Chest pain of recent onset (acute) update
Consultation on draft guideline - Stakeholder comments table
30/06/2016 to 28/07/2016

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Cardiovascular Society	Full	General	General	The terms acute coronary syndrome (ACS) and acute myocardial infarction (AMI) seem to be used interchangeably in the document (perhaps simply mirroring the common mistake that is also made in clinical medicine). The 2 terms are not the same thing. ACS is one specific cause of AMI. There are many other causes of AMI as defined in the universal definition. In addition ACS occasionally does not result in AMI (a condition we then often refer to as unstable angina – ACS). Using the correct terminology is important as the management and prognosis for ACS is different to other causes of AMI	Thank you for your comment. We have reviewed the use of the terms ACS and AMI to ensure that they are used in the correct context throughout the guideline.
British Cardiovascular Society	Full	General	General	This document refers solely to the management of patients with chest pain. A significant minority of ACS and AMI patients present with other symptoms (eg dyspnoea, syncope, epigastric pain, arm pain, delirium) or are extremely unwell and therefore simply do not or cannot describe symptoms (eg those that present with cardiac arrest, shock, or acute pulmonary oedema). There is a danger that clinicians reading this guidance will be discouraged from considering a diagnosis of ACS in those patients not presenting with chest pain. Different thresholds for diagnostic tests such as hs troponin need to be considered in such patients presenting with "atypical" symptoms (reference: Biener et al (2015) Impact of leading presentation on the diagnostic performance of high-sensitivity troponin T and on outcomes in patients with suspected acute coronary syndrome. Clinical Chemistry 61:5. 1-8	Thank you for your comment. This guideline is partial update of Chest pain of recent onset (NICE clinical guideline 95). We have added a sentence on the symptoms people may present with to the 'other considerations' section of the linking evidence to recommendation (High sensitivity cardiac troponins section 6.4.1.4.2.). We have also added a sentence to highlight that a different threshold may be necessary for people presenting with atypical chest pain. The study you refer to did not meet the inclusion criteria specified in the protocol. The review question was to ascertain how different levels of risk impact on diagnostic accuracy. We have added it to the excluded studies list.
British Cardiovascular Society	Full	General	General	I do not feel that enough has been highlighted about the disadvantages of high sensitivity troponins over "standard" troponin assays. Although they are more sensitive for detecting myocardial injury, they are less specific for a	Thank you for your comment. The Guideline Committee noted that the use of high-sensitivity troponin over standard troponin comes at the

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				diagnosis of acute coronary syndrome. Pathologies other than ACS can cause a rise in troponin, but the rise is often small and below the detection limit of standard troponin assays. High sensitivity troponin assays can pick up these small rises and although this means a potential benefit in diagnosing a few more true ACS cases, in the real world (and certainly in my hospital) this benefit is outweighed by the harm of wrongful ACS diagnosis and its treatment in those patients with small hs troponin rises due to other causes of myocardial injury.	expense of specificity and recognised that there are more false positives as a result, This has been addressed in the linking evidence to recommendation (High sensitivity cardiac troponins section 6.4.1.4.2.) and a new recommendation (Ensure that patients understand that a detectable troponin on the first high-sensitivity test does not necessarily indicate that they have had an MI) has been included in the guideline to ensure that clinicians convey to patients that a detectable troponin on the first test does not necessarily mean they have had an Myocardial Infarction.
British Cardiovascular Society	Full	22	9	Typo: there is a parenthesis that shouldn't be there	Thank you for your comment. The recommendation that you refer to has not been updated in this review so no changes to the text have been made.
British Cardiovascular Society	Full	23	11 13	Refers to patients with negative troponin and normal ECG as "Stable" chest pain. This is often not the case. Patients who present to the acute medical services normally do so because the chest pain is new, or increasing in frequency, or is more prolonged, or more severe in nature. In these circumstances, if the chest pain has typical ischaemic / angina characteristics, it should not be referred to as stable chest pain. It should be diagnosed as unstable angina. Unstable angina patients should not be discharged and followed up along the lines of stable angina patients. They require admission, antiplatelet and anticoagulatant therapy (assuming no contraindications) and consideration for coronary angiography along the lines of CG95.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
British Cardiovascular Society	Full	113	27 28	"Cardiac biomarkers are proteins that are released into the cardiac interstitium due to the compromised integrity of myocyte cell membranes as a result of myocardial ischaemia"	Thank you for your comment. We have edited this sentence as suggested.

