability of requiring an ICA was calculated using only the ICAs that did not then go on to receive a PCI. This was done to avoid double counting the ICA cost for those that did go on to receive PCI treatment. To estimate the proportion of ICAs (with no PCIs) that occurred at and after the index visit, the same proportion was assumed as the total ICAs that occurred at and after the index visit reported in the study.

Costs of treatments and repeat admissions

Table 22 gives details on the average cost of treatments, repeat ED visits and hospital admissions per patient for both groups. These were calculated using the numbers reported in the study, UK costs and results from the test-and-treat clinical review.

Table 22: Costs of treatment and repeat admissions per patient

Test	Unit cost	Proportion (n/total n)		Average cost per patient (unit cost * proportion)	
		CCTA	SOC	CCTA	SOC
ED visit non-admitted	£107.00	0.024 (6/245)	0.02 (5/245)	£2.57	£2.14
ED visit admitted	£132.00	0.029 (7/245)	0.057 (14/245)	£3.70	£7.52
Hospital admission	£280.00	0.029 (7/245)	0.057 (14/245)	£8.12	£15.95
PCI (inc. ICA)	£2242.00	0.0615(a)	0.0368(a) (31/842)	£137.84	£82.54
CABG	£7303.00	0.0085(a)	0.0095(a) (8/842)	£61.76	£69.39
			Total	£214.11	£177.55

(a) Probabilities estimated using results from the test-and-treat clinical review.

Most probabilities in Table 22 were calculated from the Netherlands study results, except for the probabilities of requiring PCI or CABG treatment. These were estimated using the meta-analysed

results from the test-and-treat clinical review. The meta-analysed results were calculated from the results of three studies (including the Netherlands study) [243 ,300 ,333] on 1,687 people in total, therefore they are likely to be more accurate than the results of the Netherlands study alone. As the costs of these treatments are significantly more expensive than any other unit costs included in the analysis, it was considered more appropriate to use the meta-analysed results in order to reduce the level of bias in the average costs. In the Netherlands study, no one in the CCTA group received a CABG, but four people in the SOC group did. As the guideline committee felt that the probability of a patient receiving a CABG is not likely to be affected by whether they received a CCTA at their ED index visit or not, but insteaddetermined by the underlying condition that they have, they believed using the original results would have led to an unfair bias in favour of CCTA.

Base case results

Table 23 shows the base case results of the cost minimisation analysis.

Table 23: Base case results – average cost per patient

	SOC	CCTA
Test at index visit (Table 20)	£162.28	£237.82
Tests after index visit (Table 21)	£42.50	£26.54
Treatment and admissions (Table 22)	£177.55	£214.11
Total	£382.33	£478.47

The results in Table 23 show that in a UK setting, the SOC group is estimated to have lower average costs over 30 days than the CCTA group: £382.33 compared to £478.47. This is the opposite result to the results reported in the Netherlands study, where the SOC group appeared to have higher average patient costs (£284 versus £430). The study reported that a reason for the CCTA group having lower costs was due to less outpatient testing occurring in that group. Although this is the case, the results above imply that the costs of tests after the index visit are relatively low in both groups. Significantly higher costs occur from the index visit tests and treatment and admissions.

The main explanation for why the results of our analysis conflicted with the results from the original study is that the Netherlands study only reported the median costs, not the mean costs. The distribution of costs in the study was extremely skewed as many people were discharged straight from the ED with low costs while a few people had very high costs due to expensive treatments. These high costs would not be captured in a median cost statistic. Another reason is that the costs used in the study were from the Netherlands not the UK, where there is likely to be some variation. Finally, the probabilities of requiring PCI or CABG treatment were taken from the clinical review and included the combined results of three studies.

Probabilistic analysis

To account for parameter uncertainty and to see how robust the base case results were to changes in resource use or costs, a probabilistic sensitivity analysis (PSA) was undertaken. The guideline committee acknowledged that NHS reference costs are average costs and that the costs of tests, treatments, ED visits and hospital admissions vary by different hospitals and geographically. They also acknowledged that most of the probabilities in the analysis were based on only one study that was not conducted in the UK; therefore they also have a degree of uncertainty and in reality will vary.

For the PSA, beta distributions were attached to all of the proportions and gamma distributions were attached to all of the costs. To define the distributions around the proportions, alpha and beta parameters were calculated from the events recorded in the study. To define the distributions around the costs, alpha and beta parameters were calculated from the interquartile ranges. For the costs that were calculated as weighted averages (for example the cost of a PCI treatment),

distributions were attached to each individual cost, and then new probabilistic weighted averages were calculated from the probabilistic costs. Ten-thousand simulations were run, each simulation simultaneously randomly selecting a value from each distribution and calculating the average cost results. Averages were then taken of the 10,000 simulation results to give the probabilistic results shown in Table 24.

Table 24: Probabilistic results (averages of 10,000 simulations) – average cost per patient

	SOC	CCTA
Test at index visit	£162.02	£237.64
Tests after index visit	£43.01	£26.80
Treatment	£177.50	£224.62
Total	£382 (CI £272, £493)	£489 (CI £286, £692)
Number of simulations with the lowest cost	8883 (88.83%)	1117 (11.17%)

The results in Table 24 show that the base case results are robust to changes in the parameter values. On average, the SOC group total costs were £382 compared to £489 for the CCTA group. The PSA results also show that for 8,883 (89%) of the 10,000 simulations, the SOC group had the lowest costs per person.

Economic considerations

Evidence from the literature suggests that routine CCTA for low to intermediate risk people with acute chest pain can lower costs by increasing emergency department discharge rates or decreasing hospital length of stay. [299 ,333 ,430] The studies that report these findings were conducted before the routine use of high-sensitivity troponin assays, therefore their results are not considered applicable to current UK practice. One study conducted after the introduction of high sensitivity Troponin [243] found that CCTA had lower median costs after 30 days than SOC. However, when UK costs were applied, more accurate estimates for the proportion of people that would require expensive treatments were used, and mean costs were reported, the CCTA group became the group with the highest average costs over 30 days. These results are robust to changes in parameter values.

The cost minimisation results suggest that CCTA is likely to be more costly than standard care and therefore not likely to be cost-effective for a low risk population; however the guideline committee acknowledged that it might be cost effective for other populations, for example an intermediate risk population.

Other considerations

The guideline committee acknowledged that the outcomes reported in the clinical review and in the Netherlands study were only 30-day outcomes and that no long-term health outcomes were reported. The cost minimisation analysis also only included costs that would occur over a 30-day time horizon. Although the guideline committee felt that 30 days may be long enough to capture all the important costs and outcomes, they were aware of the limitations a short time horizon has on the results.

The Netherlands study reported that the mean radiation dose in the CCTA group was higher than the SOC group (7.3 6.6 mSv versus 2.6 6.5 mSv). As 30-day outcomes are estimated to be equivalent and average costs are estimated to be higher with CCTA, it should be considered whether it is worth putting patients at increased risk through the use of CCTA testing.

Appendix N: How this guideline was updated

N.1 Recommendations to be deleted

Recommendation in 2010 guideline	Comment
Take a blood sample for troponin I or T measurement on initial assessment in hospital. These are the preferred biochemical markers to diagnose acute MI. (1.2.5.1)	Replaced by: Perform high sensitivity troponin test as recommended in the NICE diagnostics guidance on myocardial infarction (DG15) for people at high and moderate risk of MI. (1.2.5.2)
Take a second blood sample for troponin I or T measurement 10–12 hours after the onset of symptoms. (1.2.5.2)	Replaced by: Perform high sensitivity troponin test as recommended in the NICE diagnostics guidance on myocardial infarction (DG15) for people at high and moderate risk of MI. (1.2.5.2) Consider a single high sensitivity tropnin test at presentation to rule out ACS in people at low risk of MI if the first tropinin test is below the lower limit of detection. (1.2.5.2)
Novel cardiac biomarkers in people with acute chest pain (research recommendation 4.2)	Research question has been addressed by this 2016 update of CG95.

N.2 Amended recommendation wording (change to meaning)

Recommendation in 2010 guideline	Recommendation in current guideline	Reason for change
Take a resting 12-lead ECG and a blood sample for troponin I or T measurement (see section 1.2.5) on arrival in hospital. (1.2.4.1)	Take a resting 12-lead ECG and a blood sample for high sensitivity troponin I or T measurement (see recommendations 1.2.30-1.2.36) on arrival in hospital. (1.2.4.1)	Updated to clarify the use of high sensitivity troponin testing.
Take into account the clinical presentation, the time from onset of symptoms and the resting 12-lead ECG findings when interpreting high sensitivity troponin measurements. (1.2.5.5)	Take into account the clinical presentation, the time from onset of symptoms and the resting 12-lead ECG findings when interpreting high sensitivity troponin measurements. (1.2.5.7)	Updated to clarify the use of high sensitivity troponin testing.
When diagnosing MI, use the universal definition of myocardial infarction [2]. This is the detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit, together with evidence of myocardial ischaemia with at least one of the following: • Symptoms of ischaemia • New or presumed new significant ST-segment-T wave(ST-T)	When diagnosing MI, use the universal definition of myocardial infarction. 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 (URL) with 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	Updated reference to universal definition of MI.

Recommendation in 2010 guideline	Recommendation in current guideline	Reason for change
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 . • Identification of an intracoronary thrombus by angiography or autopsy (1.2.6.1)	block (LBBB) • Development of pathological Q waves in the ECG • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality . • Identification of an intracoronary thrombus by angiography or autopsy (1.2.6.1)	
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. (1.2.6.2)	When a raised high sensitivity 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. (1.2.6.2)	Updated to clarify the use of high sensitivity troponin testing.
When a raised troponin level is detected in people with a suspected ACS, follow the appropriate guidance ('Unstable angina and NSTEMI' [NICE clinical guideline 94] or local protocols for STEMI) until a firm diagnosis is made. Continue to monitor (see recommendation 1.2.3.4). (1.2.6.3)	When a raised high sensitivity troponin level is detected in people with a suspected ACS, follow the appropriate guidance ('Unstable angina and NSTEMI' [NICE clinical guideline 94] or local protocols for STEMI) until a firm diagnosis is made. Continue to monitor (see recommendation 1.2.3.4). (1.2.6.3)	Updated to clarify the use of high sensitivity troponin testing.
Reassess people with chest pain without raised troponin levels (determined from appropriately timed samples) 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. (1.2.6.5)	Reassess people with chest pain without raised high sensitivity troponin levels (determined from appropriately timed samples) 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. (1.2.6.5)	Updated to clarify the use of high sensitivity troponin testing.

Appendix O: Sections from CG95 which have been updated

O.1 Methods chapter

O.1.1 Introduction

This chapter sets out in detail the methods used to generate the recommendations for clinical practice that are presented in the subsequent chapters of this guideline. The methods are in accordance with those set out by the Institute in 'The guidelines manual'. April 2007. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidelinesmanual. The Guideline Development Process – an overview for stakeholders, the public and the NHS describes how organisations can become involved in the development of a guideline.

O.1.2 Developing key clinical questions (KCQs)

The first step in the development of the guideline was to refine the guideline scope into a series of key clinical questions (KCQs). These KCQs formed the starting point for the subsequent review and as a guide to facilitate the development of recommendations by the Guideline Development Group (GDG).

The KCQs were developed by the GDG and with assistance from the methodology team. The KCQs were refined into specific evidence-based questions (EBQs) specifying interventions to search and outcomes to be searched for by the methodology team and these EBQs formed the basis of the literature searching, appraisal and synthesis.

The total list of KCQs identified is listed in Appendix C1. The development team, in liaison with the GDG, identified those KCQs where a full literature search and critical appraisal were essential.

O.1.3 Literature search strategy

Systematic literature searches are undertaken to identify published evidence to answer the clinical questions identified by the methodology team and the GDG. The information scientist developed search strategies for each question, with guidance from the GDG, using relevant MeSH (medical subject headings) or indexing terms, and free text terms. Searches were conducted between May 2007 and November 2008. Update searches for all questions were carried out in April 2009 identify any recently published evidence. Full details of the sources and databases searched and the strategies are available in Appendix C2.

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or websites: National Library for Health (NLH) Guidelines Finder, National Guidelines Clearinghouse, National Institute for Health and Clinical Excellence (NICE) Guidelines, Scottish Intercollegiate Guidelines Network (SIGN), Canadian Medical Association (CMA) Infobase (Canadian guidelines), National Health and Medical Research Council (NHMRC) Clinical Practice Guidelines (Australian Guidelines), New Zealand Guidelines Group, Guidelines International Network (GIN), OMNI, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and Heath Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHSEED), TRIP, Health Evidence Bulletin Wales, BMJ Clinical Evidence, DH Data, and King's Fund.

For each clinical question the following bibliographic databases were searched from their inception to the latest date available: Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Database (HTA), MEDLINE, EMBASE, CINAHL, and CENTRAL (Cochrane Controlled Trials Register). When appropriate to the question PsycINFO and AMED were also searched.

The search strategies were developed in MEDLINE and then adapted for searching in other bibliographic databases. Methodological search filters designed to limit searches to systematic reviews or randomised controlled trials were used. These were developed by the Centre for Reviews and Dissemination (CRD) and The Cochrane Collaboration. For all other questions, no restriction was placed on study design.

The economic literature was identified by conducting searches in NHS Economic Evaluations Database (NHSEED) and in MEDLINE, EMBASE and CINAHL using an economics search strategy developed by ScHARR at the University of Sheffield.

Databases of the results of the searches for each question or topic area were created using the bibliographic management software Reference Manager.

O.1.4 Identifying the evidence

After the search of titles and abstracts was undertaken, full papers were obtained if they appeared to address the KCQ. The highest level of evidence was sought. Systematic reviews were initially selected. Where systematic reviews had recently been published, the identification of further studies was not done. Where systematic reviews were not available, diagnostic cohort studies were selected for intervention KCQs, and cohort studies were selected for other KCQs. Surveys were not selected. Expert consensus was used when no studies were available that addressed the KCQ. Following a critical review of the full text paper, articles not relevant to the subject in question were excluded. Cohort and diagnostic studies were excluded if they were conducted on an inappropriate patient population. Diagnostic studies were excluded if the test being evaluated was not compared with a reference standard (that would confirm or refute the diagnosis), and if the test and the reference standard were not evaluated in all patients in the study. Diagnostic studies that did not provide test accuracy statistics (for example sensitivity, specificity) were also excluded.

O.1.5 Critical appraisal of the evidence

From the papers retrieved, the Senior Health Service Research Fellow (SHSRF) synthesised the evidence for each question or questions into a narrative summary. These form the basis of this guideline. Each study was critically appraised using the Institute's criteria for quality assessment and the information extracted for included studies is given in Appendix D. Background papers, for example those used to set the clinical scene in the narrative summaries, were referenced but not extracted.

O.1.6 Health economics

O.1.6.1 Health economic evidence reviews

A broad search of health economics literature was developed based on the original scoping search for the Guideline. The economic literature was identified by conducting searches in NHS Economic Evaluations Database (NHSEED) and also in MEDLINE, EMBASE and CINAHL using an economics search strategy developed by ScHARR at the University of Sheffield. Towards the end of the development of the Guideline, update searches were conducted to search for studies which had been published during the development phase of the Guideline. Databases of the results of the

searches for each KCQ or topic area were created using the bibliographic management software Reference Manager™.

Identified titles and abstracts from the economic searches were reviewed by a health economist and full papers obtained as appropriate. Retrieved papers where then reviewed by a health economist, and considered for inclusion in the Guideline. No formal inclusion or exclusion criterion was applied a priori. Each paper was considered on its own merit, and in the context of availability of relevant published economic evaluations to inform the KCQs. All valid incremental cost-utility (QALY) analyses (including cost-consequence analyses where the incremental analyses could be calculated from the available study data), taking an NHS costing perspective, were included for all KCQs. In the absence of NHS based cost-utility analyses, incremental cost-effectiveness analyses using alternative outcome measures (for example the proportion of patients correctly diagnosed), were considered. For KCQs designated as high priority for economic evaluation (primarily investigations for diagnosis of stable and acute chest pain), if no UK based economic evaluations were found in the literature, then non-UK economic evaluations were considered for inclusion, if it was felt that they would inform the GDG's consideration of the cost-effectiveness for the KCQ under consideration (for example where there was dominance which was likely to be replicated in a UK based analysis).

The main reasons for exclusion were that the published study was not an economic evaluation, or that the study population did not meet the inclusion criteria for the review of clinical evidence, as set out in the NICE scope document and as agreed by the GDG. Reasons for exclusion for all requested papers were systematically recorded by the health economist using the reference manager database. A general descriptive overview of the included studies, their quality, and conclusions was presented and summarised in the form of a narrative review (see also Appendix E for the full extractions and reasons for exclusion).

O.1.6.2 Cost-effectiveness modelling

Having reviewed the health economics literature for this guideline, some de novo economic modelling was undertaken to supplement the available published economic analyses. A summary of the methods is provided here with details presented in Appendix F.

Firstly, with the cooperation of the developers of the model presented in the Mowatt 2008 HTA[510], we have replicated their short-term model for diagnosis of CAD. Outputs from the replicated model include short term costs of diagnosis, the 2*2 true, false, positive, negative matrix, and the incremental cost per correctly diagnosed patient. Only the short term cost of diagnosis was previously available from the data presented in the HTA. Both the original analysis presented in the HTA, and the new analysis produced using the replicated model found heavily in favour of 64-slice CT coronary angiography (for example dominance over MPS with SPECT). The GDG, however, had reservations about the existing model, primarily:

- Its relevance for diagnosis of angina (as opposed to coronary artery stenosis assessed by invasive coronary angiography)
- The high sensitivity of 64-slice CT coronary angiography
- Risk of radiation from 64-slice CT coronary angiography.

The latter two reservations were addressed by making revisions to model input assumptions, and by the addition of two new treatment arms respectively. The two new treatment arms explore the health economic impact of using calcium scoring as a pre-cursor to full CT scanning using 64-slice CT. That is, first line testing in the new treatment arm would be by calcium scoring. Patients testing positive or uncertain would then proceed to second line testing using full 64-slice CT coronary angiography. Patients with a negative calcium score would have no further testing, as per the existing model protocol. The difference in the two new treatment arms is inclusion, or exclusion, of invasive coronary angiography as confirmatory third line test.

Because the GDG believed that there was still a role for functional (as opposed to anatomical) testing in chest pain patient populations with moderate likelihood of CAD, a new economic model was built comparing first line functional testing using stress MPS with SPECT compared to first line anatomical testing using invasive coronary angiography. In a sensitivity analysis, invasive coronary angiography was substituted with 64-slice CT coronary angiography.

The economic evaluations presented in the Mowatt et al HTAs of 2004 and 2008,[510,511] did build "speculative" longer term cost per QALY Markov models. These models required speculative assumptions to be made about the re-presentations of false-negatives, which of the coronary arteries had significant stenosis, and how these would be treated, as well as the survival and health related quality of life assumptions that would result for treated patients. The results of the longer term model analysis presented in Mowatt 2008[510], indicated that the difference in QALY outcomes was less than one quarter of one percent. Also, results presented in the MPS HTA of 2004[511] (tables 39 and 40) indicate that for all but the lowest CAD prevalence populations, the ICERs of the short term cost per proportion of cases correctly diagnosed and the speculative longer term costs per QALY, have similar values, indicating that the former might be a useful proxy for the latter. Based on the above, and because of the diagnostic scope of this guideline, the incremental economic analysis from our de novo models has been confined to the short term incremental cost per correct diagnosis. The GDG was consulted during the construction and interpretation of the model to ensure that appropriate assumptions, model structure, and data sources were used. The results of the de novo health economic analysis are presented in Chapter 5 of this Guideline with further detail of the results and methods presented in Appendix F.

O.1.7 Assigning levels to the evidence

The evidence levels and recommendation are based on the Institute's technical manual 'The guidelines manual'. April 2006. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidelinesmanual. Evidence levels for included studies were assigned based upon details in Table 2.

Table 25

Levels of evidence	
Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example, case reports, case series)
4	Expert opinion, formal consensus

O.1.8 Forming recommendations

In preparation for each meeting, the narrative and extractions for the questions being discussed were made available to the GDG one week before the scheduled GDG meeting. These documents were available on a closed intranet site and sent by post to those members who requested it.

GDG members were expected to have read the narratives and extractions before attending each meeting. The GDG discussed the evidence at the meeting and agreed evidence statements and recommendations. Any changes were made to the electronic version of the text on a laptop and projected onto a screen until the GDG were satisfied with these.

Recommendations were also documented in a care pathway which was reviewed regularly by the GDG.

All work from the meetings was posted on the closed intranet site following the meeting as a matter of record and for referral by the GDG members.

O.1.9 Areas without evidence and consensus methodology

The table of clinical questions in Appendix C1 indicates which questions were searched.

In cases where evidence was sparse, the GDG derived the recommendations via informal consensus methods, using extrapolated evidence where appropriate. All details of how the recommendations were derived can be seen in the 'Evidence to recommendations' section of each of the chapters.

O.1.10 Consultation

The guideline has been developed in accordance with the Institute's guideline development process. This has included allowing registered stakeholders the opportunity to comment on the scope of the guideline and the draft of the full and short form guideline. In addition, the draft was reviewed by an independent Guideline Review Panel (GRP) established by the Institute.

The comments made by the stakeholders, peer reviewers and the GRP were collated and presented for consideration by the GDG. All comments were considered systematically by the GDG and the development team responded to comments.

O.1.11 Relationship between the guideline and other national guidance

O.1.11.1 Related NICE Guidance

It was identified that this guideline intersected with the following NICE guidelines published or in development. Cross reference was made to the following guidance as appropriate.

Published

- Unstable angina and NSTEMI. NICE clinical guideline 94 (2010). Available from www.nice.org.uk/guidance/CG94
- Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 67 (2008). Available from www.nice.org.uk/guidance/CG67
- Secondary prevention in primary and secondary care for patients following a myocardial infarction. NICE clinical guideline 48 (2007). Available from www.nice.org.uk/CG48
- Hypertension: management of hypertension in adults in primary care. NICE clinical guideline 34 (2006). Available from www.nice.org.uk/CG34

- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006). Available from www.nice.org.uk/TA94
- Anxiety (amended). NICE clinical guideline 22 (2007). Available from www.nice.org.uk/guidance/CG22
- Dyspepsia (amended). NICE clinical guideline 17 (2005). Available from www.nice.org.uk/guidance/CG17
- Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. NICE technology appraisal guidance 73 (2003). Available from www.nice.org.uk/TA73

Under development

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

- The management of stable angina. NICE clinical guideline. Publication expected July 2011.
- Prevention of cardiovascular disease. NICE public health guideline. Publication date to be confirmed.

Appendix P: NICE technical team

Name	Role
Christine Carson	Guideline Lead
Phil Alderson	Clinical Advisor
Rachel O'Mahony	Technical Lead
Ross Maconachie	Health Economist
Ben Doak	Guideline Commissioning Manager
Helen Dickinson	Guideline Coordinator
Anne-Louise Clayton	Editor

Appendix Q: References

1. Abbasi SA, Heydari B, Shah RV, Murthy VL, Zhang YY, Blankstein R et al. Risk stratification by regadenoson stress magnetic resonance imaging in patients with known or suspected coronary artery disease. American Journal of Cardiology. 2014; 114(8):1198-1203

2. Abbott BG, Jain D. Nuclear cardiology in the evaluation of acute chest pain in the emergency department. Echocardiography. 2000; 17(6 Pt 1):597-604

3. Abbott BG, Jain D. Impact of myocardial perfusion imaging on clinical management and the utilization of hospital resources in suspected acute coronary syndromes. Nuclear Medicine Communications. 2003; 24(10):1061-1069

4. Abd TT, George RT. Association of coronary plaque burden with fractional flow reserve: should we keep attempting to derive physiology from anatomy? Cardiovascular Diagnosis & Therapy. 2015; 5(1):67-70

5. Abdel-Rahman AS, Aly HI, Saleh MA, Ibrahim AS, Arafa HMH. Alternative technique using dual source CT imaging for assessment of myocardial perfusion. Egyptian Journal of Radiology and Nuclear Medicine. 2015; 46(2):339-354

6. Abdel-Salam Z, El-Hammady W, Abdel-Sattar A, Nammas W. Left Atrial Volume Index at Peak Dobutamine Stress Echocardiography Predicts the Extent of Coronary Artery Disease in Patients with Normal Resting Wall Motion. Echocardiography. 2015; 32(11):1662-1669

7. Abdelmoneim S, Bernier M, Dhoble A, Moir S, Hagen ME, Ness S et al. Diagnostic accuracy of contrast echocardiography during adenosine stress for detection of abnormal myocardial perfusion:prospective comparison with single-photon emission computed tomography. European Heart Journal. 2009; 30:627

8. Abdelmoneim SS, Basu A, Bernier M, Dhoble A, Abdel-Kader SS, Pellikka PA et al. Detection of myocardial microvascular disease using contrast echocardiography during adenosine stress in type 2 diabetes mellitus: Prospective comparison with single-photon emission computed tomography. Diabetes and Vascular Disease Research. 2011; 8(4):254-261

9. Abdelmoneim SS, Bernier M, Dhoble A, Moir S, Hagen ME, Ness SA et al. Diagnostic accuracy of contrast echocardiography during adenosine stress for detection of abnormal myocardial perfusion: a prospective comparison with technetium-99 m sestamibi single-photon emission computed tomography. Heart and Vessels. 2010; 25(2):121-130

10. Abdelmoneim SS, Bernier M, Dhoble A, Moir S, Hagen ME, Ness SAC et al. Assessment of myocardial perfusion during adenosine stress using real time three-dimensional and two-dimensional myocardial contrast echocardiography: Comparison with single-photon emission computed tomography. Echocardiography. 2010; 27(4):421-429

11. Abdelmoneim SS, Dhoble A, Bernier M, Erwin PJ, Korosoglou G, Senior R et al. Quantitative myocardial contrast echocardiography during pharmacological stress for diagnosis of coronary artery disease: a systematic review and meta-analysis of diagnostic accuracy studies. European Journal of Echocardiography. 2009; 10(7):813-825

12. Abdelmoneim SS, Dhoble A, Bernier M, Moir S, Hagen ME, Ness SA et al. Absolute myocardial blood flow determination using real-time myocardial contrast echocardiography during adenosine stress: comparison with single-photon emission computed tomography. Heart. 2009; 95(20):1662-1668

13. Abdelmoneim SS, Mulvagh SL, Xie F, O'Leary E, Adolphson M, Omer MA et al. Regadenoson Stress Real-Time Myocardial Perfusion Echocardiography for Detection of Coronary Artery Disease: Feasibility and Accuracy of Two Different Ultrasound Contrast Agents. Journal of the American Society of Echocardiography. 2015; 28(12):1393-1400

14. Abdool MA, Ashrafi R, Davies M, Raga S, Lewis-Jones H, Thwaite E et al. A UK cardiac centre experience of low-risk, stable chest pain patients with calcium score of zero. British Journal of Cardiology. 2014; 21(2):78

15. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E, Kober L, Torp-Pedersen C. 64-Multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: A systematic review and meta-analysis. European Heart Journal. 2007; 28(24):3042-3050

16. Abdulla J, Pedersen KS, Budoff M, Kofoed KF. Influence of coronary calcification on the diagnostic accuracy of 64-slice computed tomography coronary angiography: a systematic review and meta-analysis. The International Journal of Cardiovascular Imaging. 2012; 28(4):943-953

17. Abraham A, Nichol G, Williams KA, Guo A, deKemp RA, Garrard L et al. 18F-FDG PET imaging of myocardial viability in an experienced center with access to 18F-FDG and integration with clinical management teams: the Ottawa-FIVE substudy of the PARR 2 trial. Journal of Nuclear Medicine. 2010; 51(4):567-574

18. Abramowicz A, Daubert M, Malhotra V, Ferraro S, Ring J, Goldenberg R et al. Computer-aided analysis of 64-slice coronary computed tomography angiography: a comparison with manual interpretation. Heart International. 2013; 8(1):e2

19. Abramson BL, Ruddy TD, deKemp RA, Laramee LA, Marquis JF, Beanlands RS. Stress perfusion/metabolism imaging: a pilot study for a potential new approach to the diagnosis of coronary disease in women. Journal of Nuclear Cardiology. 2000; 7(3):205-212

20. Achenbach S, Daniel WG. Non-invasive imaging - Cardiac imaging in the patient with chest pain: Coronary CT angiography. Heart. 2010; 96(15):1241-1246