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				Biomarkers are generally not specific for ischaemic injury. They rise in any form of myocyte injury (eg myocarditis, cardiac contusion). Therefore should read: "Cardiac biomarkers are proteins that are released into the cardiac interstitium due to the compromised integrity of myocyte cell membranes as a result of myocardial ischaemia or non-ischaemic injury"	
British Cardiovascular Society	Full	138 143	General	Tables 25 and 26 are very difficult to interpret – for example, what does row 3, 1st column of Table 25 mean? *"Index test at peak threshold of 14 minus admission."* What is a "peak threshold" and "minus admission" what? I find all the entries in Column 1 of Tables 25 and 26 are difficult to understand and are potentially inconsistent – for example, in Table 26, page 142, column 1, row 3 refers to "index test at 14 threshold", whereas the next row down states "index test at threshold 14". Does the reversal of "14" and "threshold" in these 2 adjacent rows mean anything different or are they 2 different ways of referring to the same thing? There are multiple other examples of the way thresholds and potentially associated numbers are arranged relative to one another throughout these Tables. It is clear that all the high sensitivity troponin assays behave differently from one another and the troponin values produced are not equivalent. It would greatly aid interpretation of Tables 25 and 26, if the Troponin assay evaluated in each row of the Tables was made clear. A threshold of 14 with the Roche	Thank you for your comment. Tables 25 and 26 have been edited. It has been made clearer that all of the results are for the Roche assay except for one. The recommendation refers to limit of detection because of the point you raise regarding the different thresholds for different assays. The threshold is defined as when a high sensitivity troponin result is positive. The threshold is based on testing of reference populations, which vary widely from assay to assay. It is measured in ng/l .Peak threshold refers to the peak troponin levels for the assay. Minus admission refers to the time, 0 hours was admission and minus admission refers to measurements before admission to the emergency department or hospital.

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				Assay will mean something very different from a threshold of 14 on the Beckman-Coulter Assay.	
British Cardiovascular Society	Full	138 141	General	Table 25: I could not understand what this table was trying to illustrate and which troponin assays were being evaluated. It seems to say that the quality of evidence is LOW or VERY LOW for all the studies. If this is the case how can one recommend high sensitivity troponin?	Thank you for your comment. Table 25 has been edited to make it clearer. Table 26 specifies which assays were being evaluated. The studies were rated at low or very low quality due to risk of bias as assessed using QUADAS 2 and if there was uncertainty regarding the results (assessed by the confidence intervals). Risk of bias and indirectness of evidence for diagnostic data were evaluated by study using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) Please see the method chapter section 4.2.6.2 for detail on QUADAS 2,The linking evidence to recommendation (High sensitivity cardiac troponins section 6.4.1.4.2).explains the rationale for the recommendations. The ratings were mostly a result of a lack of blinding of those applying the reference standard to the result of the high-sensitivity troponins and a large number of patients not having the reference standard investigation. The GC considered that the diagnostic criteria used in these studies were an accurate reflection of current clinical practice and that this source of bias did not reduce confidence in the results.

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British Cardiovascular Society	Full	144 5	6	As above, it is clear that all the high sensitivity troponin assays behave differently from one another and the troponin values produced are not equivalent. Each evidence statement should therefore make clear which assay it refers to.	Thank you for your comment. The recommendation refers to limit of detection because the assays differ. The tables and evidence statements have been edited to make it clear what assays were used.
British Cardiovascular Society	Full	145	Rec 1	I strongly agree. It would be great if this did have a strong impact on clinical practice. Sadly, I suspect it wont. It is commonplace for troponin assays to be requested by triage nurses / healthcare professionals in A+E or on acute medical units. This is before a comprehensive clinical evaluation has taken place. This often leads to troponin assays requested in patients in whom the most likely diagnosis is not ACS. Unfortunately this then influences the doctors who see the patients and incorrect diagnoses of ACS based solely on a small troponin rise. Guidelines such as this one are read predominantly by cardiologists. I suspect they are rarely read and digested by A+E and acute medical department consultants. The challenge therefore is to change practice at the front door.	Thank you for your comment.
British Cardiovascular Society	Full	145	Rec 2	There appears to be no evidence presented at all for the Abbott ARCHITECT STAT assay that is recommended for use in NICE DG 15, yet the guideline states that we should follow NICE DG 15. How is this? A large study from a UK group using high sensitivity troponin I testing with the Abbot ARCHITECT STAT assay does not appear to have been considered for review (Shah et al, Lancet (2015);386:2481-88)	Thank you for your comment. The purpose of this partial update was not to re-examine the evidence in DG15 or to replace the recommendations made. Our review questions were on diagnostic accuracy of high-sensitivity troponins according to risk of Acute Coronary Syndrome and on non-invasive imaging. The paper you refer to was excluded because it did not meet the criteria set out in the protocol for the review question.