21. Achenbach S, Giesler T, Ropers D, Ulzheimer S, Derlien H, Schulte C et al. Detection of coronary artery stenoses by contrast-enhanced, retrospectively electrocardiographically-gated, multislice spiral computed tomography. Circulation. 2001; 103(21):2535-2538

22. Achenbach S, Moshage W, Ropers D, Nossen J, Daniel WG. Value of electron-beam computed tomography for the noninvasive detection of high-grade coronary-artery stenoses and occlusions. New England Journal of Medicine. 1998; 339(27):1964-1971

23. Achenbach S, Ropers U, Kuettner A, Anders K, Pflederer T, Komatsu S et al. Randomized comparison of 64-slice single- and dual-source computed tomography coronary angiography for the detection of coronary artery disease. JACC: Cardiovascular Imaging. 2008; 1(2):177-186

24. Adams GL, Shaw LK, Tuttle RH, Hanson MW, Pagnanelli R, Borges-Neto S. Prediction of mortality in patients with coronary artery disease undergoing vasodilator stress testing: a comparison between 99mTc-tetrofosmin and 99mTc-sestamibi. Nuclear Medicine Communications. 2007; 28(6):457-463

25. Adil M, Hafizullah M, Jan H, Paracha MM, Qazi S. Diagnostic yield of stress echocardiography in coronary artery disease patients. JPMI - Journal of Postgraduate Medical Institute. 2011; 25(4):331-337

26. Agarwal R, Gosain P, Kirkpatrick JN, Alyousef T, Doukky R, Singh G et al. Tissue Doppler imaging for diagnosis of coronary artery disease: a systematic review and meta-analysis. Cardiovascular Ultrasound. 2012; 10:47

27. Aggarwal NR, Drozdova A, Askew JW, 3rd, Kemp BJ, Chareonthaitawee P. Feasibility and diagnostic accuracy of exercise treadmill nitrogen-13 ammonia PET myocardial perfusion imaging of obese patients. Journal of Nuclear Cardiology. 2015; 22(6):1273-1280

28. Aggeli C, Felekos I, Roussakis G, Kazazaki C, Lagoudakou S, Pietri P et al. Value of real-time three-dimensional adenosine stress contrast echocardiography in patients with known or suspected coronary artery disease. European Journal of Echocardiography. 2011; 12(9):648-655

29. Aggeli C, Giannopoulos G, Misovoulos P, Roussakis G, Christoforatou E, Kokkinakis C et al. Real-time three-dimensional dobutamine stress echocardiography for coronary artery disease diagnosis: validation with coronary angiography. Heart. 2007; 93(6):672-675

30. Ahmad M, Xie T, McCulloch M, Abreo G, Runge M. Real-time three-dimensional dobutamine stress echocardiography in assessment stress echocardiography in assessment of ischemia: comparison with two-dimensional dobutamine stress echocardiography. Journal of the American College of Cardiology. 2001; 37(5):1303-1309

31. Ahmadvazir S, Zacharias K, Shah BN, Pabla JS, Senior R. Role of simultaneous carotid ultrasound in patients undergoing stress echocardiography for assessment of chest pain with no previous history of coronary artery disease. American Heart Journal. 2014; 168(2):229-236

32. Ahn JM, Kang SJ, Mintz GS, Oh JH, Kim WJ, Lee JY et al. Validation of minimal luminal area measured by intravascular ultrasound for assessment of functionally significant coronary stenosis comparison with myocardial perfusion imaging. JACC: Cardiovascular Interventions. 2011; 4(6):665-671

33. Ahn SJ, Kang DK, Sun JS, Yoon MH. Accuracy and predictive value of coronary computed tomography angiography for the detection of obstructive coronary heart disease in patients with an Agatston calcium score above 400. Journal of Computer Assisted Tomography. 2013; 37(3):387-394

34. Aidi H, Adams A, Moons KG, Ruijter HM, Mali WP, Doevendans PA et al. Cardiac magnetic resonance imaging findings and the risk of cardiovascular events in patients with recent myocardial infarction or suspected or known coronary artery disease ? a systematic review of prognostic studies (Provisional abstract). Journal of the American College of Cardiology. 2014; 63(11):1031-1045

35. Akbar AM, Hameed S, Azhar M, Sheikh SS, Sattar A, Naveed T. Significance of chest pain without ST changes during exercise treadmill testing. Journal of Ayub Medical College, Abbottabad: JAMC. 2010; 22(2):146-151

36. Akram K, Voros S. Absolute coronary artery calcium scores are superior to MESA percentile rank in predicting obstructive coronary artery disease. The International Journal of Cardiovascular Imaging. 2008; 24(7):743-749

37. Al-Kaylani H, Britton KE, Beslic N, Canizales A. Can the estimation of ejection fraction during gated single photon emission computed tomography at rest add information to the cardiac perfusion study? Nuclear Medicine Communications. 2002; 23(9):899-906

38. Al-Mallah M, Achenbach S, Berman D, Budoff MJ, Cademartiri F, Callister T et al. Incremental prognostic value of coronary CT angiography over coronary calcium score in symptomatic patients with suspected coronary disease: Results from the CONFIRM registry (COronary CT

Angiography evaluation for clinical outcomes: An international multicenter registry). Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1)

39. Al-Mallah MH, Qureshi W, Lin FY, Achenbach S, Berman DS, Budoff MJ et al. Does coronary CT angiography improve risk stratification over coronary calcium scoring in symptomatic patients with suspected coronary artery disease? Results from the prospective multicenter international CONFIRM registry. European Heart Journal Cardiovascular Imaging. 2014; 15(3):267-274

40. al-Saadi N, Gross M, Paetsch I, Schnackenburg B, Bornstedt A, Fleck E et al. Dobutamine induced myocardial perfusion reserve index with cardiovascular MR in patients with coronary artery disease. Journal of Cardiovascular Magnetic Resonance. 2002; 4(4):471-480

41. Al-Saadi N, Nagel E, Gross M, Bornstedt A, Schnackenburg B, Klein C et al. Noninvasive detection of myocardial ischemia from perfusion reserve based on cardiovascular magnetic resonance. Circulation. 2000; 101(12):1379-1383

42. Al Moudi M, Sun Z, Lenzo N. Diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease: A systematic review. Biomedical Imaging & Intervention Journal. 2011; 7(2):e9

43. Al Moudi M, Sun ZH. Diagnostic value of (18)F-FDG PET in the assessment of myocardial viability in coronary artery disease: A comparative study with (99m)Tc SPECT and echocardiography. Journal of Geriatric Cardiology. 2014; 11(3):229-236

44. Aldous SJ, Florkowski CM, Crozier IG, Elliott J, George P, Lainchbury JG et al. Comparison of high sensitivity and contemporary troponin assays for the early detection of acute myocardial infarction in the emergency department. Annals of Clinical Biochemistry. 2011; 48(Pt:3):3-8

45. Aldous SJ, Florkowski CM, Crozier IG, Than MP. The performance of high sensitivity troponin for the diagnosis of acute myocardial infarction is underestimated. Clinical Chemistry and Laboratory Medicine. 2012; 50(4):727-729

46. Aldous SJ, Richards AM, Cullen L, Than MP. Early dynamic change in high-sensitivity cardiac troponin T in the investigation of acute myocardial infarction. Clinical Chemistry. 2011; 57(8):1154-1160

47. Aldweib N, Negishi K, Seicean S, Jaber WA, Hachamovitch R, Cerqueira M et al. Appropriate test selection for single-photon emission computed tomography imaging: association with clinical risk, posttest management, and outcomes. American Heart Journal. 2013; 166(3):581-588

48. Alessandri N, Di Matteo A, Rondoni G, Petrassi M, Tufani F, Ferrari R et al. Heart imaging: the accuracy of the 64-MSCT in the detection of coronary artery disease. European Review for Medical and Pharmacological Sciences. 2009; 13(3):163-171

49. Alexanderson E, Mannting F, Gomez-Martin D, Fermon S, Meave A. Technetium-99m-Sestamibi SPECT myocardial perfusion imaging in patients with complete left bundle branch block. Archives of Medical Research. 2004; 35(2):150-156

50. Alexanderson E, Ricalde A, Romero-Ibarra JL, Meave A. Comparison of 18FDG PET with thallium SPECT in the assessment of myocardial viability. A segmental model analysis. Archivos de Cardiología de México. 2006; 76(1):9-15

51. Alexanderson Rosas E, Slomka PJ, Garcia-Rojas L, Calleja R, Jacome R, Jimenez-Santos M et al. Functional Impact of Coronary Stenosis Observed on Coronary Computed Tomography Angiography: Comparison with ¹³N-Ammonia PET. Archives of Medical Research. 2010; 41(8):642-648

52. Alexopoulos D, Stathopoulos C, Kotrsaridis A, Chiladakis J, Hahalis G. Coronary artery calcium by digital cinefluoroscopy in patients with pain suggestive of an acute coronary syndrome. Clinical Cardiology. 2005; 28(2):81-84

53. Ali M, Mallick NH, Abid AR, Haq S, Ayub M. Significance of perfusion defects on dipyridamole thallium cardiac SPECT in patients with left bundle branch block. Journal of Ayub Medical College, Abbottabad: JAMC. 2007; 19(4):21-25

54. AlJaroudi WA, Alraies MC, Wazni O, Cerqueira MD, Jaber WA. Yield and diagnostic value of stress myocardial perfusion imaging in patients without known coronary artery disease presenting with syncope. Circulation Cardiovascular imaging. 2013; 6(3):384-391

55. Alkadhi H, Scheffel H, Desbiolles L, Gaemperli O, Stolzmann P, Plass A et al. Dual-source computed tomography coronary angiography: Influence of obesity, calcium load, and heart rate on diagnostic accuracy. European Heart Journal. 2008; 29(6):766-776

56. Alkadhi H, Stolzmann P, Desbiolles L, Baumueller S, Goetti R, Plass A et al. Low-dose, 128-slice, dual-source CT coronary angiography: accuracy and radiation dose of the high-pitch and the step-and-shoot mode. Heart. 2010; 96(12):933-938

57. Allajbeu I, Hajro E, Temali I, Cekrezi B, Preza K. The Role of CT Angiography of Coronaries in Early Diagnosis of Coronary Artery Plaques in Albanian People with No History of Cardiovascular Disease in Correlation with Traditional Risk Factors. Materia Sociomedica. 2014; 26(3):163-167

58. Almeida AG, Mesquita Gabriel H, Coutinho CA, Sargento L, David C, Oliveira J et al. Myocardial perfusion and angioplasty. Comparison of myocardial contrast echocardiography and scintigraphy. [Portuguese, English]. Revista Portuguesa de Cardiologia. 2002; 21(7-8):859-868

59. Almoudi M, Sun ZH. A head-to-head comparison of the coronary calcium score by computed tomography with myocardial perfusion imaging in predicting coronary artery disease. Journal of Geriatric Cardiology. 2012; 9(4):349-354

60. Alqaisi F, Albadarin F, Jaffery Z, Tzogias L, Dawod M, Jacobsen G et al. Prognostic predictors and outcomes in patients with abnormal myocardial perfusion imaging and angiographically insignificant coronary artery disease. Journal of Nuclear Cardiology. 2008; 15(6):754-761

61. Altinmakas S, Dagdeviren B, Turkmen M, Gursurer M, Say B, Tezel T et al. Usefulness of pulse-wave Doppler tissue sampling and dobutamine stress echocardiography for identification of false positive inferior wall defects in SPECT. Japanese Heart Journal. 2000; 41(2):141-152

62. Altiok E, Neizel M, Tiemann S, Krass V, Becker M, Zwicker C et al. Layer-specific analysis of myocardial deformation for assessment of infarct transmurality: comparison of strain-encoded cardiovascular magnetic resonance with 2D speckle tracking echocardiography. European Heart Journal Cardiovascular Imaging. 2013; 14(6):570-578

63. Altiok E, Neizel M, Tiemann S, Krass V, Kuhr K, Becker M et al. Quantitative analysis of endocardial and epicardial left ventricular myocardial deformation - Comparison of strain-encoded cardiac magnetic resonance imaging with two-dimensional speckle-tracking

echocardiography. Journal of the American Society of Echocardiography. 2012; 25(11):1179-1188

64. Altiok E, Tiemann S, Becker M, Koos R, Zwicker C, Schroeder J et al. Myocardial deformation imaging by two-dimensional speckle-tracking echocardiography for prediction of global and segmental functional changes after acute myocardial infarction: a comparison with late gadolinium enhancement cardiac magnetic resonance. Journal of the American Society of Echocardiography. 2014; 27(3):249-257

65. Altun A, Durmus-Altun G, Birsin A, Gultekin A, Tatli E, Ozbay G. Normalization of negative T waves in the chronic stage of Q wave anterior myocardial infarction as a predictor of myocardial viability. Cardiology. 2005; 103(2):73-78

66. Altunkeser BB, Ozdemir K, Ozdil H, Gok H, Aydin M. Value of the corrected QT interval dispersion obtained exercise electrocardiography in determining remote vessel disease in patients with healed Q-wave myocardial infarction. Annals of Noninvasive Electrocardiology. 2002; 7(3):228-233

67. Alunni G, Marra S, Meynet I, D'Amico M, Elisa P, Fanelli A et al. The beneficial effect of extracorporeal shockwave myocardial revascularization in patients with refractory angina. Cardiovascular Revascularization Medicine. 2015; 16(1):6-11

68. Alvarez Tamargo JA, Simarro Martin-Ambrosio E, Romero Tarin E, Martin Fernandez M, Hevia Nava S, Barriales Alvarez V et al. Angiographic correlates of the treadmill scores in non-high-risk patients with unstable angina. Cardiology. 2008; 109(1):1-9

69. Amanuma M, Kondo T, Sano T, Sekine T, Takayanagi T, Matsutani H et al. Subtraction coronary computed tomography in patients with severe calcification. International Journal of Cardiovascular Imaging. 2015; 31(8):1635-1642

70. American College of R, Society of Cardiovascular Computed T, Society for Cardiovascular Magnetic R, American Society of Nuclear C, North American Society for Cardiac I, Society for Cardiovascular A et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging. A report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group. Journal of the American College of Radiology. 2006; 3(10):751-771

71. Amit G, Granot Y, Abboud S. Quantifying QRS changes during myocardial ischemia: Insights from high frequency electrocardiography. Journal of Electrocardiology. 2014; 47(4):505-511

72. Amsterdam EA, Kirk JD, Diercks DB, Lewis WR, Turnipseed SD. Immediate exercise testing to evaluate low-risk patients presenting to the emergency department with chest pain. Journal of the American College of Cardiology. 2002; 40(2):251-256

73. Anagnostopoulos C, Georgakopoulos A, Pianou N, Nekolla SG. Assessment of myocardial perfusion and viability by positron emission tomography. International Journal of Cardiology. 2013; 167(5):1737-1749

74. Anand DV, Lahiri A. Myocardial perfusion imaging versus biochemical markers in acute coronary syndromes. Nuclear Medicine Communications. 2003; 24(10):1049-1054

75. Anantharam B, Chahal N, Chelliah R, Ramzy I, Gani F, Senior R. Safety of contrast in stress echocardiography in stable patients and in patients with suspected acute coronary syndrome but negative 12-hour troponin. American Journal of Cardiology. 2009; 104(1):14-18

76. Anders K, Achenbach S, Petit I, Daniel WG, Uder M, Pflederer T. Accuracy of automated software-guided detection of significant coronary artery stenosis by CT angiography: Comparison with invasive catheterisation. European Radiology. 2013; 23(5):1218-1225

77. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey-Donald-E-Jr et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST- Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. Journal of the American College of Cardiology. 2007; 50(7):e1-e157

78. Andrade JM, Gowdak LH, Giorgi MC, de Paula FJ, Kalil-Filho R, de Lima JJ et al. Cardiac MRI for detection of unrecognized myocardial infarction in patients with end-stage renal disease: comparison with ECG and scintigraphy. AJR American Journal of Roentgenology. 2009; 193(1):W25-32

79. Andrassy M, Volz HC, Riedle N, Gitsioudis G, Seidel C, Laohachewin D et al. HMGB1 as a predictor of infarct transmurality and functional recovery in patients with myocardial infarction. Journal of Internal Medicine. 2011; 270(3):245-253

80. Andreini D, Martuscelli E, Guaricci AI, Carrabba N, Magnoni M, Tedeschi C et al. Clinical recommendations on Cardiac-CT in 2015: a position paper of the Working Group on Cardiac-CT and Nuclear Cardiology of the Italian Society of Cardiology. Journal of Cardiovascular Medicine. 2016; 17(2):73-84

81. Andreini D, Pontone G, Bartorelli AL, Agostoni P, Mushtaq S, Antonioli L et al. Comparison of the diagnostic performance of 64-slice computed tomography coronary angiography in diabetic and non-diabetic patients with suspected coronary artery disease. Cardiovascular Diabetology. 2010; 9:80

82. Annuar BR, Liew CK, Chin SP, Ong TK, Seyfarth MT, Chan WL et al. Assessment of global and regional left ventricular function using 64-slice multislice computed tomography and 2D echocardiography: A comparison with cardiac magnetic resonance. European Journal of Radiology. 2008; 65(1):112-119

83. Antony R, Daghem M, McCann GP, Daghem S, Moon J, Pennell DJ et al. Cardiovascular magnetic resonance activity in the United Kingdom: a survey on behalf of the British Society of Cardiovascular Magnetic Resonance. Journal of Cardiovascular Magnetic Resonance. 2011; 13:57

84. Anwar AM. Accuracy of two-dimensional speckle tracking echocardiography for the detection of significant coronary stenosis. Journal of Cardiovascular Ultrasound. 2013; 21(4):177-182

85. Aoyagi K, Inoue T, Yamauchi Y, Iwasaki T, Endo K. Does myocardial thallium-201 SPECT combined with electron beam computed tomography improve the detectability of coronary artery disease?--comparative study of diagnostic accuracy. Annals of Nuclear Medicine. 1998; 12(4):197-204

86. Apostolopoulos DJ, Davlouros P, Alexiou S, Patsouras N, Spyridonidis T, Vassilakos PJ et al. ST-segment depression during vasodilator stress is of minor clinical importance in women with normal myocardial perfusion imaging and low or intermediate risk of coronary artery disease. European Journal of Nuclear Medicine and Molecular Imaging. 2012; 39(3):437-445

87. Apple FS, Smith SW, Pearce LA, Murakami MM. Assessment of the multiple-biomarker approach for diagnosis of myocardial infarction in patients presenting with symptoms suggestive of acute coronary syndrome. Clinical Chemistry. 2009; 55(1):93-100

88. Arbab-Zadeh A, Di Carli MF, Cerci R, George RT, Chen MY, Dewey M et al. Accuracy of Computed Tomographic Angiography and Single-Photon Emission Computed Tomography-Acquired Myocardial Perfusion Imaging for the Diagnosis of Coronary Artery Disease. Circulation Cardiovascular imaging. 2015; 8(10):e003533

89. Arbab-Zadeh A, Hoe J. Quantification of coronary arterial stenoses by multidetector CT angiography in comparison with conventional angiography methods, caveats, and implications. JACC: Cardiovascular Imaging. 2011; 4(2):191-202

90. Argulian E, Agarwal V, Bangalore S, Chatterjee S, Makani H, Rozanski A et al. Meta-analysis of prognostic implications of dyspnea versus chest pain in patients referred for stress testing. American Journal of Cardiology. 2014; 113(3):559-564

91. Arnold JR, Karamitsos TD, Bhamra-Ariza P, Francis JM, Searle N, Robson MD et al. Myocardial oxygenation in coronary artery disease: insights from blood oxygen level-dependent magnetic resonance imaging at 3 tesla. Journal of the American College of Cardiology. 2012; 59(22):1954-1964

92. Arnold JR, Karamitsos TD, Pegg TJ, Francis JM, Olszewski R, Searle N et al. Adenosine stress myocardial contrast echocardiography for the detection of coronary artery disease: a comparison with coronary angiography and cardiac magnetic resonance. JACC: Cardiovascular Imaging. 2010; 3(9):934-943

93. Arsanjani R, Xu Y, Dey D, Fish M, Dorbala S, Hayes S et al. Improved accuracy of myocardial perfusion SPECT for the detection of coronary artery disease using a support vector machine algorithm. Journal of Nuclear Medicine. 2013; 54(4):549-555

94. Arsanjani R, Xu Y, Dey D, Vahistha V, Shalev A, Nakanishi R et al. Improved accuracy of myocardial perfusion SPECT for detection of coronary artery disease by machine learning in a large population. Journal of Nuclear Cardiology. 2013; 20(4):553-562

95. Arsanjani R, Xu Y, Hayes SW, Fish M, Lemley M, Jr., Gerlach J et al. Comparison of fully automated computer analysis and visual scoring for detection of coronary artery disease from myocardial perfusion SPECT in a large population. Journal of Nuclear Medicine. 2013; 54(2):221-228

96. Arumugam P, Tout D, Tonge C. Myocardial perfusion scintigraphy using rubidium-82 positron emission tomography. British Medical Bulletin. 2013; 107:87-100

97. Asferg C, Usinger L, Kristensen TS, Abdulla J. Accuracy of multi-slice computed tomography for measurement of left ventricular ejection fraction compared with cardiac magnetic resonance imaging and two-dimensional transthoracic echocardiography: a systematic review and meta-analysis. European Journal of Radiology. 2012; 81(5):e757-762

98. Asher E, Reuveni H, Shlomo N, Gerber Y, Beigel R, Narodetski M et al. Clinical outcomes and cost effectiveness of accelerated diagnostic protocol in a chest pain center compared with routine care of patients with chest pain http://www.plosone.org/article/fetchObject.action?uri=info:doi/10.1371/journal.pone.0117287&representation=PDF. PloS One. 2015; 10 (1) (no pagination)(0117287)

99. Atar S, Nagai T, Cercek B, Naqvi TZ, Luo H, Siegel RJ. Pacing stress echocardiography: an alternative to pharmacologic stress testing. Journal of the American College of Cardiology. 2000; 36(6):1935-1941

100. Athappan G, Habib M, Ponniah T, Jeyaseelan L. Multi-detector computerized tomography angiography for evaluation of acute chest pain--a meta analysis and systematic review of literature. International Journal of Cardiology. 2010; 141(2):132-140

101. Babar Imran M, Aleem Khan M, Naeem Aslam M, Irfanullah J. Diagnosis of coronary artery disease by stress echocardiography and perfusion scintigraphy. Journal of the College of Physicians and Surgeons Pakistan. 2003; 13(8):465-470

102. Bahrmann P, Christ M, Bahrmann A, Rittger H, Heppner HJ, Achenbach S et al. A 3-hour diagnostic algorithm for non-ST-elevation myocardial infarction using high-sensitivity cardiac troponin T in unselected older patients presenting to the emergency department. Journal of the American Medical Directors Association. 2013; 14(6):409-416

103. Balaravi B, Miller TD, Hodge DO, Gibbons RJ. The value of stress single photon emission computed tomography in patients without known coronary artery disease presenting with dyspnea. American Heart Journal. 2006; 152(3):551-557

104. Balmelli C, Meune C, Twerenbold R, Reichlin T, Rieder S, Drexler B et al. Comparison of the performances of cardiac troponins, including sensitive assays, and copeptin in the diagnostic of acute myocardial infarction and long-term prognosis between women and men. American Heart Journal. 2013; 166(1):30-37

105. Bamberg F, Dannemann N, Shapiro MD, Seneviratne SK, Ferencik M, Butler J et al. Association between cardiovascular risk profiles and the presence and extent of different types of coronary atherosclerotic plaque as detected by multidetector computed tomography. Arteriosclerosis, Thrombosis & Vascular Biology. 2008; 28(3):568-574

106. Bamberg F, Marcus RP, Becker A, Hildebrandt K, Bauner K, Schwarz F et al. Dynamic myocardial CT perfusion imaging for evaluation of myocardial ischemia as determined by MR imaging. JACC: Cardiovascular Imaging. 2014; 7(3):267-277

107. Bamberg F, Truong QA, Blankstein R, Nasir K, Lee H, Rogers IS et al. Usefulness of age and gender in the early triage of patients with acute chest pain having cardiac computed tomographic angiography. American Journal of Cardiology. 2009; 104(9):1165-1170

108. Banerjee A, Newman DR, Van den Bruel A, Heneghan C. Diagnostic accuracy of exercise stress testing for coronary artery disease: a systematic review and meta-analysis of prospective studies. international journal for clinical practice. 2012; 66(5):477-492

109. Bangalore S, Gopinath D, Yao SS, Chaudhry FA. Risk stratification using stress echocardiography: incremental prognostic value over historic, clinical, and stress electrocardiographic variables across a wide spectrum of bayesian pretest probabilities for coronary artery disease. Journal of the American Society of Echocardiography. 2007; 20(3):244-252

110. Bangalore S, Yao SS, Chaudhry FA. Stress function index, a novel index for risk stratification and prognosis using stress echocardiography. Journal of the American Society of Echocardiography. 2005; 18(12):1335-1342

111. Barbirato GB, Azevedo JC, Felix RC, Correa PL, Volschan A, Viegas M et al. Use of resting myocardial scintigraphy during chest pain to exclude diagnosis of acute myocardial infarction. Arquivos Brasileiros de Cardiologia. 2009; 92(4):269-274

112. Barletta G, Gallini C, Del Bene R, Costanzo E, Fantini F. Simultaneous dobutamine stress echocardiography and 99mTc-tetrofosmin three-head single-photon emission computed tomography in patients with suspected coronary artery disease. Coronary Artery Disease. 1999; 10(7):479-487

113. Barmeyer AA, Stork A, Muellerleile K, Schofer AK, Tiburtius C, Koester R et al. Comparison of quantitative coronary angiography and first-pass perfusion magnetic resonance imaging for the detection of an impaired coronary perfusion in nonsevere coronary stenosis. Journal of Magnetic Resonance Imaging. 2008; 27(5):1005-1011

114. Barraclough K, Gale CP, Hall R. Assessment of chest pain in a low risk patient: Is the exercise tolerance test obsolete? BMJ (Online). 2015; 350 (no pagination)(h1905)

115. Baszko A, Ochotny R, Blaszyk K, Popiel M, Straburzynska-Migaj E, Cieslinski A et al. Correlation of ST-segment depression during ambulatory electrocardiographic monitoring with myocardial perfusion and left ventricular function. American Journal of Cardiology. 2001; 87(8):959-963; A953

116. Bateman TM, Heller GV, McGhie AI, Courter SA, Golub RA, Case JA et al. Multicenter investigation comparing a highly efficient half-time stress-only attenuation correction approach against standard rest-stress Tc-99m SPECT imaging. Journal of Nuclear Cardiology. 2009; 16(5):726-735

117. Bateman TM, Heller GV, McGhie AI, Friedman JD, Case JA, Bryngelson JR et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: comparison with ECG-gated Tc-99m sestamibi SPECT. Journal of Nuclear Cardiology. 2006; 13(1):24-33

118. Bauer RW, Kerl JM, Fischer N, Burkhard T, Larson MC, Ackermann H et al. Dual-energy CT for the assessment of chronic myocardial infarction in patients with chronic coronary artery disease: comparison with 3-T MRI. AJR American Journal of Roentgenology. 2010; 195(3):639-646

119. Bauernfeind T, Preda I, Szakolczai K, Szucs E, Kiss RG, Simonyi G et al. Diagnostic value of the left atrial electrical potentials detected by body surface potential mapping in the prediction of coronary artery disease. International Journal of Cardiology. 2011; 150(3):315-318

120. Beck E, Santillan O, Cecconi G, De Cicco A, Krasnov C. Dobutamine stress test specificity and sensitivity of continuous ST-segment monitoring in 12 simultaneous standard ECG leads. Revista Española de Cardiología. 2002; 55(6):616-621

121. Becker A, Leber A, White CW, Becker C, Reiser MF, Knez A. Multislice computed tomography for determination of coronary artery disease in a symptomatic patient population. The International Journal of Cardiovascular Imaging. 2007; 23(3):361-367

122. Becker CR, Kleffel T, Crispin A, Knez A, Young J, Schoepf UJ et al. Coronary artery calcium measurement: Agreement of multirow detector and electron beam CT. American Journal of Roentgenology. 2001; 176(5):1295-1298

123. Becker HCR. Cardiac computed tomography as a cost-effective approach for diagnosing coronary artery disease? Expert Review of Cardiovascular Therapy. 2012; 10(7):823-825

124. Bedetti G, Pasanisi EM, Pizzi C, Turchetti G, Lore C. Economic analysis including long-term risks and costs of alternative diagnostic strategies to evaluate patients with chest pain. Cardiovascular Ultrasound. 2008; 6:21