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					Specifically the paper used myocardial infarction, or subsequent myocardial infarction or cardiac death at 30 days as the primary outcome and not as a reference test. They also only report predictive values. The study has been added to the list of excluded studies for this review question
British Cardiovascular Society	Full	145	Rec 2	Refers to DG15 – this recommends typically taking samples for hsTn at 0 and 3 hours. This could have considerable financial and practical impacts on those trust which currently only take one troponin blood test at 6 hours post symptom onset. If the aim is to rule out myocardial injury (you cant rule out ACS with hs Tn) rapidly allowing for early discharge then perhaps a 0 and 1 hr algorithm should be used which would fit better with the 4 hour target in A+E (which they are absolutely obsessed with up and above almost any thing else!)	Thank you for your comment. DG15 does recommend samples are taken at 0 and 3hrs. The recommendations in this guideline propose that low risk patients can be discharged after the first sample taken on admission. This will reduce resource use. There was very little evidence for the accuracy of a second sample taken at less than three hours for the moderate or high risk groups. The rationale for these recommendation is in the linking evidence to recommendation
British Cardiovascular Society	Full	145	Rec 3	What is the high quality evidence for suggesting a different hsTn testing algorithm in "low risk" MI patients as opposed to "moderate or high risk MI" patients? May be I have missed it in amongst the bewildering tables and figures. Perhaps the rationale could be better illustrated.	Thank you for your comment. The linking evidence to recommendations section (High sensitivity cardiac troponins section 6.4.1.4.2). explains the rationale for the recommendations. The GC focused on the different testing for the low risk population. They noted that on the basis of a negative predictive value of 99%, a negative result on presentation would indicate that a patient did not have ACS and so might be safely discharged home without being kept in hospital for a second test.

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British Cardiovascular Society	Full	145	Recs 2 3	Q1 and 2 – biggest impact on practice and cost implications The increased sensitivity of high sensitivity troponin assays, combined with a significantly reduced time-to-detection/testing is very attractive and I am sure that recommending their use (as in recommendations 2 and 3) is the correct thing to do. However, there may be very considerable cost implications for trusts in acquiring new high sensitivity troponin assays. For example, my own trust's (very large) biochemistry lab exclusively uses Beckman Coulter assays for all biochemical testing (including troponin), but NICE DG15 states that Beckman Coulter's high sensitivity troponin assay should not be used. To acquire a standalone Roche or Abbott assay (as recommended by DG 15) would involve a considerable capital outlay of >> £100k along with additional staff resources to run the equipment alongside the main Beckman Coulter apparatus used for all other biochemistry tests. In the current NHS economic climate this is not viable.	Thank you for your comment . The recommendation of high sensitivity troponin assays was made and approved by DG15, the evaluation of which was not part of this guidance. As part of the guidance produced by DG15 a costing statement was published by NICE along with other tools to aid in implementation and can be found here: https://www.nice.org.uk/guidance/dg15/resources/costing-statement-49213
British Cardiovascular Society	Full	196	7	On the basis of the evidence reviewed, and in particular the increased use of high sensitivity troponin in routine clinical practice, the recommendation to not routinely offer non-invasive imaging or exercise ECG in the initial assessment of acute chest pain seems appropriate. This is unlikely to be many centres routine practice in any case and so is unlikely to have any major implications for most NHS hospitals.	Thank you for your comment.

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				I agree that these tests may still have a role as outlined in the "other considerations" section on page 199	
British Cardiovascular Society	Full	196	General	I agree with the recommendation. I don't think this recommendation will have much negative impact as few centres use non-invasive imaging / ETT to assess patients with acute chest pain prior to a diagnosis of ACS	Thank you for your comment.
Resuscitation Council (UK)	Short	General	general	I regret that the initial invitation to comment on this draft guideline escaped our notice. As a result, I have had a chance only to review the short version. On behalf of the Resuscitation Council (UK) I have no comments or concerns to submit on the proposed changes to this.	Thank you for your comment.
Resuscitation Council (UK)	Short	General	General	I note that the changes made are relatively few, and that you have invited comment only on these, and not on the wording that you propose to leave unchanged. This is disappointing as there are some errors in the wording of the grey sections of the draft guideline. In case it is of any assistance, in addition to some punctuation errors, these are as follows:	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates
Resuscitation Council (UK)	Short	14	10 12	"Only use CT to 'rule out' PE…". This is incorrect: CT can be used also to diagnose PE …	Thank you for your comment. We are unable to update this recommendation as it was outside of the scope of this partial update.
Resuscitation Council (UK)	Short	14	13 15	This should be worded: "Consider a CXR to help exclude or confirm complications such as pulmonary oedema." Again, the purpose of an investigation is to try to answer a question, not purely to "rule out" a diagnosis or condition.	Thank you for your comment. We are unable to update this recommendation as it was outside of the scope of this partial update.
Resuscitation Council (UK)	Short	15	16 21	Physical examination may also identify other contributing causes of angina, such as anaemia – this is mentioned only later in relation to performing blood tests, when it could have been picked up at this earlier stage.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment

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					and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates
Resuscitation Council (UK)	Short	15	23 27	p 15 lines 23-27 In some people angina may be felt in the epigastrium or in the back of the chest. This should be mentioned.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates
Resuscitation Council (UK)	Short	19	25 28	p 19 lines 25-28 This is worded very badly resulting in potential double meaning: "Consider aspirin only if the person's chest pain is likely to be stable angina, until a diagnosis is made". I think the intended meaning is "Until a diagnosis is made, consider aspirin if the person's chest pain is likely to be stable angina, but not if the cause is uncertain or is unlikely to be angina".	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates
Roche Diagnostics Ltd	Short	11 12	29 29 and 1 9	We are concerned that neither this document nor DG15 specify what a "validated tool" is or gives appropriate examples. In order to reduce variation in service provision, we would recommend giving examples (e.g. "GRACE" or "TIMI" Risk Scoring tools). Furthermore, although users are directed to DG15, which does recommend high-sensitivity troponin tests for use with early rule-out protocols, (e.g. the "three-hour protocol"), we feel that this should be made explicit here. Also, information	Thank you for your comment. The linking evidence to recommendation refers to TIMI and GRACE (High sensitivity cardiac troponins section 6.4.1.4.2).The committee recognised that GRACE is commonly used in clinical practice and that the TIMI and GRACE validated scoring system would result in a similar risk categorisation. They also acknowledged there may be other validated risk scoring tools and as such did not refer to specific tools in the recommendation.

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				on the criteria for positive and negative test results should be detailed here. Despite NICE Guidance and adoption support tools, and local and international clinical guidelines recommending early rule-out high-sensitivity troponin testing (most recently the 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation), we are aware that only 20% of trusts in the England and Wales routinely diagnose patients this way, which has been raised as a matter of national concern (re: Ministerial Medical Technology Programme meeting, 23rd March 2016, Whitehall, London). Therefore, this area of the guidelines has been particularly difficult to implement thus far and will continue to be so unless more is done. Question 3: We believe that stronger wording explicitly re-iterating the recommendations of DG15 may help to encourage a change in practice. Users would also benefit from more explicit service redesign testimonials, network support initiatives, and support from the field implementation team. We would recommend contacting the following cardiologists who have adopted the three-hour (and shorter) protocols, as excellent sources for testimonials and advice on the service changes necessary to enable implementation: • Dr. Mickey Jachuck at South Tyneside NHS Foundation Trust (mickey.jachuck@stft@nhs.uk) • Dr. Sadie Thomas at Gloucestershire Hospitals NHS Foundation Trust (sadie.thomas3@nhs.net)	The purpose of this partial update was not to re-examine the evidence in DG15 or to replace the recommendations it made. Our review questions were on diagnostic accuracy of high sensitivity troponins according to risk of ACS and on non-invasive imaging. We are unable to reproduce the recommendations in DG15. We have added an explanation to the linking evidence to recommendation (High sensitivity cardiac troponins section 6.4.1.4.2).regarding DG15. The introduction also describes the purpose of the review.

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				• Dr. Richard Harris at Kettering General Hospital (richard.harris@kgh.nhs.uk) • Dr. Aleem Khan at Aintree University Hospitals NHS Foundation Trust (aleem.khand@lhch.nhs.uk, ALEEM.KHAND@aintree.nhs.uk)	
Royal College of General Practitioners	Short	General	General	The RCGP feels that the updated chest pain guidance has little or no impact on community based general practice. (MJ)	Thank you for your comment.
Royal College of General Practitioners	Short	General	General	The updated guidance is a missed opportunity to help primary care physicians and nurses in their management of acute chest pain in the community. Starting at the point of these patients "having suspected ACS" fails to recognise the considerable clinical uncertainty that exists in these consultations and they usually are near their end when a diagnosis of ACS is being considered. (MJ)	Thank you for your comment. The review questions for this partial update were on the diagnostic accuracy of high-sensitivity troponins according to risk, the clinical and cost effectiveness of non-invasive imaging and the diagnostic accuracy of these tests. The GC were therefore unable to make recommendations on the topics you suggest.
Royal College of General Practitioners	Short	11 13	26 27 1 11	The RCGP welcomes these sections as they report new evidence and could be highlighted. Indeed the whole of 1.1 & 1.2 could be reduced to these two statements. (DJ)	Thank you for your comment.
Royal College of General Practitioners	Short	11	28	The phrase "(as indicated by a validated tool)' would benefit from expansion with examples of currently validated tools and the settings they apply. Is there a tool applicable for primary care? (MH)	Thank you for your comment. The linking evidence to recommendation refers to TIMI and GRACE (High sensitivity cardiac troponins section 6.4.1.4.2).The committee recognised that GRACE is