125. Beigel R, Oieru D, Goitein O, Chouraqui P, Konen E, Shamiss A et al. Usefulness of routine use of multidetector coronary computed tomography in the "fast track" evaluation of patients with acute chest pain. American Journal of Cardiology. 2009; 103(11):1481-1486

126. Bekler A, Altun B, Barutcu A, Temiz A, Gazi E, Erbag G et al. Electrocardiographic changes not related to coronary thrombus formation in non-st elevated acute coronary syndrome. Anatolian Journal of Clinical Investigation. 2014; 8(1):1-5

127. Belardinelli R, Lacalaprice F, Tiano L, Mucai A, Perna GP. Cardiopulmonary exercise testing is more accurate than ECG-stress testing in diagnosing myocardial ischemia in subjects with chest pain. International Journal of Cardiology. 2014; 174(2):337-342

128. Ben Bouallegue F, Roubille F, Lattuca B, Cung TT, Macia JC, Gervasoni R et al. SPECT Myocardial Perfusion Reserve in Patients with Multivessel Coronary Disease: Correlation with Angiographic Findings and Invasive Fractional Flow Reserve Measurements. Journal of Nuclear Medicine. 2015; 56(11):1712-1717

129. Benchimol D, Mazanof M, Dubroca B, Benchimol H, Bernard V, Couffinhal T et al. Detection of coronary stenoses by stress echocardiography using a previously implanted pacemaker for ventricular pacing: preliminary report of a new method. Clinical Cardiology. 2000; 23(11):842-848

130. Benedek T, Gyongyosi M, Benedek I. Multislice computed tomographic coronary angiography for quantitative assessment of culprit lesions in acute coronary syndromes. Canadian Journal of Cardiology. 2013; 29(3):364-371

131. Benedek T, Jako B, Benedek I. Plaque quantification by coronary CT and intravascular ultrasound identifies a low CT density core as a marker of plaque instability in acute coronary syndromes. International Heart Journal. 2014; 55(1):22-28

132. Benkiran M, Mariano-Goulart D, Bourdon A, Sibille L, Bouallegue FB. Is computed tomography attenuation correction more efficient than gated single photon emission computed tomography analysis in improving the diagnostic performance of myocardial perfusion imaging in patients with low prevalence of ischemic heart disease? Nuclear Medicine Communications. 2015; 36(1):69-77

133. Bennett P, Dyer P. Exercise stress test utility in patients with chest pain presumed to be of cardiac origin. Acute Medicine. 2013; 12(3):146-150

134. Berdahl CT, Vermeulen MJ, Larson DB, Schull MJ. Emergency department computed tomography utilization in the United States and Canada. Annals of Emergency Medicine. 2013; 62(5):486-494.e483

135. Bergeron S, Ommen SR, Bailey KR, Oh JK, McCully RB, Pellikka PA. Exercise echocardiographic findings and outcome of patients referred for evaluation of dyspnea. Journal of the American College of Cardiology. 2004; 43(12):2242-2246

136. Beslic N, Kucukalic-Selimovic E. Comparison of the diagnostic capabilities of noninvasive methods for early detection of coronary artery disease. Medicinski Arhiv. 2011; 65(2):96-98

137. Bettencourt N, Chiribiri A, Schuster A, Ferreira N, Sampaio F, Duarte R et al. Cardiac magnetic resonance myocardial perfusion imaging for detection of functionally significant obstructive coronary artery disease: a prospective study. International Journal of Cardiology. 2013; 168(2):765-773

138. Bettencourt N, Chiribiri A, Schuster A, Ferreira N, Sampaio F, Pires-Morais G et al. Direct comparison of cardiac magnetic resonance and multidetector computed tomography stress-rest perfusion imaging for detection of coronary artery disease. Journal of the American College of Cardiology. 2013; 61(10):1099-1107

139. Bettencourt N, Ferreira N, Chiribiri A, Schuster A, Sampaio F, Santos L et al. Additive value of magnetic resonance coronary angiography in a comprehensive cardiac magnetic resonance stress-rest protocol for detection of functionally significant coronary artery disease: a pilot study. Circulation Cardiovascular imaging. 2013; 6(5):730-738

140. Bettencourt N, Ferreira ND, Leite D, Carvalho M, Ferreira Wda S, Schuster A et al. CAD detection in patients with intermediate-high pre-test probability: low-dose CT delayed enhancement detects ischemic myocardial scar with moderate accuracy but does not improve performance of a stress-rest CT perfusion protocol. JACC: Cardiovascular Imaging. 2013; 6(10):1062-1071

141. Better N, Karthikeyan G, Vitola J, Fatima A, Peix A, Novak MD et al. Performance of rest myocardial perfusion imaging in the management of acute chest pain in the emergency room in developing nations (PREMIER trial). Journal of Nuclear Cardiology. 2012; 19(6):1146-1153

142. Beule T, Vanhoenacker P, Booij M, Ardies L, Bladt O. Cost effectiveness of multi detector CT angiography of the coronary arteries for the diagnosis of suspected non-ST elevation acute coronary syndrome (NSTE-ACS) in the emergency department: mathematical analysis with a decision model (Structured abstract). Journal Belge de Radiologie. 2010; 93(6):285-291

143. Bhardwaj A, Truong QA, Peacock WF, Yeo KT, Storrow A, Thomas S et al. A multicenter comparison of established and emerging cardiac biomarkers for the diagnostic evaluation of chest pain in the emergency department. American Heart Journal. 2011; 162(2):276-282

144. Bholasingh R, Cornel JH, Kamp O, de Winter RJ, Heidenreich PA, Brandt RR et al. Dobutamine stress echocardiography is a valuable diagnostic test for predischarge risk assessment in low-risk chest pain patients. Evidence-Based Cardiovascular Medicine. 2003; 7(4):203-205

145. Bholasingh R, Cornel JH, Kamp O, van Straalen JP, Sanders GT, Tijssen JG et al. Prognostic value of predischarge dobutamine stress echocardiography in chest pain patients with a negative cardiac troponin T. Journal of the American College of Cardiology. 2003; 41(4):596-602

146. Biagini E, Shaw LJ, Poldermans D, Schinkel AF, Rizzello V, Elhendy A et al. Accuracy of non-invasive techniques for diagnosis of coronary artery disease and prediction of cardiac events in patients with left bundle branch block: a meta-analysis. European Journal of Nuclear Medicine and Molecular Imaging. 2006; 33(12):1442-1451

147. Bialek S, Gorko D, Zajkowska A, Koltowski L, Grabowski M, Stachurska A et al. Release kinetics of circulating miRNA-208a in the early phase of myocardial infarction. Kardiologia Polska. 2015; 73(8):613-619

148. Biener M, Mueller M, Vafaie M, Keller T, Blankenberg S, White HD et al. Comparison of a 3-hour versus a 6-hour sampling-protocol using high-sensitivity cardiac troponin T for rule-out and rule-in of non-STEMI in an unselected emergency department population. International Journal of Cardiology. 2013; 167(4):1134-1140

149. Biglands JD, Magee DR, Sourbron SP, Plein S, Greenwood JP, Radjenovic A. Comparison of the Diagnostic Performance of Four Quantitative Myocardial Perfusion Estimation Methods Used in Cardiac MR Imaging: CE-MARC Substudy. Radiology. 2015; 275(2):393-402

150. Bischoff B, Kantert C, Meyer T, Hadamitzky M, Martinoff S, Schomig A et al. Cardiovascular risk assessment based on the quantification of coronary calcium in contrast-enhanced coronary computed tomography angiography. European Heart Journal Cardiovascular Imaging. 2012; 13(6):468-475

151. Blankstein R, Ahmed W, Bamberg F, Rogers IS, Schlett CL, Nasir K et al. Comparison of exercise treadmill testing with cardiac computed tomography angiography among patients presenting to the emergency room with chest pain: the Rule Out Myocardial Infarction Using Computer-Assisted Tomography (ROMICAT) study. Circulation Cardiovascular imaging. 2012; 5(2):233-242

152. Blinder G, Benhorin J, Koukoui D, Zimam R, Hiller N. The value of electrocardiography-gated multi-slice computed tomography in the evaluation of patients with chest pain. Israel Medical Association Journal: Imaj. 2005; 7(7):419-423

153. Blomstrand P, Maret E, Ohlsson J, Scheike M, Karlsson JE, Safstrom K et al. Pulsed tissue Doppler imaging for the detection of myocardial ischaemia, a comparison with myocardial perfusion SPECT. Clinical Physiology and Functional Imaging. 2004; 24(5):289-295

154. BlueCross BlueShield Association. Computed tomographic coronary angiography in the evaluation of patients with acute chest pain. Chicago IL. Blue Cross Blue Shield Association (BCBS), 2011. Available from: http://www.scct.org/advocacy/coverage/BCBSA_TEC_CCT.pdf

155. Body R, Carley S, McDowell G, Jaffe AS, France M, Cruickshank K et al. Rapid exclusion of acute myocardial infarction in patients with undetectable troponin using a high-sensitivity assay. Journal of the American College of Cardiology. 2011; 58(13):1332-1339

156. Bogaert J, Eitel I. Role of cardiovascular magnetic resonance in acute coronary syndrome. Global Cardiology Science and Practice. 2015; 2015 (2) (no pagination)(24)

157. Boglioli L, Taviloglu G, Minutillo J, DePasquale E, Lee K, Gleim GW et al. Effect of very early radionuclide perfusion imaging on hospital length of stay in patients presenting to the emergency department with chest pain. Cardiovascular Reviews and Reports. 2001; 22(1):33-36+45

158. Boiten HJ, Van Der Sijde JN, Ruitinga PR, Valkema R, Geleijnse ML, Sijbrands EJG et al. Long-term prognostic value of exercise technetium-99m tetrofosmin myocardial perfusion single-photon emission computed tomography. Journal of Nuclear Cardiology. 2012; 19(5):907-913

159. Bom MJ, van der Zee PM, Cornel JH, van der Zant FM, Knol RJ. Diagnostic and Therapeutic Usefulness of Coronary Computed Tomography Angiography in Out-Clinic Patients Referred for Chest Pain. American Journal of Cardiology. 2015; 116(1):30-36

160. Borna C, Frostred KL, Ekelund U. Predictive role of high sensitivity troponin T within four hours from presentation of acute coronary syndrome in elderly patients. BMC Emergency Medicine. 2016; 16:1

161. Boussel L, Gamondes D, Staat P, Elicker BM, Revel D, Douek P. Acute chest pain with normal coronary angiogram: role of contrast-enhanced multidetector computed tomography in the differential diagnosis between myocarditis and myocardial infarction. Journal of Computer Assisted Tomography. 2008; 32(2):228-232

162. Bouzas-Mosquera A, Peteiro J, Broullon FJ, Alvarez-Garcia N, Rodriguez-Garrido JL, Mosquera VX et al. Incremental value of exercise echocardiography over exercise electrocardiography in a chest pain unit. European Journal of Internal Medicine. 2015; 26(9):720-725

163. Bradburn M, Goodacre SW, Fitzgerald P, Coats T, Gray A, Hassan T et al. Interhospital variation in the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers). Emergency Medicine Journal. 2012; 29(3):233-238

164. Branch KR, Bresnahan BW, Veenstra DL, Shuman WP, Weintraub WS, Busey JM et al. Economic outcome of cardiac CT-based evaluation and standard of care for suspected acute coronary syndrome in the emergency department: a decision analytic model. Academic Radiology. 2012; 19(3):265-273

165. Branch KR, Busey J, Mitsumori LM, Strote J, Caldwell JH, Busch JH et al. Diagnostic performance of resting CT myocardial perfusion in patients with possible acute coronary syndrome. AJR American Journal of Roentgenology. 2013; 200(5):W450-457

166. Branch KR, Strote J, Shuman WP, Mitsumori LM, Busey JM, Rue T et al. Diagnostic accuracy and clinical outcomes of ECG-gated, whole chest CT in the emergency department. PLoS ONE [Electronic Resource]. 2013; 8(4):e61121

167. Brodoefel H, Burgstahler C, Tsiflikas I, Reimann A, Schroeder S, Claussen CD et al. Dual-source CT: effect of heart rate, heart rate variability, and calcification on image quality and diagnostic accuracy. Radiology. 2008; 247(2):346-355

168. Brodoefel H, Reimann A, Burgstahler C, Schumacher F, Herberts T, Tsiflikas I et al. Noninvasive coronary angiography using 64-slice spiral computed tomography in an unselected patient collective: effect of heart rate, heart rate variability and coronary calcifications on image quality and diagnostic accuracy. European Journal of Radiology. 2008; 66(1):134-141

169. Brodoefel H, Tsiflikas I, Burgstahler C, Reimann A, Thomas C, Schroeder S et al. Cardiac dual-source computed tomography: Effect of body mass index on image quality and diagnostic accuracy. Investigative Radiology. 2008; 43(10):712-718

170. Brodov Y, Gransar H, Dey D, Shalev A, Germano G, Friedman JD et al. Combined Quantitative Assessment of Myocardial Perfusion and Coronary Artery Calcium Score by Hybrid 82Rb PET/CT Improves Detection of Coronary Artery Disease. Journal of Nuclear Medicine. 2015; 56(9):1345-1350

171. Brogsitter C, Gruning T, Weise R, Wielepp P, Lindner O, Korfer R et al. 18F-FDG PET for detecting myocardial viability: validation of 3D data acquisition. Journal of Nuclear Medicine. 2005; 46(1):19-24

172. Brown TL, Merrill J, Hill P, Bengel FM. Relationship of coronary calcium and myocardial perfusion in individuals with chest pain. Assessed by integrated rubidium-82 PET-CT. Nuclear-Medizin. 2008; 47(6):255-260

173. Bruins Slot MH, van der Heijden GJ, Rutten FH, van der Spoel OP, Mast EG, Bredero AC et al. Heart-type Fatty acid-binding protein in Acute Myocardial infarction Evaluation (FAME): background and design of a diagnostic study in primary care. BMC Cardiovascular Disorders. 2008; 8:8

174. Bruins Slot MH, van der Heijden GJ, Stelpstra SD, Hoes AW, Rutten FH. Point-of-care tests in suspected acute myocardial infarction: a systematic review. International Journal of Cardiology. 2013; 168(6):5355-5362

175. Bruins Slot MHE, Reitsma JB, Rutten FH, Hoes AW, Van Der Heijden GJMG. Heart-type fatty acid-binding protein in the early diagnosis of acute myocardial infarction: A systematic review and meta-analysis. Heart. 2010; 96(24):1957-1963

176. Buccelletti F, Galiuto L, Marsiliani D, Iacomini P, Mattogno P, Carroccia A et al. Comparison of diagnostic accuracy between three different rules of interpreting high sensitivity troponin T results. Internal and Emergency Medicine. 2012; 7(4):365-370

177. Bucerius J, Joe AY, Lindstaedt I, Manka-Waluch A, Reichmann K, Ezziddin S et al. Single- vs. dual-head SPECT for detection of myocardial ischemia and viability in a large study population. Clinical Imaging. 2007; 31(4):228-233

178. Buckert D, Mariyadas M, Walcher T, Rasche V, Wohrle J, Rottbauer W et al. Angiographic validation of magnetic resonance assessment of myocardium at risk in non-ST-elevation myocardial infarction. The International Journal of Cardiovascular Imaging. 2013; 29(6):1295-1301

179. Budge LP, Salerno M. The role of cardiac magnetic resonance in the evaluation of patients presenting with suspected or confirmed acute coronary syndrome. Cardiology Research and Practice. 2011; 1 (1) (no pagination)(605785)

180. Budoff MJ, Achenbach S, Duerinckx A. Clinical utility of computed tomography and magnetic resonance techniques for noninvasive coronary angiography. Journal of the American College of Cardiology. 2003; 42(11):1867-1878

181. Budoff MJ, Jollis JG, Dowe D, Min J, Group VCTS. Diagnostic accuracy of coronary artery calcium for obstructive disease: results from the ACCURACY trial. International Journal of Cardiology. 2013; 166(2):505-508

182. Budoff MJ, Rasouli ML, Shavelle DM, Gopal A, Gul KM, Mao SS et al. Cardiac CT angiography (CTA) and nuclear myocardial perfusion imaging (MPI)-a comparison in detecting significant coronary artery disease. Academic Radiology. 2007; 14(3):252-257

183. Burris AC, Boura JA, Raff GL, Chinnaiyan KM. Triple Rule Out Versus Coronary CT Angiography in Patients with Acute Chest Pain Results from the ACIC Consortium. JACC: Cardiovascular Imaging. 2015; 8(7):817-825

184. Busch JL, Alessio AM, Caldwell JH, Gupta M, Mao S, Kadakia J et al. Myocardial hypo-enhancement on resting computed tomography angiography images accurately identifies myocardial hypoperfusion. Journal of Cardiovascular Computed Tomography. 2011; 5(6):412-420

185. Cabeda EV, Falcao AM, Soares J, Jr., Rochitte CE, Nomura CH, Avila LF et al. Dipyridamole stress myocardial perfusion by computed tomography in patients with left bundle branch block. Arquivos Brasileiros de Cardiologia. 2015; 105(6):614-624

186. Cademartiri F, Maffei E, Notarangelo F, Ugo F, Palumbo A, Lina D et al. 64-slice computed tomography coronary angiography: diagnostic accuracy in the real world. Radiologia Medica. 2008; 113(2):163-180

187. Cademartiri F, Maffei E, Palumbo A, Malago R, Alberghina F, Aldrovandi A et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in patients with low-to-intermediate risk. Radiologia Medica. 2007; 112(7):969-981

188. Cadth. Assessment of high sensitivity cardiac troponin T assay for the rapid diagnosis of acute coronary syndrome and acute myocardial infarction in the emergency room: a review of the clinical and economic evidence. Ottawa. 2012. Available from: http://www.ncbi.nlm.nih.gov/books/NBK168953/pdf/Bookshelf_NBK168953.pdf

189. Candell-Riera J, Oller-Martinez G, de Leon G, Castell-Conesa J, Aguade-Bruix S. Yield of early rest and stress myocardial perfusion single-photon emission computed tomography and electrocardiographic exercise test in patients with atypical chest pain, nondiagnostic electrocardiogram, and negative biochemical markers in the emergency department. American Journal of Cardiology. 2007; 99(12):1662-1666

190. Candell-Riera J, Oller-Martínez G, Pereztol-Valdés O, Castell-Conesa J, Aguadé-Bruix S, García-Alonso C et al. [Early myocardial perfusion gated-SPECT in patients with chest pain and non-diagnostic ECG in the emergency department]. Revista Española de Cardiología. 2004; 57(3):225-233

191. Carlsson M, Hedeer F, Engblom H, Arheden H. Head-to-head comparison of a 2-day myocardial perfusion gated SPECT protocol and cardiac magnetic resonance late gadolinium enhancement for the detection of myocardial infarction. Journal of Nuclear Cardiology. 2013; 20(5):797-803

192. Carrinho M, Moraes A, Morcerf F, Medeiros C, Castier M, Romeo LJ. Myocardial contrast echocardiography in patients with suspected or known coronary artery disease: comparison with myocardial nuclear scintigraphy. Arquivos Brasileiros de Cardiologia. 2004; 83(5):419-423; 414-418

193. Carroll C, Al KM, Stevens JW, Leaviss J, Goodacre S, Collinson PO et al. Heart-type fatty acid binding protein as an early marker for myocardial infarction: systematic review and meta-analysis. [Review]. Emergency Medicine Journal. 2013; 30(4):280-286

194. Caymaz O, Fak AS, Tezcan H, Inanir SS, Toprak A, Tokay S et al. Correlation of myocardial fractional flow reserve with thallium-201 SPECT imaging in intermediate-severity coronary artery lesions. Journal of Invasive Cardiology. 2000; 12(7):345-350

195. Celik A, Ozturk A, Ozbek K, Kadi H, Koc F, Ceyhan K et al. Heart rate variability and turbulence to determine true coronary artery disease in patients with ST segment depression without angina during exercise stress testing. Clinical & Investigative Medicine - Medecine Clinique et Experimentale. 2011; 34(6):E349

196. Ceriani E, Rusconi AM, Gruppo di Autoformazione M. Highly sensitive troponin and diagnostic accuracy in acute myocardial infarction. Internal and Emergency Medicine. 2012; 7(5):471-473

197. Chammas E, Yatim A, Hage C, Sokhn K, Tarcha W, Ghanem G. Evaluation of Tc-99m tetrofosmin scan for coronary artery disease diagnosis. Asian Cardiovascular & Thoracic Annals. 2002; 10(3):244-247

198. Chan GW, Sites FD, Shofer FS, Hollander JE. Impact of stress testing on 30-day cardiovascular outcomes for low-risk patients with chest pain admitted to floor telemetry beds. American Journal of Emergency Medicine. 2003; 21(4):282-287

199. Chandra A, Rudraiah L, Zalenski RJ. Stress testing for risk stratification of patients with low to moderate probability of acute cardiac ischemia. Emergency Medicine Clinics of North America. 2001; 19(1):87-103

200. Chandraratna PA, Kuznetsov VA, Mohar DS, Sidarous PF, Scheutz J, Krinochkin DV et al. Comparison of squatting stress echocardiography and dobutamine stress echocardiography for the diagnosis of coronary artery disease. Echocardiography. 2012; 29(6):695-699

201. Chandraratna PA, Mohar DS, Sidarous PF, Brar P, Miller J, Shah N et al. Evaluation of non-ST segment elevation acute chest pain syndromes with a novel low-profile continuous imaging ultrasound transducer. Echocardiography. 2012; 29(8):895-899

202. Chang AM, Shofer FS, Weiner MG, Synnestvedt MB, Litt HI, Baxt WG et al. Actual financial comparison of four strategies to evaluate patients with potential acute coronary syndromes. Academic Emergency Medicine. 2008; 15(7):649-655

203. Chang SA, Choi SI, Choi EK, Kim HK, Jung JW, Chun EJ et al. Usefulness of 64-slice multidetector computed tomography as an initial diagnostic approach in patients with acute chest pain. American Heart Journal. 2008; 156(2):375-383

204. Chao SP, Law WY, Kuo CJ, Hung HF, Cheng JJ, Lo HM et al. The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. European Heart Journal. 2010; 31(15):1916-1923

205. Chaosuwannakit N, Kiatchoosakun S, Makarawate P. Diagnostic accuracy of 128-row multidetector computed tomography coronary angiography in the diagnosis of significant

coronary artery stenosis. Journal of the Medical Association of Thailand. 2012; 95(12):1548-1555

206. Cheezum MK, Bittencourt MS, Hulten EA, Scirica BM, Villines TC, Blankstein R. Coronary computed tomographic angiography in the emergency room: state of the art. Expert Review of Cardiovascular Therapy. 2014; 12(2):241-253

207. Chen GB, Wu H, He XJ, Huang JX, Yu D, Xu WY et al. Adenosine stress thallium-201 myocardial perfusion imaging for detecting coronary artery disease at an early stage. Journal of X-Ray Science & Technology. 2013; 21(2):317-322

208. Chen JW, Hsu NW, Ting CT, Lee WL, Lin SJ, Chang MS. Clinical strategy for coronary microvascular dysfunction in patients with chest pain of unknown cause - The role of treadmill exercise testing. Acta Cardiologica Sinica. 1999; 15(2):81-92

209. Chen L, Wang X, Bao J, Geng C, Xia Y, Wang J. Direct comparison of cardiovascular magnetic resonance and single-photon emission computed tomography for detection of coronary artery disease: a meta-analysis. PLoS ONE [Electronic Resource]. 2014; 9(2):e88402

210. Chen LC, Ding PY, Chen JW, Wu MH, Liu JC, Lan GY et al. Coronary artery calcium determined by electron beam computed tomography for predicting angiographic coronary artery disease in moderate- to high-risk Chinese patients. Cardiology. 2001; 95(4):183-189

211. Chen ML, Mo YH, Wang YC, Lo HS, Wang PC, Chao IM et al. 64-slice CT angiography for the detection of functionally significant coronary stenoses: comparison with stress myocardial perfusion imaging. British Journal of Radiology. 2012; 85(1012):368-376

212. Chen SJ, Kuo LT, Wang CH, Cherng WJ, Yang NI, Cheng CW. The diagnostic value of computed tomographic coronary angiography in patients with acute myocardial infarction versus stable angina pectoris: a preliminary report. Chang Gung Medical Journal. 2011; 34(3):268-277

213. Chen Z, Duan Q, Xue X, Chen L, Ye W, Jin L et al. Noninvasive detection of coronary artery stenoses with contrast-enhanced whole-heart coronary magnetic resonance angiography at 3.0 T. Cardiology. 2010; 117(4):284-290

214. Chenevier-Gobeaux C, Meune C, Freund Y, Wahbi K, Claessens YE, Doumenc B et al. Influence of age and renal function on high-sensitivity cardiac troponin T diagnostic accuracy for the diagnosis of acute myocardial infarction. American Journal of Cardiology. 2013; 111(12):1701-1707

215. Cheng AS, Pegg TJ, Karamitsos TD, Searle N, Jerosch-Herold M, Choudhury RP et al. Cardiovascular magnetic resonance perfusion imaging at 3-tesla for the detection of coronary artery disease: a comparison with 1.5-tesla. Journal of the American College of Cardiology. 2007; 49(25):2440-2449

216. Cheng C, Wang Q, You W, Chen M, Xia J. MiRNAs as biomarkers of myocardial infarction: A meta-analysis. PloS One. 2014; 9(2)

217. Cheng L, Jing S, Zhang Y. A comparison study between CT angiography with 64-multislice spiral computed tomography and selective X-ray coronary angiography. Experimental and Therapeutic Medicine. 2013; 5(3):969-971

218. Cheng L, Ma L, Schoenhagen P, Ye H, Lou X, Gao Y et al. Comparison of three-dimensional volume-targeted thin-slab FIESTA magnetic resonance angiography and 64-multidetector computed tomographic angiography for the identification of proximal coronary stenosis. International Journal of Cardiology. 2013; 167(6):2969-2976

219. Cheng SL, Agarwal P, Selvester RH, Ellestad MH. Significance of QT dispersion in exercise testing in patients with chest pain. Cardiovascular Reviews and Reports. 2000; 21(11):618-623

220. Cheng W, Zeng M, Arellano C, Mafori W, Goldin J, Krishnam M et al. Detection of myocardial perfusion abnormalities: standard dual-source coronary computed tomography angiography versus rest/stress technetium-99m single-photo emission CT. British Journal of Radiology. 2010; 83(992):652-660

221. Chiou KR, Huang WC, Lin SL, Hsieh PL, Liu CP, Tsay DG et al. Real-time dobutamine stress myocardial contrast echocardiography for detecting coronary artery disease: correlating abnormal wall motion and disturbed perfusion. Canadian Journal of Cardiology. 2004; 20(12):1237-1243

222. Chiu CW, So NM, Lam WW, Chan KY, Sanderson JE. Combined first-pass perfusion and viability study at MR imaging in patients with non-ST segment-elevation acute coronary syndromes: feasibility study. Radiology. 2003; 226(3):717-722

223. Choo KS, Hwangbo L, Kim JH, Park YH, Kim JS, Kim J et al. Adenosine-stress low-dose single-scan CT myocardial perfusion imaging using a 128-slice dual-source CT: a comparison with fractional flow reserve. Acta Radiologica. 2013; 54(4):389-395

224. Chow BJ, Dennie C, Hoffmann U, So D, de Kemp RA, Ruddy TD et al. Comparison of computed tomographic angiography versus rubidium-82 positron emission tomography for the detection of patients with anatomical coronary artery disease. Canadian Journal of Cardiology. 2007; 23(10):801-807

225. Christ M, Popp S, Pohlmann H, Poravas M, Umarov D, Bach R et al. Implementation of high sensitivity cardiac troponin T measurement in the emergency department. American Journal of Medicine. 2010; 123(12):1134-1142

226. Christiaens L, Duchat F, Boudiaf M, Tasu JP, Fargeaudou Y, Ledref O et al. Impact of 64-slice coronary CT on the management of patients presenting with acute chest pain: results of a prospective two-centre study. European Radiology. 2012; 22(5):1050-1058

227. Collinson P, Gaze D, Goodacre S, Bradburn M. RATPAC CBE (Randomised Assessment of Treatment using Panel Assay of Cardiac markers - Contemporary Biomarker Evaluation). Health Technology Assessment. 2013; 17(15):1-17