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					commonly used in clinical practice and that the TIMI and GRACE validated scoring system would result in a similar risk categorisation. They also acknowledged there may be other validated risk scoring tools and as such did not refer to specific tools in the recommendation.
Royal College of General Practitioners	Short	17	17 20	1. Important statement. Why is this only invoked at probability of angina >90%? The RCGP would recommend to opt for standard medical treatment at a probability considerably below this, and use treatment as a therapeutic trial. Applying the data in table 1 the RCGP finds an unclear conclusion. For instance, according to the guideline, men with typical angina below the age of 60 but with no other risk factors, and all women with or without risk factors are to be offered coronary angiography. Patients may refuse it and ask for medical treatment. It would be appropriate if the guidance recommends some kind of shared decision making over this. Two things need to be pointed out: first that all doctors, and certainly all GPs take decisions when certainty is a long way below the 90% threshold; second this will may lead to a huge amount of over investigation, lots of unnecessary, potentially pointless, and potentially dangerous stent insertion. 2. The RCGP misses further advice when the guidance says 'Manage as angina'. Is the guidance in another NICE document? Some clarification would be much appreciated. Looking in vain for a reminder that percutaneous stenting in stable angina appears to confer no advantage over medical treatment. (DJ)	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates

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Royal College of General Practitioners	Short	4 14	General	Section 1.1 is restatement of principles governing clinical care in all specialties. Does it need saying at all? Ditto section 1.2, which is the same, only specifically directed to ACS. Both sections are too general and does not give appropriate guideline for more experienced doctors. (DJ)	Thank you for your comment. The section of the guideline that you refer to was not updated.
Royal College of General Practitioners	Short	16 17	10 16	Inconsistency between treating men and women the same, and the statement in 1.3.3.4 to take male gender into account. (DJ)	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates
Royal College of Nursing	General	General	General	The Royal College of Nursing welcomes proposals to update these guidelines. The RCN invited members who care for people with cardiac issues to review the draft guidelines update on its behalf. The comments below include the views of our reviewers.	Thank you for your comment.
Royal College of Nursing	General	General	General	The updated version of the guidelines seem more realistic with less significant changes from the 2010 version and will be much easier to implement in clinical practice.	Thank you for your comment.
Royal College of Psychiatrists	Full	7	General	It would have been helpful to have a Consultant Liaison Psychiatrist on the guideline group given the frequency of atypical chest pain in acute presentations of chest pain.	Thank you for your comment. The review questions for this partial update were on the diagnostic accuracy of high-sensitivity troponins according to risk, the clinical and cost effectiveness of non-invasive

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					imaging and the diagnostic accuracy of these tests. The assessment of people with chest pain was not within our remit. We have added a sentence to the 'other considerations' section of the linking evidence to recommendations (High sensitivity cardiac troponins section 6.4.1.4.2.) to highlight that people may present with chest pain that is psychological in origin and this may require a referral to mental health services.
Royal College of Psychiatrists	Full	13	General	This is simple to implement but risks no diagnosing atypical (psychologically triggered) chest pain. This may be due to panic attacks or a somatoform disorder. If the patient does not receive a diagnosis and brief management advice they are much more likely to re-present. They will also fail to receive appropriate treatment for their actual diagnosis. This problem could be overcome where there is an on-site Hospital Liaison Psychiatry team who could provide training on such psychoeducation and could also provide a fuller psychosocial assessment or brief intervention with appropriate commissioning.	Thank you for your comment. The review questions for this partial update were on the diagnostic accuracy of high-sensitivity troponins according to risk, the clinical and cost effectiveness of non-invasive imaging and the diagnostic accuracy of these tests. The assessment of people with chest pain was not within our remit. We have added a sentence to the 'other considerations' section of the linking evidence to recommendations (High sensitivity cardiac troponins section 6.4.1.4.2.) to highlight that people may present with chest pain that is psychological in origin and this may require a referral to mental health services.
Royal College of Psychiatrists	Full	13	General	There is not a pathway for those patients who are admitted for further assessment and then deemed not to have cardiac chest pain. This group of patients forms a significant group in many acute admissions units. The response (as for point 2) is make the diagnosis (muscle strain, panic attack, somatoform disorder) and follow with appropriate brief management advice. This could be helped by on site Liaison Psychiatry.	Thank you for your comment. The review questions for this partial update were on the diagnostic accuracy of high-sensitivity troponins according to risk, the clinical and cost effectiveness of non-invasive imaging and the diagnostic accuracy of these tests. The assessment of people with chest pain was not within our remit. We have added a sentence to the 'other considerations' section of the linking evidence to recommendations (High sensitivity cardiac troponins section