228. Conti A, Alesi A, Aspesi G, Bigiarini S, Bianchi S, Angeli E et al. Comparison of exercise electrocardiogram and exercise echocardiography in intermediate-risk chest pain patients. American Journal of Emergency Medicine. 2015; 33(1):7-13

229. Conti A, Gallini C, Costanzo E, Ferri P, Matteini M, Paladini B et al. Early detection of myocardial ischaemia in the emergency department by rest or exercise (99m)Tc tracer myocardial SPET in patients with chest pain and non-diagnostic ECG. European Journal of Nuclear Medicine. 2001; 28(12):1806-1810

230. Conti A, Luzzi M, Borchi N, Donati M, Viviani G, Boni V et al. Early predicition of myocardial ischaemia with adenosine stress perfusion imaging in patients presenting with chest pain. European Heart Journal. 2010; 31:576

231. Conti A, Luzzi M, Borchi N, Poggioni C, Zanobetti M, Vincidomini S et al. Adenosine stress perfusion imaging and prediction of myocardial ischemia in patients with hypertension and low-risk chest pain in the emergency setting. Journal of Hypertension. 2010; 28:e151

232. Conti A, Sammicheli L, Gallini C, Costanzo EN, Antoniucci D, Barletta G. Assessment of patients with low-risk chest pain in the emergency department: Head-to-head comparison of exercise stress echocardiography and exercise myocardial SPECT. American Heart Journal. 2005; 149(5):894-901

233. Conti A, Vanni S, Sammicheli L, Raveggi S, Camaiti A, Pieralli F et al. Yield of nuclear scan strategy in chest pain unit evaluation of special populations. Nuclear Medicine Communications. 2008; 29(12):1106-1112

234. Coronary computed tomographic angiography in clinical practice: State of the art. Radiologic Clinics of North America. 2015; 53(2):287-296

235. CT angiography outperforms stress testing in diagnosing coronary artery disease. Cardiovascular Journal of Africa. 2009; 20(3):191

236. Cuda G, Lentini M, Gallo L, Lucia FG, Giacinto CL, Mancuso S et al. High sensitive troponin T in individuals with chest pain of presumed ischemic origin. Frontiers in Bioscience. 2012; 4:2322-2327

237. Cullen L, Mueller C, Parsonage WA, Wildi K, Greenslade JH, Twerenbold R et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. Journal of the American College of Cardiology. 2013; 62(14):1242-1249

238. Cury RC, Feuchtner GM, Batlle JC, Pena CS, Janowitz W, Katzen BT et al. Triage of patients presenting with chest pain to the emergency department: implementation of coronary CT angiography in a large urban health care system.[Erratum appears in AJR Am J Roentgenol. 2013 Mar;200(3):705]. AJR American Journal of Roentgenology. 2013; 200(1):57-65

239. Dall Armellina E, Choudhury RP. The role of cardiovascular magnetic resonance in patients with acute coronary syndromes. Progress in Cardiovascular Diseases. 2011; 54(3):230-239

240. de Winter RJ, Lijmer JG, Koster RW, Hoek FJ, Sanders GT. Diagnostic accuracy of myoglobin concentration for the early diagnosis of acute myocardial infarction. Annals of Emergency Medicine. 2000; 35(2):113-120

241. Dedic A, Genders TS, Nieman K, Hunink MG. Imaging strategies for acute chest pain in the emergency department. AJR American Journal of Roentgenology. 2013; 200(1):W26-38

242. Dedic A, Kurata A, Lubbers M, Meijboom WB, van Dalen B, Snelder S et al. Prognostic implications of non-culprit plaques in acute coronary syndrome: non-invasive assessment with coronary CT angiography. European Heart Journal Cardiovascular Imaging. 2014; 15(11):1231-1237

243. Dedic A, Lubbers MM, Schaap J, Lammers J, Lamfers EJ, Rensing BJ et al. Coronary CT Angiography for Suspected ACS in the Era of High-Sensitivity Troponins: Randomized Multicenter Study. Journal of the American College of Cardiology. 2016; 67(1):16-26

244. Dedic A, Ten Kate GJ, Neefjes LA, Rossi A, Dharampal A, Rood PP et al. Coronary CT angiography outperforms calcium imaging in the triage of acute coronary syndrome. International Journal of Cardiology. 2013; 167(4):1597-1602

245. Department of Science and Technology - Brazilian Health Technology Assessment General Coordination (DECIT-CGATS). BRATS 04: Multiple-detector computed tomography for the diagnosis of coronary artery disease Brasilia. Department of Science and Technology - Brazilian Health Technology Assessment General Coordination (DECIT-CGATS), 2008.

246. Diercks DB, Kirk JD, Naser S, Turnipseed S, Amsterdam EA. Value of high-sensitivity C-reactive protein in low risk chest pain observation unit patients. International Journal of Emergency Medicine. 2011; 4:37

247. Diercks DB, Mumma BE, Frank Peacock W, Hollander JE, Safdar B, Mahler SA et al. Incremental value of objective cardiac testing in addition to physician impression and serial contemporary troponin measurements in women. Academic Emergency Medicine. 2013; 20(3):265-270

248. Diercks DB, Peacock WFt, Hollander JE, Singer AJ, Birkhahn R, Shapiro N et al. Diagnostic accuracy of a point-of-care troponin I assay for acute myocardial infarction within 3 hours after presentation in early presenters to the emergency department with chest pain. American Heart Journal. 2012; 163(1):74-80.e74

249. Dodd JD, Kalva S, Pena A, Bamberg F, Shapiro MD, Abbara S et al. Emergency cardiac CT for suspected acute coronary syndrome: qualitative and quantitative assessment of coronary, pulmonary, and aortic image quality. AJR American Journal of Roentgenology. 2008; 191(3):870-877

250. Dorgelo J, Willems TP, Geluk CA, van Ooijen PM, Zijlstra F, Oudkerk M. Multidetector computed tomography-guided treatment strategy in patients with non-ST elevation acute coronary syndromes: a pilot study. European Radiology. 2005; 15(4):708-713

251. Duchenne J, Mestres S, Dublanchet N, Combaret N, Marceau G, Caumon L et al. Diagnostic accuracy of copeptin sensitivity and specificity in patients with suspected non-ST-elevation myocardial infarction with troponin I below the 99th centile at presentation. BMJ Open. 2014; 4(3):e004449

252. Durand E, Delos A, Chaib A, Lepillier A, Beretti S, Collin M et al. Performance assessment of a chest pain unit: Preliminary 2-year experience in the European Georges Pompidou Hospital. Archives of Cardiovascular Diseases. 2009; 102(12):803-809

253. Duvall WL, Levine E, Baber U, Croft LB, Sahni S, Sethi S et al. A simple scoring tool for the evaluation of patients in an emergency department chest pain unit. Connecticut Medicine. 2014; 78(8):465-474

254. Edmond JJ, French JK, Henny H, Belz LM, West T, Stewart R et al. Prospective evaluation of a chest pain pathway at Green Lane Hospital. New Zealand Medical Journal. 2002; 115(1158):U103

255. Eggers KM, Venge P, Lindahl B. High-sensitive cardiac troponin T outperforms novel diagnostic biomarkers in patients with acute chest pain. Clinica Chimica Acta. 2012; 413(13-14):1135-1140

256. Einstein AJ, Johnson LL, DeLuca AJ, Kontak AC, Groves DW, Stant J et al. Radiation dose and prognosis of ultra-low-dose stress-first myocardial perfusion SPECT in patients with chest pain using a high-efficiency camera. Journal of Nuclear Medicine. 2015; 56(4):545-551

257. Estrada JN, Rolandi F, Bansilal S, Averbuj P, Natale E, Zafar MU et al. Stress testing and troponin in unstable coronary syndromes: the status trial-clinical outcomes and resource use. American Heart Hospital Journal. 2006; 4(4):252-258; quiz 259-260

258. Fanaroff AC, Rymer JA, Goldstein SA, Simel DL, Newby LK. Does This Patient With Chest Pain Have Acute Coronary Syndrome?: The Rational Clinical Examination Systematic Review. JAMA. 2015; 314(18):1955-1965

259. Ferencik M, Schlett CL, Bamberg F, Truong QA, Nichols JH, Pena AJ et al. Comparison of traditional cardiovascular risk models and coronary atherosclerotic plaque as detected by computed tomography for prediction of acute coronary syndrome in patients with acute chest pain. Academic Emergency Medicine. 2012; 19(8):934-942

260. Ferencik M, Schlett CL, Ghoshhajra BB, Kriegel MF, Joshi SB, Maurovich-Horvat P et al. A computed tomography-based coronary lesion score to predict acute coronary syndrome among patients with acute chest pain and significant coronary stenosis on coronary computed tomographic angiogram. American Journal of Cardiology. 2012; 110(2):183-189

261. Fernandez-Friera L, Garcia-Alvarez A, Bagheriannejad-Esfahani F, Malick W, Mirelis JG, Sawit ST et al. Diagnostic value of coronary artery calcium scoring in low-intermediate risk patients evaluated in the emergency department for acute coronary syndrome. American Journal of Cardiology. 2011; 107(1):17-23

262. Fesmire FM, Buchheit RC, Cao Y, Severance HW, Jang Y, Heath GW. Risk stratification in chest pain patients undergoing nuclear stress testing: the Erlanger Stress Score. Critical Pathways in Cardiology: A Journal of Evidence-Based Medicine. 2012; 11(4):171-176

263. Fesmire FM, Hughes AD, Fody EP, Jackson AP, Fesmire CE, Gilbert MA et al. The Erlanger chest pain evaluation protocol: a one-year experience with serial 12-lead ECG monitoring, two-hour delta serum marker measurements, and selective nuclear stress testing to identify and exclude acute coronary syndromes. Annals of Emergency Medicine. 2002; 40(6):584-594

264. Fesmire FM, Hughes AD, Stout PK, Wojcik JF, Wharton DR. Selective dual nuclear scanning in low-risk patients with chest pain to reliably identify and exclude acute coronary syndromes. Annals of Emergency Medicine. 2001; 38(3):207-215

265. Fitzgerald P, Goodacre SW, Cross E, Dixon S. Cost-effectiveness of point-of-care biomarker assessment for suspected myocardial infarction: the randomized assessment of treatment using panel Assay of cardiac markers (RATPAC) trial. Academic Emergency Medicine. 2011; 18(5):488-495

266. Forberg JL, Hilmersson CE, Carlsson M, Arheden H, Bjork J, Hjalte K et al. Negative predictive value and potential cost savings of acute nuclear myocardial perfusion imaging in low risk patients with suspected acute coronary syndrome: a prospective single blinded study. BMC Emergency Medicine. 2009; 9:12

267. Freund Y, Chenevier-Gobeaux C, Bonnet P, Claessens YE, Allo JC, Doumenc B et al. High-sensitivity versus conventional troponin in the emergency department for the diagnosis of acute myocardial infarction. Critical Care (London, England). 2011; 15(3):R147

268. Gaemperli O, Husmann L, Schepis T, Koepfli P, Valenta I, Jenni W et al. Coronary CT angiography and myocardial perfusion imaging to detect flow-limiting stenoses: a potential gatekeeper for coronary revascularization? European Heart Journal. 2009; 30(23):2921-2929

269. Gaemperli O, Schepis T, Koepfli P, Valenta I, Soyka J, Leschka S et al. Accuracy of 64-slice CT angiography for the detection of functionally relevant coronary stenoses as assessed with myocardial perfusion SPECT. European Journal of Nuclear Medicine and Molecular Imaging. 2007; 34(8):1162-1171

270. Gaibazzi N, Reverberi C, Badano L. Usefulness of contrast stress-echocardiography or exercise-electrocardiography to predict long-term acute coronary syndromes in patients presenting with chest pain without electrocardiographic abnormalities or 12-hour troponin elevation. American Journal of Cardiology. 2011; 107(2):161-167

271. Gaibazzi N, Reverberi C, Squeri A, De Iaco G, Ardissino D, Gherli T. Contrast stress echocardiography for the diagnosis of coronary artery disease in patients with chest pain but without acute coronary syndrome: incremental value of myocardial perfusion. Journal of the American Society of Echocardiography. 2009; 22(4):404-410

272. Gaibazzi N, Rigo F, Reverberi C. Detection of coronary artery disease by combined assessment of wall motion, myocardial perfusion and coronary flow reserve: a multiparametric contrast stress-echocardiography study. Journal of the American Society of Echocardiography. 2010; 23(12):1242-1250

273. Gaibazzi N, Rigo F, Squeri A, Ugo F, Reverberi C. Incremental value of contrast myocardial perfusion to detect intermediate versus severe coronary artery stenosis during stress-echocardiography. Cardiovascular Ultrasound. 2010; 8:16

274. Galassi AR, Azzarelli S, Lupo L, Mammana C, Foti R, Tamburino C et al. Accuracy of exercise testing in the assessment of the severity of myocardial ischemia as determined by means of technetium-99m tetrofosmin SPECT scintigraphy. Journal of Nuclear Cardiology. 2000; 7(6):575-583

275. Gallagher MJ, Ross MA, Raff GL, Goldstein JA, O'Neill WW, O'neil B. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low-risk chest pain patients. Annals of Emergency Medicine. 2007; 49(2):125-136

276. Gao D, Ning N, Guo Y, Ning W, Niu X, Yang J. Computed tomography for detecting coronary artery plaques: a meta-analysis. Atherosclerosis. 2011; 219(2):603-609

277. Gargiulo P, Dellegrottaglie S, Bruzzese D, Savarese G, Scala O, Ruggiero D et al. The prognostic value of normal stress cardiac magnetic resonance in patients with known or suspected coronary artery disease: a meta-analysis. Circulation Cardiovascular imaging. 2013; 6(4):574-582

278. Gargiulo P, Petretta M, Bruzzese D, Cuocolo A, Prastaro M, D'Amore C et al. Myocardial perfusion scintigraphy and echocardiography for detecting coronary artery disease in hypertensive patients: a meta-analysis. European Journal of Nuclear Medicine and Molecular Imaging. 2011; 38(11):2040-2049

279. Garrido IP, Peteiro J, Garcia-Lara J, Montserrat L, Aldama G, Vazquez-Rodriguez JM et al. Prognostic value of exercise echocardiography in patients with diabetes mellitus and known or suspected coronary artery disease. American Journal of Cardiology. 2005; 96(1):9-12

280. Gaudio C, Mirabelli F, Alessandra L, Nguyen BL, Di Michele S, Corsi F et al. Noninvasive assessment of coronary artery stenoses by multidetector-row spiral computed tomography: comparison with conventional angiography. European Review for Medical and Pharmacological Sciences. 2005; 9(1):13-21

281. Gayed IW, Raslan OA, Bhosale PR, Perrier ND, Wei W, Gladish G. Significant coronary calcification detected using contrast-enhanced computed tomography: Is it an indication for further investigation? Clinical Nuclear Medicine. 2010; 35(6):404-408

282. Gebker R, Frick M, Jahnke C, Berger A, Schneeweis C, Manka R et al. Value of additional myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of intermediate coronary artery disease. The International Journal of Cardiovascular Imaging. 2012; 28(1):89-97

283. Gebker R, Jahnke C, Paetsch I, Kelle S, Schnackenburg B, Fleck E et al. Diagnostic performance of myocardial perfusion MR at 3 T in patients with coronary artery disease. radiolgoy. 2008; 247(1):57-63

284. Geleijnse ML, Elhendy A, Kasprzak JD, Rambaldi R, van Domburg RT, Cornel JH et al. Safety and prognostic value of early dobutamine-atropine stress echocardiography in patients with spontaneous chest pain and a non-diagnostic electrocardiogram. European Heart Journal. 2000; 21(5):397-406

285. Genders TS, Ferket BS, Dedic A, Galema TW, Mollet NR, de Feyter PJ et al. Coronary computed tomography versus exercise testing in patients with stable chest pain: comparative effectiveness and costs. International Journal of Cardiology. 2013; 167(4):1268-1275

286. Gentile R, Vitarelli A, Schillaci O, Lagana B, Gianni C, Rossi-Fanelli F et al. Diagnostic accuracy and prognostic implications of stress testing for coronary artery disease in the elderly. Italian Heart Journal: Official Journal of the Italian Federation of Cardiology. 2001; 2(7):539-545

287. George RT, Arbab-Zadeh A, Miller JM, Kitagawa K, Chang HJ, Bluemke DA et al. Adenosine stress 64- and 256-row detector computed tomography angiography and perfusion imaging: a pilot study evaluating the transmural extent of perfusion abnormalities to predict atherosclerosis causing myocardial ischemia. Circulation Cardiovascular imaging. 2009; 2(3):174-182

288. George RT, Arbab-Zadeh A, Miller JM, Vavere AL, Bengel FM, Lardo AC et al. Computed tomography myocardial perfusion imaging with 320-row detector computed tomography accurately detects myocardial ischemia in patients with obstructive coronary artery disease. Circulation Cardiovascular imaging. 2012; 5(3):333-340

289. George RT, Mehra VC, Chen MY, Kitagawa K, Arbab-Zadeh A, Miller JM et al. Myocardial CT perfusion imaging and SPECT for the diagnosis of coronary artery disease: a head-to-head comparison from the CORE320 multicenter diagnostic performance study.[Erratum appears in Radiology. 2015 Feb;274(2):626; PMID: 25625749]. Radiology. 2014; 272(2):407-416

290. Gerbaud E, Harcaut E, Coste P, Erickson M, Lederlin M, Labeque JN et al. Cardiac magnetic resonance imaging for the diagnosis of patients presenting with chest pain, raised troponin, and unobstructed coronary arteries. The International Journal of Cardiovascular Imaging. 2012; 28(4):783-794

291. Gerber BL, Coche E, Pasquet A, Ketelslegers E, Vancraeynest D, Grandin C et al. Coronary artery stenosis: direct comparison of four-section multi-detector row CT and 3D navigator MR imaging for detection--initial results. Radiology. 2005; 234(1):98-108

292. Ghoshhajra BB, Maurovich-Horvat P, Techasith T, Medina HM, Verdini D, Sidhu MS et al. Infarct detection with a comprehensive cardiac CT protocol. Journal of Cardiovascular Computed Tomography. 2012; 6(1):14-23

293. Ghostine S, Caussin C, Daoud B, Habis M, Perrier E, Pesenti-Rossi D et al. Non-invasive detection of coronary artery disease in patients with left bundle branch block using 64-slice computed tomography. Journal of the American College of Cardiology. 2006; 48(10):1929-1934

294. Giannitsis E, Becker M, Kurz K, Hess G, Zdunek D, Katus HA. High-sensitivity cardiac troponin T for early prediction of evolving non-ST-segment elevation myocardial infarction in patients with suspected acute coronary syndrome and negative troponin results on admission. Clinical Chemistry. 2010; 56(4):642-650

295. Giannitsis E, Kehayova T, Vafaie M, Katus HA. Combined testing of high-sensitivity troponin T and copeptin on presentation at prespecified cutoffs improves rapid rule-out of non-ST-segment elevation myocardial infarction. Clinical Chemistry. 2011; 57(10):1452-1455

296. Giavarina D, Carta M, Fortunato A, Wratten ML, Hartmann O, Soffiati G. Copeptin and high sensitive troponin for a rapid rule out of acute myocardial infarction? Clinical Laboratory. 2011; 57(9-10):725-730

297. Girzadas M, Varga P, Dajani K. A single-center experience of detecting coronary anomalies on 64-slice computed tomography. Journal of Cardiovascular Medicine. 2009; 10(11):842-847

298. Goldenberg R, Eilot D, Begelman G, Walach E, Ben-Ishai E, Peled N. Computer-aided simple triage (CAST) for coronary CT angiography (CCTA). International Journal of Computer Assisted Radiology and Surgery. 2012; 7(6):819-827

299. Goldstein JA, Chinnaiyan KM, Abidov A, Achenbach S, Berman DS, Hayes SW et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. Journal of the American College of Cardiology. 2011; 58(14):1414-1422

300. Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. Journal of the American College of Cardiology. 2007; 49(8):863-871

301. Gonzalez P, Dussaillant G, Gutierrez D, Berrocal I, Alay R, Otarola S. Single-photon emission computed tomography for the assessment of ventricular perfusion and function. Revista Medica de Chile. 2013; 141(9):1136-1142

302. Gonzalez P, Massardo T, Jofre MJ, Yovanovich J, Prat H, Munoz A et al. 201Tl myocardial SPECT detects significant coronary artery disease between 50% and 75% angiogram stenosis. Revista Española de Medicina Nuclear. 2005; 24(5):305-311

303. Goodacre S, Locker T, Arnold J, Angelini K, Morris F. Which diagnostic tests are most useful in a chest pain unit protocol? BMC Emergency Medicine. 2005; 5:6

304. Goodacre S, Thokala P, Carroll C, Stevens JW, Leaviss J, Al Khalaf M et al. Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome. Health Technology Assessment (Winchester, England). 2013; 17(1):v-vi, 1-188

305. Gouya H, Varenne O, Trinquart L, Touze E, Vignaux O, Spaulding C et al. Coronary artery stenosis in high-risk patients: 64-Section CT and coronary angiography - Prospective study and analysis of discordance. Radiology. 2009; 252(2):377-385

306. Graf S, Khorsand A, Gwechenberger M, Novotny C, Kletter K, Sochor H et al. Typical chest pain and normal coronary angiogram: cardiac risk factor analysis versus PET for detection of microvascular disease. Journal of Nuclear Medicine. 2007; 48(2):175-181

307. Greenslade JH, Parsonage W, Ho A, Scott A, Dalton E, Hammett C et al. Utility of Routine Exercise Stress Testing among Intermediate Risk Chest Pain Patients Attending an Emergency Department. Heart, Lung & Circulation. 2015; 24(9):879-884

308. Greenwood JP, Motwani M, Maredia N, Brown JM, Everett CC, Nixon J et al. Comparison of cardiovascular magnetic resonance and single-photon emission computed tomography in women with suspected coronary artery disease from the Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease (CE-MARC) Trial. Circulation. 2014; 129(10):1129-1138

309. Greif M, von Ziegler F, Bamberg F, Tittus J, Schwarz F, D'Anastasi M et al. CT stress perfusion imaging for detection of haemodynamically relevant coronary stenosis as defined by FFR. Heart. 2013; 99(14):1004-1011

310. Greulich S, Bruder O, Parker M, Schumm J, Grun S, Schneider S et al. Comparison of exercise electrocardiography and stress perfusion CMR for the detection of coronary artery disease in women. Journal of Cardiovascular Magnetic Resonance. 2012; 14:36

311. Greupner J, Zimmermann E, Grohmann A, Dubel HP, Althoff TF, Borges AC et al. Head-to-head comparison of left ventricular function assessment with 64-row computed tomography, biplane left cineventriculography, and both 2- and 3-dimensional transthoracic echocardiography: comparison with magnetic resonance imaging as the reference standard.[Erratum appears in J Am Coll Cardiol. 2012 Jul 31;60(5):481 Note: Althoff, Till [corrected to Althoff, Till F]]. Journal of the American College of Cardiology. 2012; 59(21):1897-1907

312. Groothuis JG, Beek AM, Meijerink MR, Brinckman SL, Heymans MW, van Kuijk C et al. Positive predictive value of computed tomography coronary angiography in clinical practice. International Journal of Cardiology. 2012; 156(3):315-319

313. Guo SL, Guo YM, Zhai YN, Ma B, Wang P, Yang KH. Diagnostic accuracy of first generation dual-source computed tomography in the assessment of coronary artery disease: a meta-analysis from 24 studies. The International Journal of Cardiovascular Imaging. 2011; 27(6):755-771

314. Gupta M, Kadakia J, Jug B, Mao SS, Budoff MJ. Detection and quantification of myocardial perfusion defects by resting single-phase 64-slice cardiac computed tomography angiography compared with SPECT myocardial perfusion imaging. Coronary Artery Disease. 2013; 24(4):290-297

315. Haaf P, Drexler B, Reichlin T, Twerenbold R, Reiter M, Meissner J et al. High-sensitivity cardiac troponin in the distinction of acute myocardial infarction from acute cardiac noncoronary artery disease. Circulation. 2012; 126(1):31-40

316. Haberl R, Tittus J, Bohme E, Czernik A, Richartz BM, Buck J et al. Multislice spiral computed tomographic angiography of coronary arteries in patients with suspected coronary artery disease: an effective filter before catheter angiography? American Heart Journal. 2005; 149(6):1112-1119

317. Hamilton-Craig C, Fifoot A, Hansen M, Pincus M, Chan J, Walters DL et al. Diagnostic performance and cost of CT angiography versus stress ECG--a randomized prospective study of suspected acute coronary syndrome chest pain in the emergency department (CT-COMPARE). International Journal of Cardiology. 2014; 177(3):867-873

318. Hammerer-Lercher A, Ploner T, Neururer S, Schratzberger P, Griesmacher A, Pachinger O et al. High-sensitivity cardiac troponin T compared with standard troponin T testing on emergency department admission: how much does it add in everyday clinical practice? Journal of the American Heart Association. 2013; 2(3):e000204

319. Han PP, Fang W, Tian YQ, Gao Y, Yang MF, Zhang XL et al. Comparison of coronary CT angiography and stress/rest myocardial perfusion SPECT imaging in a Chinese population. Clinical Nuclear Medicine. 2013; 38(10):798-804

320. Hansen M, Ginns J, Seneviratne S, Slaughter R, Premaranthe M, Samardhi H et al. The value of dual-source 64-slice CT coronary angiography in the assessment of patients presenting to an acute chest pain service. Heart, Lung & Circulation. 2010; 19(4):213-218

321. Hartlage G, Janik M, Anadiotis A, Veledar E, Oshinski J, Kremastinos D et al. Prognostic value of adenosine stress cardiovascular magnetic resonance and dobutamine stress echocardiography in patients with low-risk chest pain. The International Journal of Cardiovascular Imaging. 2012; 28(4):803-812

322. Hascoet S, Bongard V, Chabbert V, Marachet MA, Rousseau H, Charpentier S et al. Early triage of emergency department patients with acute coronary syndrome: contribution of 64-slice computed tomography angiography. Archives of Cardiovascular Diseases. 2012; 105(6-7):338-346

323. Heitner JF, Klem I, Rasheed D, Chandra A, Kim HW, Van Assche LM et al. Stress cardiac MR imaging compared with stress echocardiography in the early evaluation of patients who present to the emergency department with intermediate-risk chest pain. Radiology. 2014; 271(1):56-64

324. Hermann LK, Weingart SD, Duvall WL, Henzlova MJ. The limited utility of routine cardiac stress testing in emergency department chest pain patients younger than 40 years. Annals of Emergency Medicine. 2009; 54(1):12-16

325. Heuschmid M, Burgstahler C, Reimann A, Brodoefel H, Mysal I, Haeberle E et al. Usefulness of noninvasive cardiac imaging using dual-source computed tomography in an unselected population with high prevalence of coronary artery disease. American Journal of Cardiology. 2007; 100(4):587-592

326. Heydari B, Leipsic J, Mancini GB, Min JK, Labounty T, Taylor C et al. Diagnostic performance of high-definition coronary computed tomography angiography performed with multiple radiation dose reduction strategies. Canadian Journal of Cardiology. 2011; 27(5):606-612

327. Hjortshoj S, Venge P, Ravkilde J. Clinical performance of a new point-of-care cardiac troponin I assay compared to three laboratory troponin assays. Clinica Chimica Acta. 2011; 412(3-4):370-375

328. Hochholzer W, Reichlin T, Stelzig C, Hochholzer K, Meissner J, Breidthardt T et al. Impact of soluble fms-like tyrosine kinase-1 and placental growth factor serum levels for risk stratification and early diagnosis in patients with suspected acute myocardial infarction. European Heart Journal. 2011; 32(3):326-335

329. Hoeller R, Rubini Gimenez M, Reichlin T, Twerenbold R, Zellweger C, Moehring B et al. Normal presenting levels of high-sensitivity troponin and myocardial infarction. Heart. 2013; 99(21):1567-1572

330. Hoffmann U, Bamberg F, Chae CU, Nichols JH, Rogers IS, Seneviratne SK et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. Journal of the American College of Cardiology. 2009; 53(18):1642-1650

331. Hoffmann U, Pena AJ, Moselewski F, Ferencik M, Abbara S, Cury RC et al. MDCT in early triage of patients with acute chest pain. AJR American Journal of Roentgenology. 2006; 187(5):1240-1247

332. Hoffmann U, Truong QA, Fleg JL, Goehler A, Gazelle S, Wiviott S et al. Design of the rule out myocardial ischemia/infarction using computer assisted tomography: A multicenter randomized comparative effectiveness trial of cardiac computed tomography versus alternative triage strategies in patients with acute chest pain in the emergency department. American Heart Journal. 2012; 163(3):330-338.e331