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					6.4.1.4.2.) to highlight that people may present with chest pain that is psychological in origin and this may require a referral to mental health services.
Royal College of Psychiatrists	Full	15	General	This risks mental health diagnoses being forgotten and therefore appropriate advice not being given. We suggest adding 'including mental health disorders)	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The algorithm you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016.
Royal College of Psychiatrists	Full	18	26	Referring non cardiac chest pain for further investigation where a mental health cause is likely or confirmed, risks delay and associated worsening of the underlying disorder. If a mental health diagnosis is likely or certain then this should be explained to the patient. If further investigation is required to exclude organic causes, then the predicted likelihood of this compared to an ultimate diagnosis of panic/somatoform disorder should be discussed. If a mental health disorder is thought to be causing the pain then the patient should be referred back to their GP, or to a Liaison Psychiatry service.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	18	6	This risks mental health diagnoses being forgotten and therefore appropriate advice not being given. We suggest adding 'including mental health disorders such as panic disorder or medically unexplained symptoms/somatoform disorder. Where a clear diagnosis of health anxiety or somatoform disorder is made, evidence shows a firm diagnosis improves prognosis compared to a diagnosis linked to lots of uncertainty.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	19	18	This risks missing signs and symptoms to aid diagnosis of non-cardiac chest pain. We suggest adding a statement that where some features are atypical or non-cardiac chest pain is suspected, then ask appropriate questions for the diagnosis.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				For example, rapid onset, central start, paraesthesia, rapid thoughts of impending death	and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	19	29 33	This section relates to suspected ACS with normal ECG. The omission of advice about potential non cardiac chest pain increases the risk of poorer prognosis if the pain is due to a mental health disorder. Non cardiac chest pain is a differential to ACS and should be mentioned to the patient to reduce the risk of subsequent health anxiety or recurrent panic attacks	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	19	9	This risks missing signs and symptoms to aid diagnosis of non-cardiac chest pain. We suggest adding a statement that where some features are atypical or non-cardiac chest pain is suspected, then ask appropriate questions for the diagnosis. For example, relatives or friends with recent cardiac event, recent life events, previous unexplained symptoms	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	22	1	These items in the history risk missing features to diagnose the cause of non-cardiac chest pain. We suggest adding: recent stresses or life events, friends or family with recent illness, psychiatric history, recent mood	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	25	25	This misses mental health causes of non-cardiac chest pain so risks such disorders being missed and then becoming chronic due to health anxiety or uncertainty. We suggest	Thank you for your comment.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				adding 'mental health disorders' to gastrointestinal and respiratory pain.	This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	26	41	This clear explanation explains why the risk of radiation with further investigation is thought to outweigh the risk of cancer in potential ACS. However, the challenge is for the small group of frequent attenders with what repeatedly turns out to be troponin negative, non-cardiac chest pain. In addition to the long term risk of cancer, recurrent investigation is known to increase the risk of developing a severe and chronic somatoform disorder. We would therefore suggest that there is a statement about ensuring a specialist psychosocial assessment, from Liaison Psychiatry or Psychological Medicine Services where patients have repeated investigations for what turns out to be non-cardiac chest pain, including in those people with a history of significant cardiac disease.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	27	20 24	These groups have a significant likelihood of having non cardiac chest pain (40-70% and 71-90%). If the pain has a mental health origin, then further investigations increase the risk of the diagnosis being missed and the disorder being or becoming more chronic and severe. To overcome this challenge, we suggest in addition to the proposed tests, adding 'and an explanation that there is a good chance that the test will be negative and their chest pain eventually being diagnosed as non-cardiac.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	29	18	This group includes people with non-cardiac chest pain. We suggest in addition to the effect to diagnosing cardiac pain,	Thank you for your comment.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				the research also describes the proportion of people who end up having non cardiac chest pain – ideally broken down by system cause (respiratory, gastrointestinal, mental health, other)	This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	30	5	This risks including people with non-cardiac causes of ongoing chest pain in registries of cardiac disease and therefore more intensive monitoring which is not targeted to their actual diagnosis or treatment needs. Safeguards for this would need to be built in.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Royal College of Psychiatrists	Full	31	21	This helpful research question helps engage patients in their care. The challenge is that a significant group of patients being initially investigated for chest pain end up with non-cardiac causes, including mental health disorders. A focus on explanations about cardiac disease and delay in making a mental health diagnosis (such as panic disorder or health anxiety or somatoform disorder) is known to worsen prognosis. We suggest therefore also looking at the group of people who end up with non-cardiac chest pain. And also including a group with explanations at the start raising either cardiac or non-cardiac final diagnoses. This is in line with government demands for more integration of physical and mental health such as by improving Liaison Psychiatry availability.	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
School of Health and Related	Full	144	1	Sections 6.4.1.2.2 and 6.4.1.2.3 state that no relevant economic evaluations were identified for high sensitivity troponins. The reason given in Appendix F for excluding the	Thank you for your comment.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Research (ScHARR)				outputs above was given as lack of stratification of the study population into high, medium and low risk groups. This seems to be a rather arbitrary reason for exclusion since the study population was deliberately selected to be the clinically relevant population and subgroups analysis examined those with and without known CAD. The new recommendations for use of high sensitivity troponin (1.2.5.2 and 1.2.5.3) are based on NICE diagnostics guidance on myocardial infarction (DG15). This guidance was based upon an economic model that was developed from the model described in the two outputs above, was subsequently published (Westwood, 2015, reference 728) but has also been excluded from the economic evidence for the same reason given above. Therefore it appears that the guidance for use of high sensitivity troponin is based upon evidence that has not been acknowledged and has indeed been apparently excluded	The work undertaken for DG15 identified the cost-effectiveness of high-sensitivity Troponin assays, and the evidence that the DG15 recommendations were based on was all appropriately referenced within that guidance. This guideline update did not duplicate the work of DG15. The review questions on high-sensitivity Troponins were regarding whether the assays should be used differently for different risk groups therefore the reason for exclusion of the outputs in the economic studies review was that the populations were not stratified by risk. The recommendations 1.2.5.2 and 1.2.5.3 were drafted by the committee based on the clinical evidence that was presented during this guideline update. They are similar to the recommendations made in DG15 however the recommended use of the assays on people at low risk has been refined. This guideline update follows on from the work of DG15. To make this more explicit we have added an explanation into the report in the linking evidence to recommendations section of the high sensitivity Troponin review.
School of Health and Related Research (ScHARR)	Full	188	1	Section 6.4.2.5 states that no relevant economic evaluations for were found for non-invasive imaging for the identification of people with NSTEMI/unstable angina. Output 1 above includes a relevant economic evaluation that does not seem to have been identified by the review. This may be because the economic evaluation of CT coronary angiography and exercise testing is buried in the detail of the abstract so it is easy to see how it could be missed. If this is the case then we	Thank you for your comment. Output 1 was not identified in the economic review on non-invasive imaging therefore we thank you for highlighting the 'prognostic model' to us. Unfortunately it cannot be added to the evidence supporting the recommendations for this update as the population that received CTCA imaging in the study had received a negative standard troponin result and not a