333. Hoffmann U, Truong QA, Schoenfeld DA, Chou ET, Woodard PK, Nagurney JT et al. Coronary CT angiography versus standard evaluation in acute chest pain. New England Journal of Medicine. 2012; 367(4):299-308

334. Hollander JE, Chang AM, Shofer FS, McCusker CM, Baxt WG, Litt HI. Coronary computed tomographic angiography for rapid discharge of low-risk patients with potential acute coronary syndromes. Annals of Emergency Medicine. 2009; 53(3):295-304

335. Hollander JE, Litt HI, Chase M, Brown AM, Kim W, Baxt WG. Computed tomography coronary angiography for rapid disposition of low-risk emergency department patients with chest pain syndromes. Academic Emergency Medicine. 2007; 14(2):112-116

336. Holubkov R, Pepine CJ, Rickens C, Reichek N, Rogers WJ, Sharaf BL et al. Electrocardiogram abnormalities predict angiographic coronary artery disease in women with chest pain: results from the NHLBI WISE Study. Clinical Cardiology. 2002; 25(12):553-558

337. Hou Y, Ma Y, Fan W, Wang Y, Yu M, Vembar M et al. Diagnostic accuracy of low-dose 256-slice multi-detector coronary CT angiography using iterative reconstruction in patients with suspected coronary artery disease. European Radiology. 2014; 24(1):3-11

338. Hsu CC, Chen YW, Hao CL, Chong JT, Lee CI, Tan HT et al. Comparison of automated 4D-MSPECT and visual analysis for evaluating myocardial perfusion in coronary artery disease. Kaohsiung Journal of Medical Sciences. 2008; 24(9):445-452

339. Hulten E, Villines TC, Cheezum MK, Berman DS, Dunning A, Achenbach S et al. Usefulness of coronary computed tomography angiography to predict mortality and myocardial infarction among Caucasian, African and East Asian ethnicities (from the CONFIRM [Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter] Registry). American Journal of Cardiology. 2013; 111(4):479-485

340. Husmann L, Gaemperli O, Schepis T, Scheffel H, Valenta I, Hoefflinghaus T et al. Accuracy of quantitative coronary angiography with computed tomography and its dependency on plaque composition. International Journal of Cardiovascular Imaging. 2008; 24(8):895-904

341. Husmann L, Herzog BA, Gaemperli O, Tatsugami F, Burkhard N, Valenta I et al. Diagnostic accuracy of computed tomography coronary angiography and evaluation of stress-only single-photon emission computed tomography/computed tomography hybrid imaging: comparison of prospective electrocardiogram-triggering vs. retrospective gating. European Heart Journal. 2009; 30(5):600-607

342. Husmann L, Scheffel H, Valenta I, Schepis T, Gaemperli O, Aepli U et al. Impact of hypertension on the diagnostic accuracy of coronary angiography with computed tomography. The International Journal of Cardiovascular Imaging. 2008; 24(7):763-770

343. Husmann L, Wiegand M, Valenta I, Gaemperli O, Schepis T, Siegrist PT et al. Diagnostic accuracy of myocardial perfusion imaging with single photon emission computed tomography and positron emission tomography: A comparison with coronary angiography. International Journal of Cardiovascular Imaging. 2008; 24(5):511-518

344. Hwang IC, Kim YJ, Kim KH, Shin DH, Lee SP, Kim HK et al. Diagnostic yield of coronary angiography in patients with acute chest pain: role of noninvasive test. American Journal of Emergency Medicine. 2014; 32(1):1-6

345. Identifying acute ischemia in the ED: How useful are the available tests? Consultant. 1997; 37(6):1719-1720

346. Iglesias-Garriz I, Rodriguez MA, Garcia-Porrero E, Ereno F, Garrote C, Suarez G. Emergency nontraumatic chest pain: use of stress echocardiography to detect significant coronary artery stenosis. Journal of the American Society of Echocardiography. 2005; 18(11):1181-1186

347. Imran S, Ali L, Abid AR, Mohyuddin MT, Aziz ur R. Role of exercise stress testing in evaluation of patients presenting with chest pain. Journal of Postgraduate Medical Institute. 2006; 20(1):25-29

348. Inoue K, Suwa S, Ohta H, Itoh S, Maruyama S, Masuda N et al. Heart fatty acid-binding protein offers similar diagnostic performance to high-sensitivity troponin T in emergency room patients presenting with chest pain. Circulation Journal. 2011; 75(12):2813-2820

349. investigators S-H. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial.[Erratum appears in Lancet. 2015 Jun 13;385(9985):2354; PMID: 26088642]. Lancet. 2015; 385(9985):2383-2391

350. Irfan A, Reichlin T, Twerenbold R, Meister M, Moehring B, Wildi K et al. Early diagnosis of myocardial infarction using absolute and relative changes in cardiac troponin concentrations. American Journal of Medicine. 2013; 126(9):781-788.e782

351. Isoda H, Itagaki Y, Nomura N, Urushida T, Naitou A, Watanabe A et al. Usefulness of dual SPECT with Tc-99m pyrophosphate and Tl-201 to predict further events after acute myocardial infarction with single-vessel coronary artery disease. Clinical Nuclear Medicine. 1999; 24(4):227-231

352. Iyengar SS, Morgan-Hughes G, Ukoumunne O, Clayton B, Davies EJ, Nikolaou V et al. diagnostic accuracy of high-definition CT cononary angiograpgy in high-risk patients. Clinical Radiology. 2016; 71(2):151-158

353. Jahnke C, Nagel E, Gebker R, Kokocinski T, Kelle S, Manka R et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. Circulation. 2007; 115(13):1769-1776

354. Jahnke C, Paetsch I, Schnackenburg B, Gebker R, Kohler U, Bornstedt A et al. Comparison of radial and Cartesian imaging techniques for MR coronary angiography. Journal of Cardiovascular Magnetic Resonance. 2004; 6(4):865-875

355. Jang JY, Sohn IS, Kim JN, Park JH, Park CB, Jin ES et al. Treadmill exercise stress echocardiography in patients with no history of coronary artery disease: a single-center experience in korean population. Sunhwangi. 2011; 41(9):528-534

356. Januzzi JL, Jr., Bamberg F, Lee H, Truong QA, Nichols JH, Karakas M et al. High-sensitivity troponin T concentrations in acute chest pain patients evaluated with cardiac computed tomography. Circulation. 2010; 121(10):1227-1234

357. Jeetley P, Burden L, Senior R. Stress echocardiography is superior to exercise ECG in the risk stratification of patients presenting with acute chest pain with negative Troponin. European Journal of Echocardiography. 2006; 7(2):155-164

358. Jimenez-Hoyuela Garcia JM, Robledo Carmona J, Ortega Lozano S, Martinez del Valle Torres M, Delgado Garcia A, Gomez Doblas JJ. Myocardial perfusion scintigraphy in the emergency department for the evaluation and triage of patients with chest pain and a non-diagnostic electrocardiogram. [Spanish, English]. Investigacion Cardiovascular. 2006; 9(1):7-18

359. Johnson TR, Nikolaou K, Becker A, Leber AW, Rist C, Wintersperger BJ et al. Dual-source CT for chest pain assessment. European Radiology. 2008; 18(4):773-780

360. Johnson TR, Nikolaou K, Wintersperger BJ, Knez A, Boekstegers P, Reiser MF et al. ECG-gated 64-MDCT angiography in the differential diagnosis of acute chest pain. AJR American Journal of Roentgenology. 2007; 188(1):76-82

361. Jug B, Gupta M, Papazian J, Li D, Tsang J, Bhatia H et al. Diagnostic performance of 64-slice multidetector coronary computed tomographic angiography in women. Journal of Nuclear Cardiology. 2012; 19(6):1154-1161

362. Kadokami T, Ando S, Momii H, Yoshida M, Narita S, Fukunaga T et al. Diagnostic performance of cardiac fusion images from myocardial perfusion imaging and multislice computed tomography coronary angiography for assessment of hemodynamically significant coronary artery lesions: an observational study. Nuclear Medicine Communications. 2012; 33(1):60-68

363. Kajander S, Joutsiniemi E, Saraste M, Pietila M, Ukkonen H, Saraste A et al. Cardiac positron emission tomography/computed tomography imaging accurately detects anatomically and functionally significant coronary artery disease. Circulation. 2010; 122(6):603-613

364. Kaminek M, Myslivecek M, Husak V, Koranda P, Skvarilova M, Ostransky J et al. The accuracy of myocardial perfusion SPECT imaging in the evaluation of coronary artery disease in women and men. Nuclear Medicine Review. 2001; 4(2):69-72

365. Kamiya K, Sakakibara M, Asakawa N, Yamada S, Yoshitani T, Iwano H et al. Cardiac magnetic resonance performs better in the detection of functionally significant coronary artery stenosis compared to single-photon emission computed tomography and dobutamine stress echocardiography. Circulation Journal. 2014; 78(10):2468-2476

366. Kang DH, Kang SJ, Song JM, Choi KJ, Hong MK, Song JK et al. Efficacy of myocardial contrast echocardiography in the diagnosis and risk stratification of acute coronary syndrome. American Journal of Cardiology. 2005; 96(11):1498-1502

367. Kang X, Berman DS, Lewin H, Miranda R, Erel J, Friedman JD et al. Comparative ability of myocardial perfusion single-photon emission computed tomography to detect coronary artery disease in patients with and without diabetes mellitus. American Heart Journal. 1999; 137(5):949-957

368. Karacavus S, Tutus A, Topsakal R, Kula M, Celik A, Abdulrezzak U et al. Evaluation of the diagnostic and prognostic use of gated myocardial perfusion single-photon emission computed tomography in patients with acute chest pain: comparison with the SYNTAX score. Nuclear Medicine Communications. 2015; 36(9):945-951

369. Kaul S, Senior R, Firschke C, Wang XQ, Lindner J, Villanueva FS et al. Incremental value of cardiac imaging in patients presenting to the emergency department with chest pain and without ST-segment elevation: a multicenter study. American Heart Journal. 2004; 148(1):129-136

370. Kawai Y, Morita K, Nozaki Y, Ohkusa T, Sakurai M, Tamaki N. Diagnostic value of ¹²³I-betamethyl-p-iodophenyl-pentadecanoic acid (BMIPP) single photon emission computed tomography (SPECT) in patients with chest pain - Comparison with rest-stress ^{99m}Tc-tetrofosmin SPECT and coronary angiography. Circulation Journal. 2004; 68(6):547-552

371. Kawecki D, Morawiec B, Monney P, Pellaton C, Wojciechowska C, Jojko J et al. Diagnostic contribution of cardiac magnetic resonance in patients with acute coronary syndrome and culprit-free angiograms. Medical Science Monitor. 2015; 21:171-180

372. Keijer JT, van Rossum AC, van Eenige MJ, Bax JJ, Visser FC, Teule JJ et al. Magnetic resonance imaging of regional myocardial perfusion in patients with single-vessel coronary artery

disease: quantitative comparison with (201)Thallium-SPECT and coronary angiography. Journal of Magnetic Resonance Imaging. 2000; 11(6):607-615

373. Keller T, Tzikas S, Zeller T, Czyz E, Lillpopp L, Ojeda FM et al. Copeptin improves early diagnosis of acute myocardial infarction. Journal of the American College of Cardiology. 2010; 55(19):2096-2106

374. Keller T, Zeller T, Ojeda F, Tzikas S, Lillpopp L, Sinning C et al. Serial changes in highly sensitive troponin I assay and early diagnosis of myocardial infarction. JAMA. 2011; 306(24):2684-2693

375. Keller T, Zeller T, Peetz D, Tzikas S, Roth A, Czyz E et al. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. New England Journal of Medicine. 2009; 361(9):868-877

376. Khan DA, Sharif MS, Khan FA. Diagnostic performance of high-sensitivity troponin T, myeloperoxidase, and pregnancy-associated plasma protein A assays for triage of patients with acute myocardial infarction. Korean Journal of Laboratory Medicine. 2011; 31(3):172-178

377. Kim RJ, Albert TS, Wible JH, Elliott MD, Allen JC, Lee JC et al. Performance of delayed-enhancement magnetic resonance imaging with gadoversetamide contrast for the detection and assessment of myocardial infarction: an international, multicenter, double-blinded, randomized trial. Circulation. 2008; 117(5):629-637

378. Kim SM, Chang SA, Shin W, Choe YH. Dual-energy CT perfusion during pharmacologic stress for the assessment of myocardial perfusion defects using a second-generation dual-source CT: a comparison with cardiac magnetic resonance imaging. Journal of Computer Assisted Tomography. 2014; 38(1):44-52

379. Kim WY, Danias PG, Stuber M, Flamm SD, Plein S, Nagel E et al. Coronary magnetic resonance angiography for the detection of coronary stenoses. New England Journal of Medicine. 2001; 345(26):1863-1869

380. Kim Y, Goto H, Kobayashi K, Sawada Y, Miyake Y, Fujiwara G et al. A new method to evaluate ischemic heart disease: combined use of rest thallium-201 myocardial SPECT and Tc-99m exercise tetrofosmin first pass and myocardial SPECT. Annals of Nuclear Medicine. 1999; 13(3):147-153

381. Kim YJ, Seo JS, Choi BW, Choe KO, Jang Y, Ko YG. Feasibility and diagnostic accuracy of whole heart coronary MR angiography using free-breathing 3D balanced turbo-field-echo with SENSE and the half-fourier acquisition technique. Korean Journal of Radiology. 2006; 7(4):235-242

382. Kirisli HA, Gupta V, Shahzad R, Al Younis I, Dharampal A, Geuns RJ et al. Additional diagnostic value of integrated analysis of cardiac CTA and SPECT MPI using the SMARTVis system in patients with suspected coronary artery disease. Journal of Nuclear Medicine. 2014; 55(1):50-57

383. Kitagawa K, Sakuma H, Nagata M, Okuda S, Hirano M, Tanimoto A et al. Diagnostic accuracy of stress myocardial perfusion MRI and late gadolinium-enhanced MRI for detecting flow-limiting coronary artery disease: a multicenter study. European Radiology. 2008; 18(12):2808-2816

384. Klem I, Greulich S, Heitner JF, Kim H, Vogelsberg H, Kispert EM et al. Value of cardiovascular magnetic resonance stress perfusion testing for the detection of coronary artery disease in women. JACC: Cardiovascular Imaging. 2008; 1(4):436-445

385. Klumpp B, Miller S, Seeger A, May AE, Gawaz MP, Claussen CD et al. Is the diagnostic yield of myocardial stress perfusion MRI impaired by three-vessel coronary artery disease? Acta Radiologica. 2015; 56(2):143-151

386. Klumpp BD, Seeger A, Doesch C, Doering J, Hoevelborn T, Kramer U et al. High resolution myocardial magnetic resonance stress perfusion imaging at 3 T using a 1 M contrast agent. European Radiology. 2010; 20(3):533-541

387. Ko BS, Cameron JD, Leung M, Meredith IT, Leong DP, Antonis PR et al. Combined CT coronary angiography and stress myocardial perfusion imaging for hemodynamically significant stenoses in patients with suspected coronary artery disease: a comparison with fractional flow reserve. JACC: Cardiovascular Imaging. 2012; 5(11):1097-1111

388. Ko SM, Choi JW, Hwang HK, Song MG, Shin JK, Chee HK. Diagnostic performance of combined noninvasive anatomic and functional assessment with dual-source CT and adenosine-induced stress dual-energy CT for detection of significant coronary stenosis. AJR American Journal of Roentgenology. 2012; 198(3):512-520

389. Ko SM, Park JH, Hwang HK, Song MG. Direct comparison of stress- and rest-dual-energy computed tomography for detection of myocardial perfusion defect. The International Journal of Cardiovascular Imaging. 2014; 30 Suppl 1:41-53

390. Ko SM, Song MG, Chee HK, Hwang HK, Feuchtner GM, Min JK. Diagnostic performance of dual-energy CT stress myocardial perfusion imaging: direct comparison with cardiovascular MRI. AJR American Journal of Roentgenology. 2014; 203(6):W605-613

391. Koide Y, Yotsukura M, Yoshino H, Ishikawa K. A new coronary artery disease index of treadmill exercise electrocardiograms based on the step-up diagnostic method. American Journal of Cardiology. 2001; 87(2):142-147

392. Kontos MC, Haney A, Ornato JP, Jesse RL, Tatum JL. Value of simultaneous functional assessment in association with acute rest perfusion imaging for predicting short- and long-term outcomes in emergency department patients with chest pain. Journal of Nuclear Cardiology. 2008; 15(6):774-782

393. Kontos MC, Jesse RL, Anderson FP, Schmidt KL, Ornato JP, Tatum JL. Comparison of myocardial perfusion imaging and cardiac troponin I in patients admitted to the emergency department with chest pain. Circulation. 1999; 99(16):2073-2078

394. Kontos MC, Kurdziel K, McQueen R, Arrowood JA, Jesse RL, Ornato JP et al. Comparison of 2-dimensional echocardiography and myocardial perfusion imaging for diagnosing myocardial infarction in emergency department patients. American Heart Journal. 2002; 143(4):659-667

395. Koo BK, Erglis A, Doh JH, Daniels DV, Jegere S, Kim HS et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. Journal of the American College of Cardiology. 2011; 58(19):1989-1997

396. Krittayaphong R, Mahanonda N, Kangkagate C, Nakyen S, Tanapibunpon P, Chaithiraphan S. Accuracy of magnetic resonance imaging in the diagnosis of coronary artery disease. Journal of the Medical Association of Thailand. 2003; 86 Suppl 1:S59-66

397. Kume N, Mitsuoka H, Hayashida K, Tanaka M. Pentraxin 3 as a biomarker for acute coronary syndrome: comparison with biomarkers for cardiac damage. Journal of Cardiology. 2011; 58(1):38-45

398. Kunimasa T, Sato Y, Matsumoto N, Chiku M, Tani S, Kasama S et al. Detection of coronary artery disease by free-breathing, whole heart coronary magnetic resonance angiography: our initial experience. Heart and Vessels. 2009; 24(6):429-433

399. Kurz K, Giannitsis E, Becker M, Hess G, Zdunek D, Katus HA. Comparison of the new high sensitive cardiac troponin T with myoglobin, h-FABP and cTnT for early identification of myocardial necrosis in the acute coronary syndrome. Clinical Research in Cardiology. 2011; 100(3):209-215

400. Kwong RY, Schussheim AE, Rekhraj S, Aletras AH, Geller N, Davis J et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. Circulation. 2003; 107(4):531-537

401. Langdorf MI, Wei E, Ghobadi A, Rudkin SE, Lotfipour S. Echocardiography to supplement stress electrocardiography in emergency department chest pain patients. The Western Journal of Emergency Medicine. 2010; 11(4):379-383

402. Langer C, Peterschroder A, Franzke K, Esdorn H, Korperich H, Meyer H et al. Noninvasive coronary angiography focusing on calcification: Multislice computed tomography compared with magnetic resonance imaging. Journal of Computer Assisted Tomography. 2009; 33(2):179-185

403. Laudon DA, Behrenbeck TR, Wood CM, Bailey KR, Callahan CM, Breen JF et al. Computed tomographic coronary artery calcium assessment for evaluating chest pain in the emergency department: long-term outcome of a prospective blind study. Mayo Clinic Proceedings. 2010; 85(4):314-322

404. Laudon DA, Vukov LF, Breen JF, Rumberger JA, Wollan PC, Sheedy PF, 2nd. Use of electron-beam computed tomography in the evaluation of chest pain patients in the emergency department. Annals of Emergency Medicine. 1999; 33(1):15-21

405. Layritz C, Schmid J, Achenbach S, Ulzheimer S, Wuest W, May M et al. Accuracy of prospectively ECG-triggered very low-dose coronary dual-source CT angiography using iterative reconstruction for the detection of coronary artery stenosis: comparison with invasive catheterization. European Heart Journal Cardiovascular Imaging. 2014; 15(11):1238-1245

406. Lazoura O, Vlychou M, Vassiou K, Kelekis A, Kanavou T, Thriskos P et al. 128-detector-row computed tomography coronary angiography assessing differences in morphology and distribution of atherosclerotic plaques between patients with and without pre-test probability of significant coronary artery disease. European Journal of Radiology. 2011; 77(1):123-130

407. Leber AW, Johnson T, Becker A, von Ziegler F, Tittus J, Nikolaou K et al. Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. European Heart Journal. 2007; 28(19):2354-2360

408. Leber AW, Knez A, Becker A, Becker C, Von Ziegler F, Nikolaou K et al. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: A comparative study with intracoronary ultrasound. Journal of the American College of Cardiology. 2004; 43(7):1241-1247

409. Leber AW, Knez A, Becker C, Becker A, White C, Thilo C et al. Non-invasive intravenous coronary angiography using electron beam tomography and multislice computed tomography. Heart. 2003; 89(6):633-639

410. Lee CP, Hoffmann U, Bamberg F, Brown DF, Chang Y, Swap C et al. Emergency physician estimates of the probability of acute coronary syndrome in a cohort of patients enrolled in a study of coronary computed tomographic angiography. CJEM Canadian Journal of Emergency Medical Care. 2012; 14(3):147-156

411. Lee DP, Fearon WF, Froelicher VF. Clinical utility of the exercise ECG in patients with diabetes and chest pain. Chest. 2001; 119(5):1576-1581

412. Lehmkuhl L, Herz F, Foldyna B, Nagel HD, Grothoff M, Nitzsche S et al. Diagnostic performance of prospectively ECG triggered versus retrospectively ECG gated 64-slice computed tomography coronary angiography in a heterogeneous patient population. European Journal of Radiology. 2011; 80(2):342-348

413. Lei Z, Gu J, Fu Q, Shi H, Xu H, Han P et al. The diagnostic evaluation of dual-source CT (DSCT) in the diagnosis of coronary artery stenoses. Pakistan Journal of Medical Sciences. 2013; 29(1):107-111

414. Lemos AA, Pezzullo JC, Fasani P, Gullo M, Giannitto C, Lo Gullo R et al. Can the unenhanced phase be eliminated from dual-phase CT angiography for chest pain? Implications for diagnostic accuracy in acute aortic intramural hematoma. AJR American Journal of Roentgenology. 2014; 203(6):1171-1180

415. Leschka S, Alkadhi H, Plass A, Desbiolles L, Grunenfelder J, Marincek B et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. European Heart Journal. 2005; 26(15):1482-1487

416. Leschka S, Stolzmann P, Desbiolles L, Baumueller S, Goetti R, Schertler T et al. Diagnostic accuracy of high-pitch dual-source CT for the assessment of coronary stenoses: First experience. European Radiology. 2009; 19(12):2896-2903

417. Leurent G, Langella B, Fougerou C, Lentz PA, Larralde A, Bedossa M et al. Diagnostic contributions of cardiac magnetic resonance imaging in patients presenting with elevated troponin, acute chest pain syndrome and unobstructed coronary arteries. Archives of Cardiovascular Diseases. 2011; 104(3):161-170

418. Li J, Li X, Wei M, Zhao H, Zheng M. Diagnostic accuracy of dual-source computed tomography in the detection of coronary chronic total occlusion:Comparison with invasive angiography. African Journal of Biotechnology. 2011; 10(19):3854-3858

419. Li JM, Li T, Shi RF, Zhang LR. Comparative Analysis between SPECT Myocardial Perfusion Imaging and CT Coronary Angiography for Diagnosis of Coronary Artery Disease. International Journal of Molecular Imaging. 2012; 2012:253475

420. Li M, Du XM, Jin ZT, Peng ZH, Ding J, Li L. The diagnostic performance of coronary artery angiography with 64-MSCT and post 64-MSCT: systematic review and meta-analysis. PLoS ONE [Electronic Resource]. 2014; 9(1):e84937

421. Lim SH, Anantharaman V, Sundram F, Chan EY, Ang ES, Yo SL et al. Stress myocardial perfusion imaging for the evaluation and triage of chest pain in the emergency department: A randomized controlled trial. Journal of Nuclear Cardiology. 2013; 20(6):1002-1012

422. Limon O, Atilla R, Oray NC, Limon G, Doylan O. Serial measurement of heart-type fatty acid binding protein for the rapid diagnosis of acute coronary syndromes in the emergency department. Hong Kong Journal of Emergency Medicine. 2014; 21(4):213-221

423. Lin CJ, Hsu JC, Lai YJ, Wang KL, Lee JY, Li AH et al. Diagnostic accuracy of dual-source CT coronary angiography in a population unselected for degree of coronary artery calcification and without heart rate modification. Clinical Radiology. 2010; 65(2):109-117

424. Lin F, Shaw LJ, Berman DS, Callister TQ, Weinsaft JW, Wong FJ et al. Multidetector computed tomography coronary artery plaque predictors of stress-induced myocardial ischemia by SPECT. Atherosclerosis. 2008; 197(2):700-709

425. Lindahl B, Venge P, James S. The new high-sensitivity cardiac troponin T assay improves risk assessment in acute coronary syndromes.[Erratum appears in Am Heart J. 2011 Feb;161(2):425]. American Heart Journal. 2010; 160(2):224-229

426. Linde JJ, Kofoed KF, Sorgaard M, Kelbaek H, Jensen GB, Nielsen WB et al. Cardiac computed tomography guided treatment strategy in patients with recent acute-onset chest pain: results from the randomised, controlled trial: CArdiac cT in the treatment of acute CHest pain (CATCH). International Journal of Cardiology. 2013; 168(6):5257-5262

427. Lipinski MJ, Escarcega RO, D'Ascenzo F, Magalhaes MA, Baker NC, Torguson R et al. A systematic review and collaborative meta-analysis to determine the incremental value of copeptin for rapid rule-out of acute myocardial infarction. [Review]. American Journal of Cardiology. 2014; 113(9):1581-1591

428. Lippi G, Mattiuzzi C, Cervellin G. Critical review and meta-analysis on the combination of heart-type fatty acid binding protein (H-FABP) and troponin for early diagnosis of acute myocardial infarction. [Review]. Clinical Biochemistry. 2013; 46(1-2):26-30

429. Lippi G, Mattiuzzi C, Comelli I, Cervellin G. Glycogen phosphorylase isoenzyme BB in the diagnosis of acute myocardial infarction: a meta-analysis. Biochemia Medica. 2013; 23(1):78-82

430. Litt HI, Gatsonis C, Snyder B, Singh H, Miller CD, Entrikin DW et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. New England Journal of Medicine. 2012; 366(15):1393-1403

431. Litt HI, Gatsonis C, Snyder B, Singh H, Miller CD, Entrikin DW et al. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial

CT angiography for safe discharge of patients with possible acute coronary syndromes. Lancet (London, England). 2015; 385(9985):2383-2391

432. Lo KY, Leung KF, Chu CM, Loke KL, Chan CK, Yue CS. Prognostic value of adenosine stress myocardial perfusion by cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease. QJM. 2011; 104(5):425-432

433. Lockie T, Ishida M, Perera D, Chiribiri A, De Silva K, Kozerke S et al. High-resolution magnetic resonance myocardial perfusion imaging at 3.0-Tesla to detect hemodynamically significant coronary stenoses as determined by fractional flow reserve.[Erratum appears in J Am Coll Cardiol. 2011 Mar 29;57(13):1501]. Journal of the American College of Cardiology. 2011; 57(1):70-75

434. Loimaala A, Groundstroem K, Pasanen M, Oja P, Vuori I. Comparison of bicycle, heavy isometric, dipyridamole-atropine and dobutamine stress echocardiography for diagnosis of myocardial ischemia. American Journal of Cardiology. 1999; 84(12):1396-1400

435. Loimaala A, Groundstroem K, Pasanen M, Vuori I. Overall and segmental agreement of stress echocardiography. Echocardiography. 1999; 16(6):531-538

436. Lotze U, Lemm H, Heyer A, Muller K. Combined determination of highly sensitive troponin T and copeptin for early exclusion of acute myocardial infarction: first experience in an emergency department of a general hospital. Vascular Health & Risk Management. 2011; 7:509-515

437. Lowenstein J, Tiano C, Marquez G, Presti C, Quiroz C. Simultaneous Analysis of Wall Motion and Coronary Flow Reserve of the Left Anterior Descending Coronary Artery by Transthoracic Doppler Echocardiography during Dipyridamole Stress Echocardiography. Journal of the American Society of Echocardiography. 2003; 16(6):607-613