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				would be keen to highlight this with the HTA monograph editors. The analysis directly addresses the issue of the cost-effectiveness of CT coronary angiography and exercise testing in people with suspected ACS and concludes that "CTCA may be a cost-effective strategy for troponin-negative patients but further research is required to estimate the effect of CTCA on event rates and health-care costs". This provides evidence to support recommendations 1.2.6.6 and 1.2.6.7 that exercise ECG and chest CT should not be routinely offered in the initial assessment of acute cardiac chest pain.	negative high-sensitivity Troponin result, which was a more relevant population of interest for the review. The costing analysis that was undertaken for this guideline update was based on an RCT conducted on a high-sensitivity Troponin negative population, therefore because the prognostic model in output 1 is based on less relevant clinical evidence it would not strengthen the evidence supporting the recommendations. We have selectively excluded the paper and have added it to the excluded studies table in Appendix O.
School of Health and Related Research (ScHARR)	General	General	General	Our recent project "Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome" (see http://www.nets.nihr.ac.uk/projects/hta/092221) was funded by the NIHR HTA programme (HTA 09/22/21) specifically to address two key research questions from the NICE 2010 chest pain guidance: (1) The use of alternative biomarker strategies to diagnose MI, including high sensitivity troponin assays, and (2) The use of multislice CT angiography as an alternative to exercise ECG for first-line investigation in patients with troponin negative suspected ACS. The relevant outputs were: 1. Goodacre S, Thokala P, Carroll C, Stevens J, Leaviss J, et al. Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome. Health Technol	Thank you for your comment. The outputs were excluded in the high-sensitivity troponin economic review as the review was looking for studies that had looked at the cost-effectiveness of high-sensitivity Troponin assays in low, medium and high risk groups and the populations in the studies were not stratified by risk. Output 1 was not identified in the review on the use of non-invasive imaging however the paper has now been critically assessed and it has been selectively excluded.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Assess 2013;17(1). http://www.journalslibrary.nihr.ac.uk/hta/volume-17/issue-1#abstract 2. Thokala P, Goodacre SW, Collinson P, Stevens JW, Mills NL, Newby DE, Morris F, Kendall J, Stevenson MD. Cost-effectiveness of presentation and delayed troponin testing for acute myocardial infarction. Heart 2012;98:1498-1503. The evidence generated by this project regarding high sensitivity troponins seems to have been excluded from the guideline evidence review and the evidence regarding CT coronary angiography and exercise ECG seems not to have been identified. We have outlined details in points 2 and 3 below. We would be very grateful if you could consider using the evidence from our HTA-funded project to inform the updated guidance. Doing this would not require any change to the recommendations but would strengthen the evidence supporting the recommendations. Alternatively, if the committee has examined our evidence and found that it was not useful then it would be helpful to have some feedback so we can ensure our efforts are better directed in future. This is an important issue for researchers and research funders. The HTA programme prioritises research that addresses NICE research recommendations. HTA 09/22/21 was specifically funded and undertaken to address research questions outlined in the 2010 guidance. If it has succeeded then it would be helpful to us and the HTA programme if this	