438. Lu B, Lu JG, Sun ML, Hou ZH, Chen XB, Tang X et al. Comparison of diagnostic accuracy and radiation dose between prospective triggering and retrospective gated coronary angiography by dual-source computed tomography. American Journal of Cardiology. 2011; 107(9):1278-1284

439. Machida H, Tanaka I, Fukui R, Shen Y, Ishikawa T, Tate E et al. Current and Novel Imaging Techniques in Coronary CT. Radiographics. 2015; 35(4):991-1010

440. Macor F, Cassin M, Pitzorno C, Dall'Armellina E, Carniel E, Marciano F et al. Usefulness of exercise test in selected patients coming to the emergency department for acute chest pain. Italian Heart Journal. 2003; 4(2):92-98

441. Maffei E, Martini C, Rossi A, Mollet N, Lario C, Castiglione Morelli M et al. Diagnostic accuracy of second-generation dual-source computed tomography coronary angiography with iterative reconstructions: a real-world experience. Radiologia Medica. 2012; 117(5):725-738

442. Maffei E, Martini C, Tedeschi C, Spagnolo P, Zuccarelli A, Arcadi T et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in a large population of patients without revascularisation: registry data on the impact of calcium score. La Radiologia Medica. 2011; 116(7):1000-1013

443. Maffei E, Martini C, Tedeschi C, Spagnolo P, Zuccarelli A, Arcadi T et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in a large population of patients without revascularisation: registry data on the comparison between male and female population. Radiologia Medica. 2012; 117(1):6-18

444. Maffei E, Martini C, Tedeschi C, Spagnolo P, Zuccarelli A, Arcadi T et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in a large population of patients without revascularisation: registry data in NSTEMI acute coronary syndrome and influence of gender and risk factors. Radiologia Medica. 2011; 116(7):1014-1026

445. Maffei E, Palumbo A, Martini C, Cuttone A, Ugo F, Emiliano E et al. Stress-ECG vs. CT coronary angiography for the diagnosis of coronary artery disease: a "real-world" experience. Radiologia Medica. 2010; 115(3):354-367

446. Maffei E, Palumbo A, Martini C, Notarangelo F, Sacco C, Ugo F et al. Predictive value of computed tomography coronary angiography for the evaluation of acute chest pain: single center preliminary experience. Acta Bio-Medica de l Ateneo Parmense. 2010; 81(3):157-164

447. Maffei E, Palumbo A, Martini C, Ugo F, Lina D, Aldrovandi A et al. Diagnostic accuracy of computed tomography coronary angiography in a high risk symptomatic population. Acta Bio-Medica de l Ateneo Parmense. 2010; 81(1):47-53

448. Magalhaes TA, Cury RC, Pereira AC, Moreira Vde M, Lemos PA, Kalil-Filho R et al. Additional value of dipyridamole stress myocardial perfusion by 64-row computed tomography in patients with coronary stents. Journal of Cardiovascular Computed Tomography. 2011; 5(6):449-458

449. Magalhaes TA, Kishi S, George RT, Arbab-Zadeh A, Vavere AL, Cox C et al. Combined coronary angiography and myocardial perfusion by computed tomography in the identification of flow-limiting stenosis - The CORE320 study: An integrated analysis of CT coronary angiography and myocardial perfusion. Journal of Cardiovascular Computed Tomography. 2015; 9(5):438-445

450. Mahajan N, Polavaram L, Vankayala H, Ference B, Wang Y, Ager J et al. Diagnostic accuracy of myocardial perfusion imaging and stress echocardiography for the diagnosis of left main and triple vessel coronary artery disease: a comparative meta-analysis. Heart. 2010; 96(12):956-966

451. Maintz D, Ozgun M, Hoffmeier A, Quante M, Fischbach R, Manning WJ et al. Whole-heart coronary magnetic resonance angiography: value for the detection of coronary artery stenoses in comparison to multislice computed tomography angiography. Acta Radiologica. 2007; 48(9):967-973

452. Majstorov V, Pop Gjorceva D, Vaskova O, Vavlukis M, Peovska I, Maksimovic J. Gender differences in detecting coronary artery disease with dipyridamole stress myocardial perfusion imaging using 99m-Tc sestamibi gated SPECT. Makedonska Akademija na Naukite i Umetnostite Oddelenie Za Bioloshki i Meditsinski Nauki Prilozi. 2005; 26(1):93-102

453. Makaryus AN, Henry S, Loewinger L, Makaryus JN, Boxt L. Multi-Detector Coronary CT Imaging for the Identification of Coronary Artery Stenoses in a "Real-World" Population. Clinical Medicine Insights Cardiology. 2014; 8(Suppl 4):13-22

454. Malago R, D'Onofrio M, Tavella D, Mantovani W, Brunelli S, Pezzato A et al. Diagnostic accuracy in coronary stenosis: Comparison between visual score and quantitative analysis (quantitative computed tomographic angiography) in coronary angiography by multidetector computed tomographyycoronary angiography and quantitative analysis (quantitative coronary angiography) in conventional coronary angiography. Journal of Computer Assisted Tomography. 2010; 34(5):652-659

455. Malago R, Pezzato A, Barbiani C, Alfonsi U, D'Onofrio M, Tavella D et al. Role of coronary angiography MDCT in the clinical setting: changes in diagnostic workup in the real world. Radiologia Medica. 2012; 117(6):939-952

456. Malago R, Pezzato A, Barbiani C, Tavella D, Vallerio P, Pasini AF et al. Role of MDCT coronary angiography in the clinical setting: economic implications. Radiologia Medica. 2013; 118(8):1294-1308

457. Maltagliati A, Berti M, Muratori M, Tamborini G, Zavalloni D, Berna G et al. Exercise echocardiography versus exercise electrocardiography in the diagnosis of coronary artery disease in hypertension. American Journal of Hypertension. 2000; 13(7):796-801

458. Manini AF, Dannemann N, Brown DF, Butler J, Bamberg F, Nagurney JT et al. Limitations of risk score models in patients with acute chest pain. American Journal of Emergency Medicine. 2009; 27(1):43-48

459. Manka R, Paetsch I, Kozerke S, Moccetti M, Hoffmann R, Schroeder J et al. Whole-heart dynamic three-dimensional magnetic resonance perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve: determination of volumetric myocardial ischaemic burden and coronary lesion location. European Heart Journal. 2012; 33(16):2016-2024

460. Manka R, Wissmann L, Gebker R, Jogiya R, Motwani M, Frick M et al. Multicenter evaluation of dynamic three-dimensional magnetic resonance myocardial perfusion imaging for the

detection of coronary artery disease defined by fractional flow reserve. Circulation Cardiovascular imaging. 2015; 8(5)

461. Mannan M, Bashar MA, Mohammad J, Jahan MU, Momenuzzaman NA, Haque MA. Comparison of coronary CT angiography with conventional coronary angiography in the diagnosis of coronary artery disease. Bangladesh Medical Research Council Bulletin. 2014; 40(1):31-35

462. Maret E, Engvall J, Nylander E, Ohlsson J. Feasibility and diagnostic power of transthoracic coronary Doppler for coronary flow velocity reserve in patients referred for myocardial perfusion imaging. Cardiovascular Ultrasound. 2008; 6:12

463. Markman Filho B, Almeida MC, Markman M, Chaves A, Moretti MA, Ramires JA et al. Stratifying the risk in unstable angina with dobutamine stress echocardiography. Arquivos Brasileiros de Cardiologia. 2006; 87(3):294-299

464. Martuscelli E, Romagnoli A, D'Eliseo A, Razzini C, Tomassini M, Sperandio M et al. Accuracy of thin-slice computed tomography in the detection of coronary stenoses. European Heart Journal. 2004; 25(12):1043-1048

465. Mas-Stachurska A, Miro O, Sitges M, de Caralt TM, Perea RJ, Lopez B et al. Exercise echocardiography and multidetector computed tomography for the evaluation of acute chest pain. Revista Española de Cardiología. 2015; 68(1):17-24

466. Mastrobuoni S, Bastarrika G, Ubilla M, Castano S, Azcarate P, Barrero EA et al. Dual-source ct coronary angiogram in heart transplant recipients in comparison with dobutamine stress echocardiography for detection of cardiac allograft vasculopathy. Transplantation. 2009; 87(4):587-590

467. Matsuda T, Kido T, Itoh T, Saeki H, Shigemi S, Watanabe K et al. Diagnostic accuracy of late iodine enhancement on cardiac computed tomography with a denoise filter for the evaluation of myocardial infarction. The International Journal of Cardiovascular Imaging. 2015; 31 Suppl 2:177-185

468. Matsumoto N, Sato Y, Suzuki Y, Yoda S, Kunimasa T, Kato M et al. Usefulness of rapid low-dose/high-dose 1-day 99mTc-sestamibi ECG-gated myocardial perfusion single-photon emission computed tomography. Circulation Journal. 2006; 70(12):1585-1589

469. Matsunari I, Kanayama S, Yoneyama T, Matsudaira M, Nakajima K, Taki J et al. Electrocardiographic-gated dual-isotope simultaneous acquisition SPECT using 18F-FDG and 99mTc-sestamibi to assess myocardial viability and function in a single study. European Journal of Nuclear Medicine and Molecular Imaging. 2005; 32(2):195-202

470. Mc Ardle BA, Dowsley TF, deKemp RA, Wells GA, Beanlands RS. Does rubidium-82 PET have superior accuracy to SPECT perfusion imaging for the diagnosis of obstructive coronary disease?: A systematic review and meta-analysis. Journal of the American College of Cardiology. 2012; 60(18):1828-1837

471. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. Journal of the American College of Cardiology. 2008; 52(25):2135-2144

472. Meijboom WB, van Mieghem CA, Mollet NR, Pugliese F, Weustink AC, van Pelt N et al. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. Journal of the American College of Cardiology. 2007; 50(15):1469-1475

473. Meijs MF, de Vries JJ, Rutten A, Budde RP, de Vos AM, Meijboom WB et al. Does slice thickness affect diagnostic performance of 64-slice CT coronary angiography in stable and unstable angina patients with a positive calcium score? Acta Radiologica. 2010; 51(4):427-430

474. Meinel FG, De Cecco CN, Schoepf UJ, Nance JW, Jr., Silverman JR, Flowers BA et al. First-arterial-pass dual-energy CT for assessment of myocardial blood supply: do we need rest, stress, and delayed acquisition? Comparison with SPECT. Radiology. 2014; 270(3):708-716

475. Meintjes M, Sathekge M, Makanjee CR, Dickson JC, Endozo R, Rheeder P et al. Comparison of rubidium-82 myocardial blood flow quantification with coronary calcium score for evaluation of coronary artery stenosis. Nuclear Medicine Communications. 2016; 37(2):197-206

476. Melki D, Lind S, Agewall S, Jernberg T. Diagnostic value of high sensitive troponin T in chest pain patients with no persistent ST-elevations. Scandinavian Cardiovascular Journal45 (4) (pp 198-204), 2011Date of Publication: August 2011. 2011; (4):198-204

477. Mendoza-Rodriguez V, Llerena LR, Llerena LD, Rodriguez L, Olivares E, Linares R et al. Ischemic heart disease diagnosed by 64 slice computed tomography coronary angiography. Internet Journal of Cardiology. 2009; 7(2)

478. Meng L, Cui L, Cheng Y, Wu X, Tang Y, Wang Y et al. Effect of heart rate and coronary calcification on the diagnostic accuracy of the dual-source CT coronary angiography in patients with suspected coronary artery disease. Korean Journal of Radiology. 2009; 10(4):347-354

479. Menon M, Lesser JR, Hara H, Birkett R, Knickelbine T, Longe T et al. Multidetector CT coronary angiography for patient triage to invasive coronary angiography: Performance and cost in ambulatory patients with equivocal or suspected inaccurate noninvasive stress tests. Catheterization and Cardiovascular Interventions. 2009; 73(4):497-502

480. Merkle N, Wohrle J, Nusser T, Grebe O, Spiess J, Torzewski J et al. Diagnostic performance of magnetic resonance first pass perfusion imaging is equally potent in female compared to male patients with coronary artery disease. Clinical Research in Cardiology. 2010; 99(1):21-28

481. Meurin P, Brandao Carreira V, Dumaine R, Shqueir A, Milleron O, Safar B et al. Incidence, diagnostic methods, and evolution of left ventricular thrombus in patients with anterior myocardial infarction and low left ventricular ejection fraction: a prospective multicenter study. American Heart Journal. 2015; 170(2):256-262

482. Meyer M, Henzler T, Fink C, Vliegenthart R, Barraza JM, Jr., Nance JW, Jr. et al. Impact of coronary calcium score on the prevalence of coronary artery stenosis on dual source CT coronary angiography in caucasian patients with an intermediate risk. Academic Radiology. 2012; 19(11):1316-1323

483. Meyer M, Schoepf UJ, Fink C, Goldenberg R, Apfaltrer P, Gruettner J et al. Diagnostic performance evaluation of a computer-aided simple triage system for coronary CT angiography in patients with intermediate risk for acute coronary syndrome. Academic Radiology. 2013; 20(8):980-986

484. Midiri M, La Grutta L, Grassedonio E, Toia P, Guglielmi G. Non invasive imaging of myocardial infarction with computed tomography and magnetic resonance. Current Vascular Pharmacology. 2015; 13(1):64-77

485. Mieres JH, Makaryus AN, Cacciabaudo JM, Donaldson D, Green SJ, Heller GV et al. Value of electrocardiographically gated single-photon emission computed tomographic myocardial

perfusion scintigraphy in a cohort of symptomatic postmenopausal women. American Journal of Cardiology. 2007; 99(8):1096-1099

486. Miller CD, Case LD, Little WC, Mahler SA, Burke GL, Harper EN et al. Stress CMR reduces revascularization, hospital readmission, and recurrent cardiac testing in intermediate-risk patients with acute chest pain. JACC: Cardiovascular Imaging. 2013; 6(7):785-794

487. Miller CD, Hwang W, Hoekstra JW, Case D, Lefebvre C, Blumstein H et al. Stress cardiac magnetic resonance imaging with observation unit care reduces cost for patients with emergent chest pain: a randomized trial. Annals of Emergency Medicine. 2010; 56(3):209-219.e202

488. Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I et al. Diagnostic performance of coronary angiography by 64-row CT. New England Journal of Medicine. 2008; 359(22):2324-2336

489. Miller JM, Rochitte CE, Dewey M, Keyhani S. Cardiac computed tomography-not ready for prime time. Journal of Clinical Outcomes Management. 2009; 16(1):18-19

490. Miller JM, Rochitte CE, Dewey M, Niinuma H, Arbab-Zadeh A, Gottlieb I et al. Quantitative and diagnostic accuracy of 64-MDCTA for segmental coronary artery stenosis detection: Results from the core-64 multicenter international study. Journal of the American College of Cardiology. 2010; 55 (10 SUPPL 1):A80.E757

491. Miller TD, Hodge DO, Christian TF, Milavetz JJ, Bailey KR, Gibbons RJ. Effects of adjustment for referral bias on the sensitivity and specificity of single photon emission computed tomography for the diagnosis of coronary artery disease. American Journal of Medicine. 2002; 112(4):290-297

492. Miszalski-Jamka T, Kuntz-Hehner S, Schmidt H, Jost P, Luderitz B, Omran H. Diagnosis of ischaemic heart disease by myocardial contrast echocardiography during supine bicycle stress. Kardiologia Polska. 2006; 64(4):355-361

493. Mohammadzadeh A, Shabestari AA, Mohammadzadeh M, Mohammadzadeh MA, Kadivar S, Mohammadzadeh V et al. Diagnostic performance of multislice CT coronary angiography in the assessment of significant coronary artery disease. Acta Medica Iranica. 2012; 50(1):31-36

494. Moir S, Haluska BA, Jenkins C, Fathi R, Marwick TH. Incremental benefit of myocardial contrast to combined dipyridamole-exercise stress echocardiography for the assessment of coronary artery disease. Circulation. 2004; 110(9):1108-1113

495. Mollet N, Maffei E, Martini C, Weustink A, van Mieghem C, Baks T et al. Coronary plaque burden in patients with stable and unstable coronary artery disease using multislice CT coronary angiography. Radiologia Medica. 2011; 116(8):1174-1187

496. Mollet NR, Cademartiri F, van Mieghem CA, Runza G, McFadden EP, Baks T et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation. 2005; 112(15):2318-2323

497. Moon JH, Park EA, Lee W, Yin YH, Chung JW, Park JH et al. The diagnostic accuracy, image quality and radiation dose of 64-slice dual-source CT in daily practice: A single institution's experience. Korean Journal of Radiology. 2011; 12(3):308-318

498. Moon JS, Yoon JS, Won KC, Cho IH, Lee HW. Diagnostic Accuracy of 64-Slice MDCT Coronary Angiography for the Assessment of Coronary Artery Disease in Korean Patients with Type 2 Diabetes. Diabetes & Metabolism Journal. 2013; 37(1):54-62

499. Moon JY, Chung N, Choi BW, Choe KO, Seo HS, Ko YG et al. The utility of multi-detector row spiral CT for detection of coronary artery stenoses. Yonsei Medical Journal. 2005; 46(1):86-94

500. Moralidis E, Spyridonidis T, Arsos G, Anagnostopoulos C. Identification of advanced coronary artery disease with exercise myocardial perfusion imaging: the clinical value of a novel approach for assessing lung thallium-201 uptake. European Journal of Nuclear Medicine and Molecular Imaging. 2007; 34(4):573-583

501. Moralidis E, Spyridonidis T, Arsos G, Skeberis V, Anagnostopoulos C, Gavrielidis S. Resting electrocardiogram and stress myocardial perfusion imaging in the determination of left ventricular systolic function: an assessment enhancing the performance of gated SPET. Hellenic Journal of Nuclear Medicine. 2010; 13(2):118-126

502. Mordi I, Stanton T, Carrick D, McClure J, Oldroyd K, Berry C et al. Comprehensive dobutamine stress CMR versus echocardiography in LBBB and suspected coronary artery disease. JACC: Cardiovascular Imaging. 2014; 7(5):490-498

503. Mordini FE, Haddad T, Hsu LY, Kellman P, Lowrey TB, Aletras AH et al. Diagnostic accuracy of stress perfusion CMR in comparison with quantitative coronary angiography: fully quantitative, semiquantitative, and qualitative assessment. JACC: Cardiovascular Imaging. 2014; 7(1):14-22

504. Morise AP. Are the American College of Cardiology/American Heart Association guidelines for exercise testing for suspected coronary artery disease correct? Chest. 2000; 118(2):535-541

505. Morton G, Chiribiri A, Ishida M, Hussain ST, Schuster A, Indermuehle A et al. Quantification of absolute myocardial perfusion in patients with coronary artery disease: comparison between cardiovascular magnetic resonance and positron emission tomography. Journal of the American College of Cardiology. 2012; 60(16):1546-1555

506. Moscariello A, Vliegenthart R, Schoepf UJ, Nance JW, Jr., Zwerner PL, Meyer M et al. Coronary CT angiography versus conventional cardiac angiography for therapeutic decision making in patients with high likelihood of coronary artery disease. Radiology. 2012; 265(2):385-392

507. Motevalli M, Ghanaati H, Firouznia K, Kargar J, Aliyari Ghasabeh M, Shahriari M et al. Diagnostic efficacy of vessel specific coronary calcium score in detection of coronary artery stenosis. Iranian Red Crescent Medical Journal. 2014; 16(12):e26010

508. Motoyama S, Sarai M, Inoue K, Kawai H, Ito H, Harigaya H et al. Morphologic and functional assessment of coronary artery disease--potential application of computed tomography angiography and myocardial perfusion imaging. Circulation Journal. 2013; 77(2):411-417

509. Motoyasu M, Sakuma H, Ichikawa Y, Ishida N, Uemura S, Okinaka T et al. Prediction of regional functional recovery after acute myocardial infarction with low dose dobutamine stress cine MR imaging and contrast enhanced MR imaging. Journal of Cardiovascular Magnetic Resonance. 2003; 5(4):563-574

510. Mowatt G, Cummins E, Waugh N, Walker S, Cook J, Jia X et al. Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease. Health Technology Assessment. 2009; 12(17):i-xi, 1-164

511. Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N et al. Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion

scintigraphy for the diagnosis and management of angina and myocardial infarction. Health Technology Assessment. 2004; 8(30):iii-89

512. Muhlenbruch G, Seyfarth T, Soo CS, Pregalathan N, Mahnken AH. Diagnostic value of 64-slice multi-detector row cardiac CTA in symptomatic patients. European Radiology. 2007; 17(3):603-609

513. Muscholl MW, Oswald M, Mayer C, von Scheidt W. Prognostic value of 2D echocardiography in patients presenting with acute chest pain and non-diagnostic ECG for ST-elevation myocardial infarction. International Journal of Cardiology. 2002; 84(2-3):217-225

514. Musto C, Simon P, Nicol E, Tanigawa J, Davies SW, Oldershaw PJ et al. 64-multislice computed tomography in consecutive patients with suspected or proven coronary artery disease: Initial single center experience. International Journal of Cardiology. 2007; 114(1):90-97

515. Nabi F, Chang SM, Pratt CM, Paranilam J, Peterson LE, Frias ME et al. Coronary artery calcium scoring in the emergency department: identifying which patients with chest pain can be safely discharged home. Annals of Emergency Medicine. 2010; 56(3):220-229

516. Nagao M, Matsuoka H, Kawakami H, Higashino H, Mochizuki T, Ohshita A et al. Detection of myocardial ischemia using 64-slice MDCT. Circulation Journal. 2009; 73(5):905-911

517. Nagao M, Matsuoka H, Kawakami H, Higashino H, Mochizuki T, Uemura M et al. Myocardial ischemia in acute coronary syndrome: assessment using 64-MDCT. American Journal of Roentgenology. 2009; 193(4):1097-1106

518. Nagori M, Narain VS, Saran RK, Dwivedi SK, Sethi R. Efficacy of multi-detector coronary computed tomography angiography in comparison with exercise electrocardiogram in the triage of patients of low risk acute chest pain. Indian Heart Journal. 2014; 66(4):435-442

519. Nair SU, Ahlberg AW, Mathur S, Katten DM, Polk DM, Heller GV. The clinical value of single photon emission computed tomography myocardial perfusion imaging in cardiac risk stratification of very elderly patients (>80 years) with suspected coronary artery disease. Journal of Nuclear Cardiology. 2012; 19(2):244-255

520. Nakazato R, Berman DS, Dey D, Le Meunier L, Hayes SW, Fermin JS et al. Automated quantitative Rb-82 3D PET/CT myocardial perfusion imaging: normal limits and correlation with invasive coronary angiography. Journal of Nuclear Cardiology. 2012; 19(2):265-276

521. Nakazato R, Slomka PJ, Fish M, Schwartz RG, Hayes SW, Thomson LE et al. Quantitative high-efficiency cadmium-zinc-telluride SPECT with dedicated parallel-hole collimation system in obese patients: results of a multi-center study. Journal of Nuclear Cardiology. 2015; 22(2):266-275

522. Nakazato R, Tamarappoo BK, Kang X, Wolak A, Kite F, Hayes SW et al. Quantitative upright-supine high-speed SPECT myocardial perfusion imaging for detection of coronary artery disease: correlation with invasive coronary angiography. Journal of Nuclear Medicine. 2010; 51(11):1724-1731

523. Nasis A, Ko BS, Leung MC, Antonis PR, Nandurkar D, Wong DT et al. Diagnostic accuracy of combined coronary angiography and adenosine stress myocardial perfusion imaging using 320-detector computed tomography: pilot study. European Radiology. 2013; 23(7):1812-1821

524. Nasis A, Leung MC, Antonis PR, Cameron JD, Lehman SJ, Hope SA et al. Diagnostic accuracy of noninvasive coronary angiography with 320-detector row computed tomography. American Journal of Cardiology. 2010; 106(10):1429-1435

525. National Horizon Scanning Centre (NHSC). Magnetic resonance angiography (MRA) imaging for the detection of coronary artery disease: horizon scanning technology briefing Birmingham. National Horizon Scanning Centre (NHSC), 2007.

526. National Horizon Scanning Centre (NHSC). Myocardial stress perfusion magnetic resonance imaging (MRI) assessment of myocardial blood flow in coronary artery disease: horizon scanning technology briefing Birmingham. National Horizon Scanning Centre (NHSC), 2007.

527. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

528. National Institute for Health and Clinical Excellence. The guidelines manual. London. National Institute for Health and Clinical Excellence. 2012. Available from: http://www.nice.org.uk/article/pmg6/

529. Nedeljkovic I, Ostojic M, Beleslin B, Djordjevic-Dikic A, Stepanovic J, Nedeljkovic M et al. Comparison of exercise, dobutamine-atropine and dipyridamole-atropine stress echocardiography in detecting coronary artery disease. Cardiovascular Ultrasound. 2006; 4:22

530. Neefjes LA, Rossi A, Genders TSS, Nieman K, Papadopoulou SL, Dharampal AS et al. Diagnostic accuracy of 128-slice dual-source CT coronary angiography: A randomized comparison of different acquisition protocols. European Radiology. 2013; 23(3):614-622

531. Neglia D, Rovai D, Caselli C, Pietila M, Teresinska A, Aguade-Bruix S et al. Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. Circulation Cardiovascular imaging. 2015; 8(3)

532. NHS Quality Improvement Scotland. The use of multislice computed tomography angiography (CTA) for the diagnosis of coronary artery disease Glasgow. NHS Quality Improvement Scotland (NHS QIS), 2005. Available from: http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/earlier_evidence_notes/evidence_note_9.aspx

533. NHSC. Computed tomography (CT) angiography for the diagnosis and management of coronary artery disease: horizon scanning technology briefing Birmingham. National Horizon Scanning Centre (NHSC), 2006.