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				were acknowledged. If it has failed then feedback would be helpful.	
Thermo Fisher Scientific	Full	General	General	Recently submitted evidence to NICE MTG4 (Copeptin), the information there is relevant to biomarkers	Thank you for your comment. Dual marker strategy was not identified as a topic for this update of this guideline. The review question for the recommendations on troponins was about their use in different risk populations. The evidence submitted to MTG4 (see below) is evaluating a dual marker strategy and not relevant to this review in the update. https://www.nice.org.uk/guidance/MTG4/chapter/1-Recommendations 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 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. 1.2 Research is recommended 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 myocardial infarction. NICE will review this guidance when new and substantive evidence becomes available.
Thermo Fisher Scientific	Full	22	2	We are concerned that Copeptin proAVP has been overlooked, it has been implemented into both the German and Italian Chest Pain Guidance, Further the European	Thank you for your comment.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Society of Cardiology (ESC) recommended Copeptin for use alongside Troponin for the early rule out of MI. The ESC guidance is important and text around Copeptin should be considered in its entirety – "*Assessment of copeptin, the C-terminal part of the vasopressin prohormone, may quantify the endogenous stress level in multiple medical conditions including MI. As the level of endogenous stress appears to be invariably high at the onset of MI, the added value of copeptin to conventional (less sensitive) cardiac troponin assays is substantial. Therefore the routine use of copeptin as an additional biomarker for the early rule-out of MI is recommended whenever sensitive or high-sensitivity cardiac troponin assays are not available. Copeptin may have some added value even over high-sensitivity cardiac troponin in the early rule-out of MI."* Note, use of Copeptin with conventional troponin receives and A-I recommendation, with hsTroponin it's B-II	The review questions were on high-sensitivity troponins and non-invasive imaging and not dual marker strategies. The guideline committee were therefore unable to consider this evidence. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.
Thermo Fisher Scientific	Full	22	8, 11, 12	The "validated" NICE guidance was recently validated by a Global team of troponin experts. Parsonage *et al*. Validation of NICE diagnostic guidance for rule out of myocardial infarction using high-sensitivity troponin tests *Heart* heartjnl-2016-309270 *Published Online First: 10 June 2016 (http://heart.bmj.com/content/early/2016/06/10/heartjnl-2016-309270.abstract)* – "*The NICE algorithms could identify patients with low probability of AMI within 2 hours; however, neither strategy performed as predicted by the NICE diagnostic guidance model. Additionally, the rate of MACE at 30 days was sufficiently high that the algorithms should only be used as*	Thank you for your comment. We have referred to this study in the linking evidence to recommendations ((High sensitivity cardiac troponins section 6.4.1.4.2).The GC noted that the algorithm in DG15 has been validated. The purpose of this review was not to replace the recommendations in DG15 but to see if additional recommendations could be made for people with different risks of ACS. The GC

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				one component of a more extensive model of risk stratification" *MACE=Major Adverse Cardiac Events* Worth drawing attention to an interventional clinical trial performed using Copeptin, the study demonstrated higher early discharge rates and lower MACE than the Parsonage NICE validation. - Möckel M, Searle J, Hamm C, Slagman A, Blankenberg S, Huber K, et al. Early discharge using single cardiac troponin and copeptin testing in patients with suspected acute coronary syndrome (ACS): a randomized, controlled clinical process study. European heart journal; 2015. p. 369-76.	The review questions were on high sensitivity troponins and non-invasive imaging and not dual marker strategies. Dual marker strategy was not identified as a topic for this update of this guideline. The review question for the recommendations on troponins was about their use in different risk populations.
Thermo Fisher Scientific	Full	23	9	This is where Copeptin would add value	Thank you for your comment. This partial update of CG95 focused only on acute chest pain. The recommendation you refer to relates to the assessment and diagnosis of stable chest pain which underwent consultation on new and updated recommendations in May 2016. The full amended guideline includes both the acute and stable chest pain updates.

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