534. Nicol ED, Stirrup J, Reyes E, Roughton M, Padley SP, Rubens MB et al. Comparison of 64-slice cardiac computed tomography with myocardial perfusion scintigraphy for assessment of global and regional myocardial function and infarction in patients with low to intermediate likelihood of coronary artery disease. Journal of Nuclear Cardiology. 2008; 15(4):497-502

535. Nicol ED, Stirrup J, Reyes E, Roughton M, Padley SP, Rubens MB et al. Sixty-four-slice computed tomography coronary angiography compared with myocardial perfusion scintigraphy for the diagnosis of functionally significant coronary stenoses in patients with a low to intermediate likelihood of coronary artery disease. Journal of Nuclear Cardiology. 2008; 15(3):311-318

536. Nieman K, Galema TW, Neefjes LA, Weustink AC, Musters P, Moelker AD et al. Comparison of the value of coronary calcium detection to computed tomographic angiography and exercise testing in patients with chest pain. American Journal of Cardiology. 2009; 104(11):1499-1504

537. Nieman K, Rensing BJ, van Geuns RJ, Munne A, Ligthart JM, Pattynama PM et al. Usefulness of multislice computed tomography for detecting obstructive coronary artery disease. American Journal of Cardiology. 2002; 89(8):913-918

538. Nikolaou K, Knez A, Rist C, Wintersperger BJ, Leber A, Johnson T et al. Accuracy of 64-MDCT in the diagnosis of ischemic heart disease. American Journal of Roentgenology. 2006; 187(1):111-117

539. Normann J, Mueller M, Biener M, Vafaie M, Katus HA, Giannitsis E. Effect of older age on diagnostic and prognostic performance of high-sensitivity troponin T in patients presenting to an emergency department. American Heart Journal. 2012; 164(5):698-705.e694

540. Ogino Y, Horiguchi Y, Ueda T, Shiomori T, Kanna M, Kawaminami T et al. A myocardial perfusion imaging system using a multifocal collimator for detecting coronary artery disease: validation with invasive coronary angiography. Annals of Nuclear Medicine. 2015; 29(4):366-370

541. Olivetti L, Mazza G, Volpi D, Costa F, Ferrari O, Pirelli S. Multislice CT in emergency room management of patients with chest pain and medium-low probability of acute coronary syndrome. Radiologia Medica. 2006; 111(8):1054-1063

542. Olivieri F, Galeazzi R, Giavarina D, Testa R, Abbatecola AM, Ceka A et al. Aged-related increase of high sensitive Troponin T and its implication in acute myocardial infarction diagnosis of elderly patients. Mechanisms of Ageing and Development. 2012; 133(5):300-305

543. Olszowska M, Kostkiewicz M, Tracz W, Przewlocki T. Assessment of myocardial perfusion in patients with coronary artery disease. Comparison of myocardial contrast echocardiography and 99mTc MIBI single photon emission computed tomography. International Journal of Cardiology. 2003; 90(1):49-55

544. Oncel D, Oncel G, Karaca M. Coronary stent patency and in-stent restenosis: Determination with 64-section multidetector CT coronary angiography - Initial experience. Radiology. 2007; 242(2):403-409

545. Oncel D, Oncel G, Tastan A, Tamci B. Detection of significant coronary artery stenosis with 64-section MDCT angiography. European Journal of Radiology. 2007; 62(3):394-405

546. Ovrehus KA, Munkholm H, Bottcher M, Botker HE, Norgaard BL. Coronary computed tomographic angiography in patients suspected of coronary artery disease: impact of observer experience on diagnostic performance and interobserver reproducibility. Journal of Cardiovascular Computed Tomography. 2010; 4(3):186-194

547. Palagi C, Mengozzi G, Rovai D, Volterrani D, Dell'Anna R, Giorgi D et al. Assessment of myocardial perfusion with intravenous contrast echocardiography: comparison with (99) Tc-tetrofosmin single photon emission computed tomography and dobutamine echocardiography. Echocardiography. 2003; 20(1):37-45

548. Palumbo AA, Maffei E, Martini C, Tarantini G, Di Tanna GL, Berti E et al. Coronary calcium score as gatekeeper for 64-slice computed tomography coronary angiography in patients with chest pain: per-segment and per-patient analysis. European Radiology. 2009; 19(9):2127-2135

549. Parato VM, Mehta A, Delfino D, Amabili S, Partemi M, Grossi P et al. Resting echocardiography for the early detection of acute coronary syndromes in chest pain unit patients. Echocardiography. 2010; 27(6):597-602

550. Park TH, Tayan N, Takeda K, Jeon HK, Quinones MA, Zoghbi WA. Supine bicycle echocardiography improved diagnostic accuracy and physiologic assessment of coronary artery disease with the incorporation of intermediate stages of exercise. Journal of the American College of Cardiology. 2007; 50(19):1857-1863

551. Parker MW. Comparison of the Diagnostic Accuracy of PET and SPECT for Coronary Artery Disease. Current Cardiovascular Imaging Reports. 2015; 8(1):1-12

552. Parker MW, Iskandar A, Limone B, Perugini A, Kim H, Jones C et al. Diagnostic accuracy of cardiac positron emission tomography versus single photon emission computed tomography for coronary artery disease: a bivariate meta-analysis. Circulation Cardiovascular imaging. 2012; 5(6):700-707

553. Patsilinakos SP, Kranidis AI, Antonelis IP, Filippatos G, Houssianakou IK, Zamanis NI et al. Detection of coronary artery disease in patients with severe aortic stenosis with noninvasive methods. Angiology. 1999; 50(4):309-317

554. Pavlovic S, Sobic-Saranovic D, Djordjevic-Dikic A, Beleslin B, Stepanovic J, Artiko V et al. Comparative utility of gated myocardial perfusion imaging and transthoracic coronary flow reserve for the assessment of coronary artery disease in patients with left bundle branch block. Nuclear Medicine Communications. 2010; 31(4):334-340

555. Pelliccia F, Pasceri V, Evangelista A, Pergolini A, Barilla F, Viceconte N et al. Diagnostic accuracy of 320-row computed tomography as compared with invasive coronary angiography in unselected, consecutive patients with suspected coronary artery disease.[Retraction in Int J Cardiovasc Imaging. 2014 Apr;30(4):833; PMID: 24671379]. The International Journal of Cardiovascular Imaging. 2013; 29(2):443-452

556. Pereira E, Bettencourt N, Ferreira N, Schuster A, Chiribiri A, Primo J et al. Incremental value of adenosine stress cardiac magnetic resonance in coronary artery disease detection. International Journal of Cardiology. 2013; 168(4):4160-4167

557. Pilz G, Eierle S, Heer T, Klos M, Ali E, Scheck R et al. Negative predictive value of normal adenosine-stress cardiac MRI in the assessment of coronary artery disease and correlation with semiquantitative perfusion analysis. Journal of Magnetic Resonance Imaging. 2010; 32(3):615-621

558. Plein S, Greenwood JP, Ridgway JP, Cranny G, Ball SG, Sivananthan MU. Assessment of non-ST-segment elevation acute coronary syndromes with cardiac magnetic resonance imaging. Journal of the American College of Cardiology. 2004; 44(11):2173-2181

559. Ponte M, Bettencourt N, Pereira E, Ferreira ND, Chiribiri A, Schuster A et al. Anatomical versus functional assessment of coronary artery disease: direct comparison of computed tomography coronary angiography and magnetic resonance myocardial perfusion imaging in patients with intermediate pre-test probability. The International Journal of Cardiovascular Imaging. 2014; 30(8):1589-1597

560. Pontone G, Andreini D, Bartorelli AL, Cortinovis S, Mushtaq S, Bertella E et al. Diagnostic Accuracy of Coronary Computed Tomography Angiography. A Comparison Between Prospective and Retrospective Electrocardiogram Triggering. Journal of the American College of Cardiology. 2009; 54(4):346-355

561. Pontone G, Andreini D, Quaglia C, Ballerini G, Nobili E, Pepi M. Accuracy of multidetector spiral computed tomography in detecting significant coronary stenosis in patient populations with differing pre-test probabilities of disease. Clinical Radiology. 2007; 62(10):978-985

562. Potocki M, Reichlin T, Thalmann S, Zellweger C, Twerenbold R, Reiter M et al. Diagnostic and prognostic impact of copeptin and high-sensitivity cardiac troponin T in patients with pre-existing coronary artery disease and suspected acute myocardial infarction. Heart. 2012; 98(7):558-565

563. Pracon R, Kruk M, Jakubczak B, Demkow M, Bilinska ZT. Superior early diagnostic performance of a sensitive cardiac troponin assay as compared to a standard troponin test in the diagnosis of acute myocardial infarction. Kardiologia Polska. 2012; 70(2):131-138

564. Previtali M, Cannizzaro G, Lanzarini L, Calsamiglia G, Poli A, Fetiveau R. Comparison of dobutamine stress echocardiography and exercise stress Thallium-201 SPECT for detection of myocardial ischemia after acute myocardial infarction treated with thrombolysis. International Journal of Cardiac Imaging. 1999; 15(3):195-204

565. Pursnani A, Lee AM, Mayrhofer T, Ahmed W, Uthamalingam S, Ferencik M et al. Early resting myocardial computed tomography perfusion for the detection of acute coronary syndrome in patients with coronary artery disease. Circulation Cardiovascular imaging. 2015; 8(3):e002404

566. Pyati AK, Devaranavadagi BB, Sajjannar SL, Nikam SV, Shannawaz M, Sudharani. Heart-Type Fatty Acid Binding Protein: A Better Cardiac Biomarker than CK-MB and Myoglobin in the Early Diagnosis of Acute Myocardial Infarction. Journal of Clinical and Diagnostic Research JCDR. 2015; 9(10):BC08-11

567. Raskovalova T, Twerenbold R, Collinson PO, Keller T, Bouvaist H, Folli C et al. Diagnostic accuracy of combined cardiac troponin and copeptin assessment for early rule-out of myocardial infarction: a systematic review and meta-analysis. European Heart Journal Acute Cardiovascular Care. 2014; 3(1):18-27

568. Rastgou F, Bitarafan-Rajabi A, Farhzadi A, Yaghoobi N, Firoozabady H, Malek H et al. Diagnostic accuracy assessment of ST-segment displacements, chest pain and stress myocardial perfusion imaging exercise test in coronary stenosis compared with angiography findings. Iranian Heart Journal. 2012; 12(4):30-36

569. Reichlin T, Hochholzer W, Bassetti S, Steuer S, Stelzig C, Hartwiger S et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. New England Journal of Medicine. 2009; 361(9):858-867

570. Reichlin T, Hochholzer W, Stelzig C, Laule K, Freidank H, Morgenthaler NG et al. Incremental value of copeptin for rapid rule out of acute myocardial infarction. Journal of the American College of Cardiology. 2009; 54(1):60-68

571. Reichlin T, Irfan A, Twerenbold R, Reiter M, Hochholzer W, Burkhalter H et al. Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction. Circulation. 2011; 124(2):136-145

572. Reichlin T, Schindler C, Drexler B, Twerenbold R, Reiter M, Zellweger C et al. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. Archives of Internal Medicine. 2012; 172(16):1211-1218

573. Reinsch N, Mahabadi AA, Lehmann N, Mohlenkamp S, Hoefs C, Sievers B et al. Comparison of dual-source and electron-beam CT for the assessment of coronary artery calcium scoring. British Journal of Radiology. 2012; 85(1015):e300-e306

574. Reiter M, Twerenbold R, Reichlin T, Benz B, Haaf P, Meissner J et al. Early diagnosis of acute myocardial infarction in patients with pre-existing coronary artery disease using more sensitive cardiac troponin assays. European Heart Journal. 2012; 33(8):988-997

575. Reiter M, Twerenbold R, Reichlin T, Haaf P, Peter F, Meissner J et al. Early diagnosis of acute myocardial infarction in the elderly using more sensitive cardiac troponin assays. European Heart Journal. 2011; 32(11):1379-1389

576. Reiter M, Twerenbold R, Reichlin T, Mueller M, Hoeller R, Moehring B et al. Heart-type fatty acid-binding protein in the early diagnosis of acute myocardial infarction. Heart. 2013; 99(10):708-714

577. Rieber J, Huber A, Erhard I, Mueller S, Schweyer M, Koenig A et al. Cardiac magnetic resonance perfusion imaging for the functional assessment of coronary artery disease: a comparison with coronary angiography and fractional flow reserve. European Heart Journal. 2006; 27(12):1465-1471

578. Rieber J, Jung P, Erhard I, Koenig A, Hacker M, Schiele TM et al. Comparison of pressure measurement, dobutamine contrast stress echocardiography and SPECT for the evaluation of intermediate coronary stenoses. The COMPRESS trial. International Journal of Cardiovascular Interventions. 2004; 6(3-4):142-147

579. Rispler S, Aronson D, Abadi S, Roguin A, Engel A, Beyar R et al. Integrated SPECT/CT for assessment of haemodynamically significant coronary artery lesions in patients with acute coronary syndrome. European Journal of Nuclear Medicine and Molecular Imaging. 2011; 38(10):1917-1925

580. Rispler S, Keidar Z, Ghersin E, Roguin A, Soil A, Dragu R et al. Integrated single-photon emission computed tomography and computed tomography coronary angiography for the assessment of hemodynamically significant coronary artery lesions. Journal of the American College of Cardiology. 2007; 49(10):1059-1067

581. Rollan MJ, San Roman JA, Vilacosta I, Ortega JR, Bratos JL. Dobutamine stress echocardiography in the diagnosis of coronary artery disease in women with chest pain: comparison with different noninvasive tests. Clinical Cardiology. 2002; 25(12):559-564

582. Ronderos RE, Boskis M, Chung N, Corneli DB, Escudero EM, Ha JW et al. Correlation between myocardial perfusion abnormalities detected with intermittent imaging using intravenous perfluorocarbon microbubbles and radioisotope imaging during high-dose dipyridamole stress echo. Clinical Cardiology. 2002; 25(3):103-111

583. Rubini Gimenez M, Hoeller R, Reichlin T, Zellweger C, Twerenbold R, Reiter M et al. Rapid rule out of acute myocardial infarction using undetectable levels of high-sensitivity cardiac troponin. International Journal of Cardiology. 2013; 168(4):3896-3901

584. Rubinshtein R, Halon DA, Gaspar T, Jaffe R, Karkabi B, Flugelman MY et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation. 2007; 115(13):1762-1768

585. Rubinshtein R, Halon DA, Gaspar T, Schliamser JE, Yaniv N, Ammar R et al. Usefulness of 64-slice multidetector computed tomography in diagnostic triage of patients with chest pain and negative or nondiagnostic exercise treadmill test result. American Journal of Cardiology. 2007; 99(7):925-929

586. Rubinshtein R, Miller TD, Williamson EE, Kirsch J, Gibbons RJ, Primak AN et al. Detection of myocardial infarction by dual-source coronary computed tomography angiography using quantitated myocardial scintigraphy as the reference standard. Heart. 2009; 95(17):1419-1422

587. Ruzsics B, Lee H, Zwerner PL, Gebregziabher M, Costello P, Schoepf UJ. Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia-initial experience. European Radiology. 2008; 18(11):2414-2424

588. Ruzsics B, Schwarz F, Schoepf UJ, Lee YS, Bastarrika G, Chiaramida SA et al. Comparison of Dual-Energy Computed Tomography of the Heart With Single Photon Emission Computed Tomography for Assessment of Coronary Artery Stenosis and of the Myocardial Blood Supply. American Journal of Cardiology. 2009; 104(3):318-326

589. Saad MAM, Azer HY. Dual-source CT coronary angiography: Diagnostic accuracy without the use of B blockers. Egyptian Journal of Radiology and Nuclear Medicine. 2011; 42(3-4):281-287

590. Saba L, Fellini F, De Filippo M. Diagnostic value of contrast-enhanced cardiac magnetic resonance in patients with acute coronary syndrome with normal coronary arteries. Japanese Journal of Radiology. 2015; 33(7):410-417

591. Sabharwal NK, Stoykova B, Taneja AK, Lahiri A. A randomized trial of exercise treadmill ECG versus stress SPECT myocardial perfusion imaging as an initial diagnostic strategy in stable patients with chest pain and suspected CAD: cost analysis.[Erratum appears in J Nucl Cardiol. 2007 May-Jun;14(3):414]. Journal of Nuclear Cardiology. 2007; 14(2):174-186

592. Saenger AK, Beyrau R, Braun S, Cooray R, Dolci A, Freidank H et al. Multicenter analytical evaluation of a high-sensitivity troponin T assay. Clinica Chimica Acta. 2011; 412(9-10):748-754

593. Sajjadieh A, Hekmatnia A, Keivani M, Asoodeh A, Pourmoghaddas M, Sanei H. Diagnostic performance of 64-row coronary CT angiography in detecting significant stenosis as compared with conventional invasive coronary angiography. ARYA Atherosclerosis. 2013; 9(2):157-163

594. Sakakura K, Yasu T, Kobayashi Y, Katayama T, Sugawara Y, Funayama H et al. Noninvasive tissue characterization of coronary arterial plaque by 16-slice computed tomography in acute coronary syndrome. Angiology. 2006; 57(2):155-160

595. Sakuma H, Suzawa N, Ichikawa Y, Makino K, Hirano T, Kitagawa K et al. Diagnostic accuracy of stress first-pass contrast-enhanced myocardial perfusion MRI compared with stress myocardial perfusion scintigraphy. AJR American Journal of Roentgenology. 2005; 185(1):95-102

596. Sampson UK, Dorbala S, Limaye A, Kwong R, Di Carli MF. Diagnostic accuracy of rubidium-82 myocardial perfusion imaging with hybrid positron emission tomography/computed tomography in the detection of coronary artery disease. Journal of the American College of Cardiology. 2007; 49(10):1052-1058

597. Sanchis J, Bardaji A, Bosch X, Loma-Osorio P, Marin F, Sanchez PL et al. Usefulness of high-sensitivity troponin T for the evaluation of patients with acute chest pain and no or minimal myocardial damage. American Heart Journal. 2012; 164(2):194-200

598. Santalo M, Martin A, Velilla J, Povar J, Temboury F, Balaguer J et al. Using high-sensitivity troponin T: the importance of the proper gold standard. American Journal of Medicine. 2013; 126(8):709-717

599. Santana CA, Garcia EV, Faber TL, Sirineni GK, Esteves FP, Sanyal R et al. Diagnostic performance of fusion of myocardial perfusion imaging (MPI) and computed tomography coronary angiography. Journal of Nuclear Cardiology. 2009; 16(2):201-211

600. Santana CA, Garcia EV, Vansant JP, Krawczynska EG, Folks RD, Cooke CD et al. Three-dimensional color-modulated display of myocardial SPECT perfusion distributions accurately assesses coronary artery disease. Journal of Nuclear Medicine. 2000; 41(12):1941-1946

601. Santos MB, Ferreira AM, De Araujo Goncalves P, Raposo L, Teles RC, Almeida M et al. Diagnostic yield of current referral strategies for elective coronary angiography in suspected coronary artery disease - An analysis of the across registry. Revista Portuguesa de Cardiologia. 2013; 32(6):483-488

602. Sara L, Rochitte CE, Lemos PA, Niinuma H, Dewey M, Shapiro EP et al. Accuracy of multidetector computed tomography for detection of coronary artery stenosis in acute coronary syndrome compared with stable coronary disease: a CORE64 multicenter trial substudy. International Journal of Cardiology. 2014; 177(2):385-391

603. Sardanelli F, Molinari G, Zandrino F, Balbi M. Three-dimensional, navigator-echo MR coronary angiography in detecting stenoses of the major epicardial vessels, with conventional coronary angiography as the standard of reference. Radiology. 2000; 214(3):808-814

604. Sato Y, Matsumoto N, Ichikawa M, Kunimasa T, Iida K, Yoda S et al. Efficacy of multislice computed tomography for the detection of acute coronary syndrome in the emergency department. Circulation Journal. 2005; 69(9):1047-1051

605. Sato Y, Matsumoto N, Kato M, Inoue F, Horie T, Kusama J et al. Noninvasive assessment of coronary artery disease by multislice spiral computed tomography using a new retrospectively ECG-gated image reconstruction technique. Circulation Journal. 2003; 67(5):401-405

606. Schaap J, Kauling RM, Boekholdt SM, Post MC, Van der Heyden JA, de Kroon TL et al. Usefulness of coronary calcium scoring to myocardial perfusion SPECT in the diagnosis of coronary artery disease in a predominantly high risk population. The International Journal of Cardiovascular Imaging. 2013; 29(3):677-684

607. Scheffel H, Alkadhi H, Leschka S, Plass A, Desbiolles L, Guber I et al. Low-dose CT coronary angiography in the step-and-shoot mode: Diagnostic performance. Heart. 2008; 94(9):1132-1137

608. Scheffel H, Stolzmann P, Alkadhi H, Azemaj N, Plass A, Baumueller S et al. Low-dose CT and cardiac MR for the diagnosis of coronary artery disease: accuracy of single and combined approaches. The International Journal of Cardiovascular Imaging. 2010; 26(5):579-590

609. Schepis T, Gaemperli O, Koepfli P, Namdar M, Valenta I, Scheffel H et al. Added value of coronary artery calcium score as an adjunct to gated SPECT for the evaluation of coronary artery disease in an intermediate-risk population. Journal of Nuclear Medicine. 2007; 48(9):1424-1430

610. Schertler T, Frauenfelder T, Stolzmann P, Scheffel H, Desbiolles L, Marincek B et al. Triple rule-out CT in patients with suspicion of acute pulmonary embolism: findings and accuracy. Academic Radiology. 2009; 16(6):708-717

611. Schlosser T, Konorza T, Hunold P, Kuhl H, Schmermund A, Barkhausen J. Noninvasive visualization of coronary artery bypass grafts using 16-detector row computed tomography. Journal of the American College of Cardiology. 2004; 44(6):1224-1229

612. Schroeder S, Kuettner A, Beck T, Kopp AF, Herdeg C, Heuschmid M et al. Usefulness of noninvasive MSCT coronary angiography as first-line imaging technique in patients with chest pain: initial clinical experience. International Journal of Cardiology. 2005; 102(3):469-475

613. Schuijf JD, Bax JJ, Salm LP, Jukema JW, Lamb HJ, van der Wall EE et al. Noninvasive coronary imaging and assessment of left ventricular function using 16-slice computed tomography. American Journal of Cardiology. 2005; 95(5):571-574

614. Schuijf JD, Pundziute G, Jukema JW, Lamb HJ, van der Hoeven BL, de Roos A et al. Diagnostic accuracy of 64-slice multislice computed tomography in the noninvasive evaluation of significant coronary artery disease. American Journal of Cardiology. 2006; 98(2):145-148

615. Schwartz JG, Johnson RB, Aepfelbacher FC, Parker JA, Chen L, Azar RR et al. Sensitivity, specificity and accuracy of stress SPECT myocardial perfusion imaging for detection of coronary artery disease in the distribution of first-order branch vessels, using an anatomical matching of angiographic and perfusion data. Nuclear Medicine Communications. 2003; 24(5):543-549

616. Schwitter J, Nanz D, Kneifel S, Bertschinger K, Buchi M, Knusel PR et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation. 2001; 103(18):2230-2235

617. Schwitter J, Wacker CM, van Rossum AC, Lombardi M, Al-Saadi N, Ahlstrom H et al. MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial. European Heart Journal. 2008; 29(4):480-489

618. Schwitter J, Wacker CM, Wilke N, Al-Saadi N, Sauer E, Huettle K et al. Superior diagnostic performance of perfusion-cardiovascular magnetic resonance versus SPECT to detect coronary artery disease: The secondary endpoints of the multicenter multivendor MR-IMPACT II (Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial). Journal of Cardiovascular Magnetic Resonance. 2012; 14:61

619. Schwitter J, Wacker CM, Wilke N, Al-Saadi N, Sauer E, Huettle K et al. MR-IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary artery disease Trial: perfusion-cardiac magnetic resonance vs. single-photon emission computed tomography for the detection of coronary artery disease: a comparative multicentre, multivendor trial. European Heart Journal. 2013; 34(10):775-781

620. Sebbane M, Lefebvre S, Kuster N, Jreige R, Jacques E, Badiou S et al. Early rule out of acute myocardial infarction in ED patients: value of combined high-sensitivity cardiac troponin T and ultrasensitive copeptin assays at admission. American Journal of Emergency Medicine. 2013; 31(9):1302-1308

621. Sehovic S. Diagnostic capabilities of 64 slice CT coronography compared to classic in coronary disease detection. Acta Informatica Medica. 2013; 21(3):208-210

622. Selcoki Y, Yilmaz OC, Kankilic MN, Akin K, Eryonucu B. Diagnostic accuracy of 64-slice computed tomography in patients with suspected or proven coronary artery disease. Turk Kardiyoloji Dernegi Arsivi. 2010; 38(2):95-100

623. Senior R, Lepper W, Pasquet A, Chung G, Hoffman R, Vanoverschelde JL et al. Myocardial perfusion assessment in patients with medium probability of coronary artery disease and no prior myocardial infarction: comparison of myocardial contrast echocardiography with 99mTc single-photon emission computed tomography. American Heart Journal. 2004; 147(6):1100-1105

624. Shabestari AA, Abdi S, Akhlaghpoor S, Azadi M, Baharjoo H, Pajouh MD et al. Diagnostic performance of 64-channel multislice computed tomography in assessment of significant

coronary artery disease in symptomatic subjects. American Journal of Cardiology. 2007; 99(12):1656-1661

625. Shah AS, Griffiths M, Lee KK, McAllister DA, Hunter AL, Ferry AV et al. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study.[Erratum appears in BMJ. 2015;350:h626; PMID: 25646958]. BMJ. 2015; 350:g7873

626. Shah AS, Newby DE, Mills NL. High sensitivity cardiac troponin in patients with chest pain. BMJ. 2013; 347:f4222

627. Shah ASV, McAllister DA, Mills R, Lee KK, Churchhouse AMD, Fleming KM et al. Sensitive Troponin Assay and the Classification of Myocardial Infarction. American Journal of Medicine. 2015; 128(5):493-501

628. Shaheen J, Luria D, Klutstein MW, Rosenmann D, Tzivoni D. Diagnostic value of 12-lead electrocardiogram during dobutamine echocardiographic studies. American Heart Journal. 1998; 136(6):1061-1064

629. Shariat M, Thavendiranathan P, Nguyen E, Wintersperger B, Paul N, Rakowski H et al. Utility of coronary CT angiography in outpatients with hypertrophic cardiomyopathy presenting with angina symptoms. Journal of Cardiovascular Computed Tomography. 2014; 8(6):429-437

630. Sharma P, Patel CD, Karunanithi S, Maharjan S, Malhotra A. Comparative accuracy of CT attenuation-corrected and non-attenuation-corrected SPECT myocardial perfusion imaging. Clinical Nuclear Medicine. 2012; 37(4):332-338

631. Sharma RK, Arbab-Zadeh A, Kishi S, Chen MY, Magalhaes TA, George RT et al. Incremental diagnostic accuracy of computed tomography myocardial perfusion imaging over coronary angiography stratified by pre-test probability of coronary artery disease and severity of coronary artery calcification: The CORE320 study. International Journal of Cardiology. 2015; 201:570-577

632. Shavelle DM, Budoff MJ, LaMont DH, Shavelle RM, Kennedy JM, Brundage BH. Exercise testing and electron beam computed tomography in the evaluation of coronary artery disease. Journal of the American College of Cardiology. 2000; 36(1):32-38

633. Sheikh M, Ben-Nakhi A, Shukkur AM, Sinan T, Al-Rashdan I. Accuracy of 64-multidetector-row computed tomography in the diagnosis of coronary artery disease. Medical Principles and Practice. 2009; 18(4):323-328

634. Sheth T, Amlani S, Ellins ML, Mehta S, Velianou J, Cappelli G et al. Computed tomographic coronary angiographic assessment of high-risk coronary anatomy in patients with suspected coronary artery disease and intermediate pretest probability. American Heart Journal. 2008; 155(5):918-923

635. Shi H, Aschoff AJ, Brambs HJ, Hoffmann MH. Multislice CT imaging of anomalous coronary arteries. European Radiology. 2004; 14(12):2172-2181

636. Shin JH, Pokharna HK, Williams KA, Mehta R, Ward RP. SPECT myocardial perfusion imaging with prone-only acquisitions: correlation with coronary angiography. Journal of Nuclear Cardiology. 2009; 16(4):590-596

637. Shivalkar B, Goovaerts I, Salgado RA, Ozsarlak O, Bosmans J, Parizel PM et al. Multislice cardiac computed tomography in symptomatic middle-aged women. Annals of Medicine. 2007; 39(4):290-297

638. Shouker MAH, Yusuf El-Shazely MA, Abd El-Aziz MFM, Samak MF. CT angiography using dual source 64-MSCT versus catheter angiography in assessment of coronary atherosclerotic disease. Egyptian Journal of Radiology and Nuclear Medicine. 2012; 43(2):147-155

639. Shuman WP, Branch KR, May JM, Mitsumori LM, Lockhart DW, Dubinsky TJ et al. Prospective versus retrospective ECG gating for 64-detector CT of the coronary arteries: Comparison of image quality and patient radiation dose. Radiology. 2008; 248(2):431-437

640. Shuman WP, Branch KR, May JM, Mitsumori LM, Strote JN, Warren BH et al. Whole-chest 64-MDCT of emergency department patients with nonspecific chest pain: Radiation dose and coronary artery image quality with prospective ECG triggering versus retrospective ECG gating. AJR American Journal of Roentgenology. 2009; 192(6):1662-1667

641. Shuman WP, May JM, Branch KR, Mitsumori LM, Strote JN, Green DE et al. Negative ECG-gated cardiac CT in patients with low-to-moderate risk chest pain in the emergency department: 1-year follow-up. AJR American Journal of Roentgenology. 2010; 195(4):923-927

642. Siriapisith T, Wasinrat J. Comparison of image quality of coronary CT angiography between 16 and 64 slices MDCT. Journal of the Medical Association of Thailand. 2008; 91(3):364-371

643. Sirol M, Sanz J, Henry P, Rymer R, Leber A. Evaluation of 64-slice MDCT in the real world of cardiology: a comparison with conventional coronary angiography. Archives of Cardiovascular Diseases. 2009; 102(5):433-439

644. Slim J, Castillo-Rojas L, Hann M, Symons J, Martinho S, Sim J et al. Computed tomography coronary angiography versus stress myocardial perfusion imaging for risk stratification in patients with high occupational risk. Journal of Thoracic Imaging. 2012; 27(1):40-43

645. Smart SC, Bhatia A, Hellman R, Stoiber T, Krasnow A, Collier BD et al. Dobutamine-atropine stress echocardiography and dipyridamole sestamibi scintigraphy for the detection of coronary artery disease: limitations and concordance. Journal of the American College of Cardiology. 2000; 36(4):1265-1273

646. Smart SC, Knickelbine T, Malik F, Sagar KB. Dobutamine-atropine stress echocardiography for the detection of coronary artery disease in patients with left ventricular hypertrophy. Importance of chamber size and systolic wall stress. Circulation. 2000; 101(3):258-263

647. So NM, Lam WW, Li D, Chan AK, Sanderson JE, Metreweli C. Magnetic resonance coronary angiography with 3D TrueFISP: breath-hold versus respiratory gated imaging. British Journal of Radiology. 2005; 78(926):116-121

648. Sommer T, Hackenbroch M, Hofer U, Schmiedel A, Willinek WA, Flacke S et al. Coronary MR angiography at 3.0 T versus that at 1.5 T: initial results in patients suspected of having coronary artery disease. Radiology. 2005; 234(3):718-725

649. Soon KH, Chaitowitz I, Cox N, Macgregor L, Eccleston D, Bell KW et al. Diagnostic accuracy of 16-slice CT coronary angiography in the evaluation of coronary artery disease. Australasian Radiology. 2007; 51(4):365-369

650. Staniak HL, Bittencourt MS, Sharovsky R, Bensenor I, Olmos RD, Lotufo PA. Calcium score to evaluate chest pain in the emergency room. Arquivos Brasileiros de Cardiologia. 2013; 100(1):90-93

651. Stolzmann P, Alkadhi H, Scheffel H, Plass A, Leschka S, Falk V et al. Combining cardiac magnetic resonance and computed tomography coronary calcium scoring: added value for the assessment of morphological coronary disease? The International Journal of Cardiovascular Imaging. 2011; 27(7):969-977

652. Stolzmann P, Goetti R, Baumueller S, Plass A, Falk V, Scheffel H et al. Prospective and retrospective ECG-gating for CT coronary angiography perform similarly accurate at low heart rates. European Journal of Radiology. 2011; 79(1):85-91

653. Sun JL, Han R, Guo JH, Li XY, Ma XL, Wang CY. The diagnostic value of treadmill exercise test parameters for coronary artery disease. Cell Biochemistry and Biophysics. 2013; 65(1):69-76

654. Sun Y, Mao D, Lu F, Chen Y, Shi K, Qi L et al. Diagnosis of Dissection of the Coronary Artery Dissection by Multidetector Computed Tomography: A Comparative Study with Coronary Angiology. Journal of Computer Assisted Tomography. 2015; 39(4):572-577

655. Sun Z, Dimpudus FJ, Nugroho J, Adipranoto JD. CT virtual intravascular endoscopy assessment of coronary artery plaques: a preliminary study. European Journal of Radiology. 2010; 75(1):e112-119

656. Suratkal V, Shirke M, Lele RD. Treadmill ECG test combined with myocardial perfusion imaging for evaluation of coronary artery disease: analysis of 340 cases. Journal of the Association of Physicians of India. 2003; 51:561-564

657. Takahashi N, Inoue T, Oka T, Suzuki A, Kawano T, Uchino K et al. Diagnostic use of T2-weighted inversion-recovery magnetic resonance imaging in acute coronary syndromes compared with 99mTc-Pyrophosphate, 123I-BMIPP and 201TlCl single photon emission computed tomography. Circulation Journal. 2004; 68(11):1023-1029

658. Takakuwa KM, Halpern EJ. Evaluation of a "triple rule-out" coronary CT angiography protocol: use of 64-Section CT in low-to-moderate risk emergency department patients suspected of having acute coronary syndrome. Radiology. 2008; 248(2):438-446

659. Takakuwa KM, Halpern EJ, Shofer FS. A time and imaging cost analysis of low-risk ED observation patients: a conservative 64-section computed tomography coronary angiography "triple rule-out" compared to nuclear stress test strategy. American Journal of Emergency Medicine. 2011; 29(2):187-195

660. Takase B, Nagata M, Kihara T, Kameyawa A, Noya K, Matsui T et al. Whole-heart dipyridamole stress first-pass myocardial perfusion MRI for the detection of coronary artery disease. Japanese Heart Journal. 2004; 45(3):475-486

661. Takeuchi M, Miura Y, Sonoda S, Kuroiwa A. Comparison of three different protocols for dobutamine stress echocardiography: Does the addition of atropine increase complications, and does it improve diagnostic accuracy? Echocardiography. 1999; 16(4):347-355

662. Takx RA, Blomberg BA, El Aidi H, Habets J, de Jong PA, Nagel E et al. Diagnostic accuracy of stress myocardial perfusion imaging compared to invasive coronary angiography with fractional flow reserve meta-analysis. Circulation Cardiovascular imaging. 2015; 8(1)

663. Tan KT, Reed D, Howe J, Challenor V, Gibson M, McGann G. CT vs conventional angiography in unselected patients with suspected coronary heart disease. International Journal of Cardiology. 2007; 121(1):125-126

664. Tanaka A, Shimada K, Yoshida K, Jissyo S, Tanaka H, Sakamoto M et al. Non-invasive assessment of plaque rupture by 64-slice multidetector computed tomography--comparison with intravascular ultrasound. Circulation Journal. 2008; 72(8):1276-1281

665. Tanaka H, Chikamori T, Hida S, Igarashi Y, Miyagi M, Ohtaki Y et al. The diagnostic utility of the Heston index in gated SPECT to detect multi-vessel coronary artery disease. Journal of Cardiology. 2008; 51(1):42-49

666. Tanaka H, Shimada K, Yoshida K, Jissho S, Yoshikawa J, Yoshiyama M. The simultaneous assessment of aortic valve area and coronary artery stenosis using 16-slice multidetector-row computed tomography in patients with aortic stenosis comparison with echocardiography. Circulation Journal. 2007; 71(10):1593-1598

667. Tanami Y, Miller JM, Vavere AL, Rochitte CE, Dewey M, Niinuma H et al. Nuclear stress perfusion imaging versus computed tomography coronary angiography for identifying patients with obstructive coronary artery disease as defined by conventional angiography: Insights from the core-64 multicenter study. Heart International. 2014; 9(1):1-6

668. Tandogan I, Yetkin E, Ileri M, Ortapamuk H, Yanik A, Cehreli S et al. Diagnosis of coronary artery disease with Tl-201 SPECT in patients with left bundle branch block: importance of alternative interpretation approaches for left anterior descending coronary lesions. Angiology. 2001; 52(2):103-108

669. Tandogan I, Yetkin E, Yanik A, Ulusoy FV, Temizhan A, Cehreli S et al. Comparison of thallium-201 exercise SPECT and dobutamine stress echocardiography for diagnosis of coronary artery disease in patients with left bundle branch block. The International Journal of Cardiovascular Imaging. 2001; 17(5):339-345

670. Tardif JC, Dore A, Chan KL, Fagan S, Honos G, Marcotte F et al. Economic impact of contrast stress echocardiography on the diagnosis and initial treatment of patients with suspected coronary artery disease. Journal of the American Society of Echocardiography. 2002; 15(11):1335-1345

671. Tas MH, Aksakal E, Gurlertop Y, Simsek Z, Gundogdu F, Sevimli S et al. Assesment of myocardial ischemia by combination of tissue synchronisation imaging and dobutamine stress echocardiography. Korean Circulation Journal. 2013; 43(6):384-390

672. Ten Kate GJR, Caliskan K, Dedic A, Meijboom WB, Neefjes LA, Manintveld OC et al. Computed tomography coronary imaging as a gatekeeper for invasive coronary angiography in patients with newly diagnosed heart failure of unknown aetiology. European Journal of Heart Failure. 2013; 15(9):1028-1034

673. Than M, Aldous S, Lord SJ, Goodacre S, Frampton CM, Troughton R et al. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. JAMA Internal Medicine. 2014; 174(1):51-58

674. The Swedish Council on Health Technology Assessment. Computed tomography for suspected coronary artery disease Stockholm. Swedish Council on Technology Assessment in Health Care (SBU), 2011. Available from: http://www.sbu.se/globalassets/publikationer/content0/3/computed_tomography_suspected_coronary_artery_disease_201103_webb.pdf

675. Thelin J, Borna C, Erlinge D, Ohlin B. The combination of high sensitivity troponin T and copeptin facilitates early rule-out of ACS: a prospective observational study. BMC Cardiovascular Disorders. 2013; 13:42

676. Thilo C, Gebregziabher M, Mayer FB, Berghaus TM, Zwerner PL, Schoepf UJ. Can Non-calcified Coronary Artery Plaques Be Detected on Non-contrast CT Calcium Scoring Studies? Academic Radiology. 2011; 18(7):858-865

677. Thokala P, Goodacre SW, Collinson PO, Stevens JW, Mills NL, Newby DE et al. Cost-effectiveness of presentation versus delayed troponin testing for acute myocardial infarction. Heart. 2012; 98(20):1498-1503

678. Thompson AG, Raju R, Blanke P, Yang TH, Mancini GBJ, Budoff MJ et al. Diagnostic accuracy and discrimination of ischemia by fractional flow reserve CT using a clinical use rule: Results from the Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography study. Journal of Cardiovascular Computed Tomography. 2015; 9(2):120-128

679. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD et al. Third universal definition of myocardial infarction. Circulation. 2012; 126(16):2020-2035

680. Tomizawa N, Hayakawa Y, Nojo T, Nakamura S. Improving the diagnostic performance of the real world coronary computed tomography angiography including uninterpretable segments. International Journal of Cardiology. 2014; 176(3):975-979

681. Tomonaga Y, Gutzwiller F, Luscher TF, Riesen WF, Hug M, Diemand A et al. Diagnostic accuracy of point-of-care testing for acute coronary syndromes, heart failure and thromboembolic events in primary care: a cluster-randomised controlled trial. BMC Family Practice. 2011; 12:12

682. Treuth MG, Reyes GA, He ZX, Cwajg E, Mahmarian JJ, Verani MS. Tolerance and diagnostic accuracy of an abbreviated adenosine infusion for myocardial scintigraphy: a randomized, prospective study. Journal of Nuclear Cardiology. 2001; 8(5):548-554

683. Truong QA, Bayley J, Hoffmann U, Bamberg F, Schlett CL, Nagurney JT et al. Multi-marker strategy of natriuretic peptide with either conventional or high-sensitivity troponin-T for acute coronary syndrome diagnosis in emergency department patients with chest pain: from the "rule out myocardial infarction using computer assisted tomography" (ROMICAT) trial. American Heart Journal. 2012; 163(6):972-979

684. Truong QA, Hayden D, Woodard PK, Kirby R, Chou ET, Nagurney JT et al. Sex differences in the effectiveness of early coronary computed tomographic angiography compared with standard emergency department evaluation for acute chest pain: the rule-out myocardial infarction with Computer-Assisted Tomography (ROMICAT)-II Trial. Circulation. 2013; 127(25):2494-2502

685. Truong QA, Knaapen P, Pontone G, Andreini D, Leipsic J, Carrascosa P et al. Rationale and design of the dual-energy computed tomography for ischemia determination compared to "gold standard" non-invasive and invasive techniques (DECIDE-Gold): A multicenter international efficacy diagnostic study of rest-stress dual-energy computed tomography angiography with perfusion. Journal of Nuclear Cardiology. 2015; 22(5):1031-1040

686. Trzaska ZJ, Cohen MC. SPECT vs CT: CT is not the first line test for the diagnosis and prognosis of stable coronary artery disease. Journal of Nuclear Cardiology. 2013; 20(3):473-478

687. Tsai IC, Lee T, Lee WL, Tsao CR, Tsai WL, Chen MC et al. Use of 40-detector row computed tomography before catheter coronary angiography to select early conservative versus early invasive treatment for patients with low-risk acute coronary syndrome. Journal of Computer Assisted Tomography. 2007; 31(2):258-264

688. Tsai JP, Yun CH, Wu TH, Yen CH, Hou CJ, Kuo JY et al. A meta-analysis comparing SPECT with PET for the assessment of myocardial viability in patients with coronary artery disease. Nuclear Medicine Communications. 2014; 35(9):947-954

689. Tsai MF, Kao PF, Tzen KY. Improved diagnostic performance of thallium-201 myocardial perfusion scintigraphy in coronary artery disease: from planar to single photon emission computed tomography imaging. Chang Gung Medical Journal. 2002; 25(8):522-530

690. Tsang JC, Min JK, Lin FY, Shaw LJ, Budoff MJ. Sex comparison of diagnostic accuracy of 64-multidetector row coronary computed tomographic angiography: results from the

multicenter ACCURACY trial. Journal of Cardiovascular Computed Tomography. 2012; 6(4):246-251

691. Tsougos E, Panou F, Paraskevaidis I, Dagres N, Karatzas D, Kremastinos DT. Exercise-induced changes in E/E' ratio in patients with suspected coronary artery disease. Coronary Artery Disease. 2008; 19(6):405-411

692. Tsougos E, Paraskevaidis I, Dagres N, Varounis C, Panou F, Karatzas D et al. Detection of high-burden coronary artery disease by exercise-induced changes of the E/E' ratio. The International Journal of Cardiovascular Imaging. 2012; 28(3):521-530

693. Tsutsui JM, Xie F, O'Leary EL, Elhendy A, Anderson JR, McGrain AC et al. Diagnostic accuracy and prognostic value of dobutamine stress myocardial contrast echocardiography in patients with suspected acute coronary syndromes. Echocardiography. 2005; 22(6):487-495

694. Turkvatan A, Biyikoglu SF, Buyukbayraktar F, Olcer T, Cumhur T, Duru E. Clinical value of 16-slice multidetector computed tomography in symptomatic patients with suspected coronary artery disease. Acta Radiologica. 2008; 49(4):400-408

695. Turnipseed SD, Trythall WS, Diercks DB, Laurin EG, Kirk JD, Smith DS et al. Frequency of acute coronary syndrome in patients with normal electrocardiogram performed during presence or absence of chest pain. Academic Emergency Medicine. 2009; 16(6):495-499

696. Uebleis C, Groebner M, Von Ziegler F, Becker A, Rischpler C, Tegtmeyer R et al. Combined anatomical and functional imaging using coronary CT angiography and myocardial perfusion SPECT in symptomatic adults with abnormal origin of a coronary artery. International Journal of Cardiovascular Imaging. 2012; 28(7):1763-1774

697. Ueno K, Anzai T, Jinzaki M, Yamada M, Kohno T, Kawamura A et al. Diagnostic capacity of 64-slice multidetector computed tomography for acute coronary syndrome in patients presenting with acute chest pain. Cardiology. 2009; 112(3):211-218

698. Ueno Y, Nakamura Y, Kinoshita M, Fujita T, Sakamoto T, Okamura H. Noninvasive assessment of significant right coronary artery stenosis based on coronary flow velocity reserve in the right coronary artery by transthoracic Doppler echocardiography. Echocardiography. 2003; 20(6):495-501

699. Ulimoen GR, Gjonnaess E, Atar D, Dahl T, Stranden E, Sandbaek G. Noninvasive coronary angiography with 64-channel multidetector computed tomography in patients with acute coronary syndrome. Acta Radiologica. 2008; 49(10):1140-1144

700. Underwood SR, Godman B, Salyani S, Ogle JR, Ell PJ. Economics of myocardial perfusion imaging in Europe--the EMPIRE Study. European Heart Journal. 1999; 20(2):157-166

701. Underwood SR, Shaw LJ, Anagnostopoulos C, Cerqueira M, Ell PJ, Flint J et al. Myocardial perfusion scintigraphy and cost effectiveness of diagnosis and management of coronary heart disease. Heart. 2004; 90 Suppl 5:v34-36

702. Utsunomiya D, Oda S, Yuki H, Yamamuro M, Tsujita K, Funama Y et al. Evaluation of appropriateness of second-generation 320-row computed tomography for coronary artery disease. Springerplus. 2015; 4:109

703. Vaidya A, Severens JL, Bongaerts BW, Cleutjens KB, Nelemans PJ, Hofstra L et al. High-sensitive troponin T assay for the diagnosis of acute myocardial infarction: an economic evaluation. BMC Cardiovascular Disorders. 2014; 14:77

704. Valenta I, Quercioli A, Schindler TH. Diagnostic value of PET-measured longitudinal flow gradient for the identification of coronary artery disease. JACC: Cardiovascular Imaging. 2014; 7(4):387-396

705. van der Wall EE. The promise study: A clear promise for functional stress testing in patients with suspected coronary artery disease. Netherlands Heart Journal. 2015; 23(6):297-298

706. Van Geuns RJM, De Bruin HG, Rensing BJWM, Wielopolski PA, Hulshoff MD, Van Ooijen PMA et al. Magnetic resonance imaging of the coronary arteries: Clinical results from three dimensional evaluation of a respiratory gated technique. Heart. 1999; 82(4):515-519

707. Van Mieghem CAG, Thury A, Meijboom WB, Cademartiri F, Mollet NR, Weustink AC et al. Detection and characterization of coronary bifurcation lesions with 64-slice computed tomography coronary angiography. European Heart Journal. 2007; 28(16):1968-1976

708. van Velzen JE, de Graaf FR, Kroft LJ, de Roos A, Reiber JH, Bax JJ et al. Performance and efficacy of 320-row computed tomography coronary angiography in patients presenting with acute chest pain: results from a clinical registry. The International Journal of Cardiovascular Imaging. 2012; 28(4):865-876

709. van Velzen JE, Schuijf JD, de Graaf FR, Boersma E, Pundziute G, Spano F et al. Diagnostic performance of non-invasive multidetector computed tomography coronary angiography to detect coronary artery disease using different endpoints: detection of significant stenosis vs. detection of atherosclerosis. European Heart Journal. 2011; 32(5):637-645

710. van Werkhoven JM, Heijenbrok MW, Schuijf JD, Jukema JW, van der Wall EE, Schreur JH et al. Combined non-invasive anatomical and functional assessment with MSCT and MRI for the detection of significant coronary artery disease in patients with an intermediate pre-test likelihood. Heart. 2010; 96(6):425-431

711. Vashist A, Collins D, Prasad Y, Blum S, Heller EN. Does cardiac SPECT using attenuation and scatter correction accurately predict coronary artery disease in a minority women population? Medical Science Monitor. 2007; 13(9):CR386-390

712. Vavere AL, Arbab-Zadeh A, Rochitte CE, Dewey M, Niinuma H, Gottlieb I et al. Coronary artery stenoses: accuracy of 64-detector row CT angiography in segments with mild, moderate, or severe calcification--a subanalysis of the CORE-64 trial. Radiology. 2011; 261(1):100-108

713. Verna E, Ceriani L, Giovanella L, Binaghi G, Garancini S. "False-positive" myocardial perfusion scintigraphy findings in patients with angiographically normal coronary arteries: insights from intravascular sonography studies. Journal of Nuclear Medicine. 2000; 41(12):1935-1940

714. Vigna C, Stanislao M, De Rito V, Russo A, Natali R, Santoro T et al. Dipyridamole stress echocardiography vs dipyridamole sestamibi scintigraphy for diagnosing coronary artery disease in left bundle-branch block. Chest. 2001; 120(5):1534-1539

715. Vijayakrishnan R, Ariyarajah V, Apiyasawat S, Spodick DH. Usefulness of diastolic time measured on electrocardiogram to improve sensitivity and specificity of exercise tolerance tests. American Journal of Cardiology. 2012; 109(2):174-179

716. Vogel-Claussen J, Skrok J, Dombroski D, Shea SM, Shapiro EP, Bohlman M et al. Comprehensive adenosine stress perfusion MRI defines the etiology of chest pain in the emergency room: Comparison with nuclear stress test. Journal of Magnetic Resonance Imaging. 2009; 30(4):753-762

717. Volz KA, McGillicuddy DC, Horowitz GL, Sanchez LD. Creatine kinase-MB does not add additional benefit to a negative troponin in the evaluation of chest pain. American Journal of Emergency Medicine. 2012; 30(1):188-190

718. von Ziegler F, Brendel M, Uebleis C, Helbig S, Greif M, Ruemmler J et al. SPECT myocardial perfusion imaging as an adjunct to coronary calcium score for the detection of hemodynamically significant coronary artery stenosis. BMC Cardiovascular Disorders. 2012; 12 (no pagination)(116)

719. von Ziegler F, Schenzle J, Schiessl S, Greif M, Helbig S, Tittus J et al. Use of multi-slice computed tomography in patients with chest-pain submitted to the emergency department. The International Journal of Cardiovascular Imaging. 2014; 30(1):145-153

720. Wagdi P, Alkadhi H. The impact of cardiac CT on the appropriate utilization of catheter coronary angiography. The International Journal of Cardiovascular Imaging. 2010; 26(3):333-344

721. Walker S, Girardin F, McKenna C, Ball SG, Nixon J, Plein S et al. Cost-effectiveness of cardiovascular magnetic resonance in the diagnosis of coronary heart disease: an economic evaluation using data from the CE-MARC study. Heart. 2013; 99(12):873-881

722. Wang Q, Qin J, Gai LY, Chen YD, Dong W, Guan ZW et al. A pilot study on diagnosis of coronary artery disease using computed tomography first-pass myocardial perfusion imaging at rest. Journal of Zhejiang University SCIENCE B. 2011; 12(6):485-491

723. Wang R, Yu W, Wang Y, He Y, Yang L, Bi T et al. Incremental value of dual-energy CT to coronary CT angiography for the detection of significant coronary stenosis: comparison with quantitative coronary angiography and single photon emission computed tomography. The International Journal of Cardiovascular Imaging. 2011; 27(5):647-656

724. Watkins MW, Hesse B, Green CE, Greenberg NL, Manning M, Chaudhry E et al. Detection of Coronary Artery Stenosis Using 40-Channel Computed Tomography With Multisegment Reconstruction. American Journal of Cardiology. 2007; 99(2):175-181

725. Weber M, Bazzino O, Navarro Estrada JL, de MR, Salzberg S, Fuselli JJ et al. Improved diagnostic and prognostic performance of a new high-sensitive troponin T assay in patients with acute coronary syndrome. American Heart Journal. 2011; 162(1):81-88

726. Wehrschuetz M, Wehrschuetz E, Schuchlenz H, Schaffler G. Accuracy of MSCT coronary angiography with 64 row CT scanner - Facing the facts. Clinical Medicine Insights: Cardiology. 2010; 4:15-22

727. Weinsaft JW, Gade CL, Wong FJ, Kim HW, Min JK, Manoushagian SJ et al. Diagnostic impact of SPECT image display on assessment of obstructive coronary artery disease. Journal of Nuclear Cardiology. 2007; 14(5):659-668

728. Westwood M, van Asselt T, Ramaekers B, Whiting P, Thokala P, Joore M et al. High-sensitivity troponin assays for the early rule-out or diagnosis of acute myocardial infarction in people with acute chest pain: a systematic review and cost-effectiveness analysis. Health Technology Assessment (Winchester, England). 2015; 19(44):1-234

729. Weustink AC, Meijboom WB, Mollet NR, Otsuka M, Pugliese F, van Mieghem C et al. Reliable high-speed coronary computed tomography in symptomatic patients. Journal of the American College of Cardiology. 2007; 50(8):786-794

730. Weustink AC, Mollet NR, Neefjes LA, Meijboom WB, Galema TW, van Mieghem CA et al. Diagnostic accuracy and clinical utility of noninvasive testing for coronary artery disease. Annals of Internal Medicine. 2010; 152(10):630-639

731. Weustink AC, Neefjes LA, Rossi A, Meijboom WB, Nieman K, Capuano E et al. Diagnostic performance of exercise bicycle testing and single-photon emission computed tomography: comparison with 64-slice computed tomography coronary angiography. The International Journal of Cardiovascular Imaging. 2012; 28(3):675-684

732. White CS, Kuo D, Kelemen M, Jain V, Musk A, Zaidi E et al. Chest pain evaluation in the emergency department: can MDCT provide a comprehensive evaluation? AJR American Journal of Roentgenology. 2005; 185(2):533-540

733. White HD, Tonkin A, Simes J, Stewart R, Mann K, Thompson P et al. Association of contemporary sensitive troponin I levels at baseline and change at 1 year with long-term coronary events following myocardial infarction or unstable angina: results from the LIPID Study (Long-Term Intervention With Pravastatin in Ischaemic Disease). Journal of the American College of Cardiology. 2014; 63(4):345-354

734. Wierzbowska-Drabik K, Roszczyk N, Sobczak M, Kurpesa M, Plonska-Gosciniak E, Kasprzak JD. Effect of sex on the diagnostic efficacy of dobutamine stress echocardiography with early atropine administration in the detection of coronary artery disease. Polskie Archiwum Medycyny Wewnetrznej. 2014; 124(3):105-113

735. Wilson SR, Min JK. The potential role for the use of cardiac computed tomography angiography for the acute chest pain patient in the emergency department. Journal of Nuclear Cardiology. 2011; 18(1):168-176

736. Winchester DE, Brandt J, Schmidt C, Allen B, Payton T, Amsterdam EA. Diagnostic yield of routine noninvasive cardiovascular testing in low-risk acute chest pain patients. American Journal of Cardiology. 2015; 116(2):204-207

737. Winchester DE, Jeffrey R, Schwarz J, Jois P. Comparing two strategies for emergency department chest pain patients: immediate computed tomography coronary angiography versus delayed outpatient treadmill testing. Critical Pathways in Cardiology: A Journal of Evidence-Based Medicine. 2013; 12(4):197-200

738. Winchester DE, Jois P, Kraft SM, Wymer DC, Hill JA. Immediate computed tomography coronary angiography versus delayed outpatient stress testing for detecting coronary artery disease in emergency department patients with chest pain. The International Journal of Cardiovascular Imaging. 2012; 28(3):667-674

739. Xu Y, Tang L, Zhu X, Xu H, Tang J, Yang Z et al. Comparison of dual-source CT coronary angiography and conventional coronary angiography for detecting coronary artery disease. The International Journal of Cardiovascular Imaging. 2010; 26 Suppl 1:75-81

740. Yamada AT, Soares J, Jr., Meneghetti JC, Araujo F, Ramires JA, Mansur AJ. Planar myocardial perfusion imaging for evaluation of patients with acute chest pain. International Journal of Cardiology. 2004; 97(3):447-453

741. Yang FB, Guo WL, Sheng M, Sun L, Ding YY, Xu QQ et al. Diagnostic accuracy of coronary angiography using 64-slice computed tomography in coronary artery disease. Saudi Medical Journal. 2015; 36(10):1156-1162

742. Yerramasu A, Lahiri A, Venuraju S, Dumo A, Lipkin D, Underwood SR et al. Diagnostic role of coronary calcium scoring in the rapid access chest pain clinic: prospective evaluation of NICE guidance. European Heart Journal Cardiovascular Imaging. 2014; 15(8):886-892

743. Zaag-Loonen HJ, Dikkers R, Bock GH, Oudkerk M. The clinical value of a negative multi-detector computed tomographic angiography in patients suspected of coronary artery disease: a meta-analysis. European Radiology. 2006; 16(12):2748-2756

744. Zancaner LF, Villa AV, Trindade EM, Rocha RPS, Dantas RN, Cabeda EV et al. Diagnostic accuracy of 320 detector-row computed tomography for detection of significant coronary artery disease in the clinical routine. Echocardiography. 2012; 29 (2):261

745. Zeb I, Abbas N, Nasir K, Budoff MJ. Coronary computed tomography as a cost-effective test strategy for coronary artery disease assessment - a systematic review. Atherosclerosis. 2014; 234(2):426-435

746. Zeb I, Nasir K, Budoff M. Coronary computed tomography reduces downstream resource utilization and is cost-effective test strategy for coronary artery disease assessment - A systematic review. Circulation Conference: American Heart Association. 2012; 126(21 SUPPL. 1)

747. Zhang L, Chen X, Su T, Li H, Huang Q, Wu D et al. Circulating miR-499 are novel and sensitive biomarker of acute myocardial infarction. Journal of Thoracic Disease. 2015; 7(3):303-308

748. Zhang LJ, Wu SY, Wang J, Lu Y, Zhang ZL, Jiang SS et al. Diagnostic accuracy of dual-source CT coronary angiography: The effect of average heart rate, heart rate variability, and calcium score in a clinical perspective. Acta Radiologica. 2010; 51(7):727-740

749. Zhang ZH, Jin ZY, Li DJ, Lin SB, Zhang SY, Kong LY et al. Non-invasive imaging of coronary artery with 16-slice spiral computed tomography. Chinese Medical Sciences Journal. 2004; 19(3):174-179

750. Zhao XJ, Li BQ, Ren JY, Chen H. Diagnostic accuracy and influence factors of mutislice ct in women versus men with suspected or proven coronary artery disease. Heart. 2011; 97:A141

751. Zorga P, Birkenfeld B, Listewnik MH, Piwowarska-Bilska H. Prognostic value of myocardial perfusion scintigraphy for patients suspected of and diagnosed with coronary artery disease. Nuclear Medicine Review. 2012; 15(1):14-21

752. Zwank MD, House CM, Isenberger KM, Quaday KA, Ziegenfuss JY, Moriarty KA et al. Early discharge with next day stress testing in low risk chest pain patients presenting to the emergency department is feasible. Annals of Emergency Medicine. 2015; 1):S18