Review decision

Review of DG15: Myocardial infarction (acute): Early rule out using high-sensitivity troponin tests (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays)

This guidance was issued in October 2014.

The review date for this guidance is October 2017.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Decision

Transfer the guidance to the 'static guidance list'.

A link will be added from the landing page of diagnostics guidance 15 to NICE’s guidance on chest pain of recent onset: assessment and diagnosis.

The evidence gathered in this report will be passed to the Centre for Guidelines surveillance team and be considered during routine surveillance of NICE’s guideline on chest pain of recent onset: assessment and diagnosis. This guideline is expected to be reviewed in November 2018.

At the Guidance Executive meeting of 3 April 2018 it was agreed that no consultation on the recommendations was required.

A list of the options that were considered, and the consequences of each option is provided in Appendix 1 at the end of this paper.
2. Rationale

Since diagnostics guidance 15 was published, evidence which addresses some of the uncertainties identified by the committee has been published. In addition, NICE’s guideline on chest pain of recent onset: assessment and diagnosis has been updated. It incorporates diagnostics guidance 15 and makes additional recommendations on the use of high sensitivity troponin test for the early rule out of NSTEMI in patients presenting with symptoms of acute coronary syndrome. The guideline addresses the use of single high sensitivity troponin tests in low risk patients and covers the use of risk scoring. Through their inclusion in the guideline, the tests are now part of the standard of care for diagnosing acute coronary syndrome in the NHS. It is, therefore, most appropriate for the new evidence to be assessed during the Centre for Guidelines routine surveillance procedures for the guideline. This could include the evidence on alternative early rule-out algorithms and on the AccuTnI+3 assay. In the interim, diagnostics guidance 15 will be transferred to the static list and a link to NICE’s guideline on chest pain of recent onset: assessment and diagnosis added to its landing page.

3. Implications for other guidance producing programmes

The evidence gathered in this report will be passed to the Centre for Guidelines surveillance team and will be considered during routine surveillance of NICE’s guidance on chest pain of recent onset: assessment and diagnosis. This guideline may need updating by the Centre for Guidelines in the future. There will be no implications for the Quality Standards programme, as the use of high sensitivity troponin tests, as recommended in DG15, is not included in the quality standard on acute coronary syndromes in adults.

4. Original objective of guidance

To assess the clinical and cost effectiveness of high-sensitivity troponin tests (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays) for acute myocardial infarction.

For the purposes of the original assessment, a high-sensitivity troponin assay was defined as an assay that has a coefficient of variation of 10% or less at the 99th percentile (the upper limit of the reference population), and which is able to detect cardiac troponin in at least 50% of the reference population.
5. Current guidance

**Recommendations**

1.1 The Elecsys Troponin T high-sensitive assay and ARCHITECT STAT High Sensitive Troponin-I assay are recommended 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 acute coronary syndrome.

1.2 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. Laboratories should report absolute values and the upper reference limit should be set at the 99th percentile. Results should be interpreted along with clinical judgement and the results of clinical assessment. Healthcare professionals should take into account the pre-test probability of NSTEMI, the length of time since the suspected acute coronary syndrome, the possibility of chronically elevated troponin levels in some patients and that 99th percentile thresholds for troponin I and T may differ between sexes. When NSTEMI is not ruled out using an 'early rule out protocol', further clinical assessment is required to determine whether a diagnosis of NSTEMI is appropriate.

1.3 The AccuTnI+3 assay is only recommended for use in clinical research, for early rule out of NSTEMI in people presenting to an emergency department with chest pain and suspected acute coronary syndrome.

1.4 Healthcare professionals using 'early rule-out protocols' including the Elecsys Troponin T high-sensitive or the ARCHITECT STAT High Sensitive Troponin-I assays should collect further information on the time taken to rule out NSTEMI in clinical practice and on the clinical outcomes of people presenting to an emergency department with chest pain and suspected acute coronary syndrome.

**Recommendations for further research**

7.1 The Committee recommended that robust evidence be generated to show the clinical effectiveness of the AccuTnI+3 assay for the early rule out of non-ST-segment elevation myocardial infarction (NSTEMI) in people presenting to an emergency department with acute chest pain. Where possible the accuracy of the AccuTnI+3 assay and its resulting clinical outcomes should be compared
with both high-sensitivity troponin assays recommended and standard troponin assays.

7.2 The Committee recommended the collection of further outcome data through clinical audit in centres adopting 'early rule-out protocols' with high-sensitivity troponin testing (see recommendation 1.4). The data collected through audit should be sufficient to allow analysis of the optimal timing of samples taken after presentation to an emergency department and the optimal high-sensitivity troponin test cut-offs for both ruling out and ruling in NSTEMI.

7.3 The Committee recommended further research comparing the clinical effectiveness of different early rule-out test protocols using high-sensitivity assays which meet the criteria applied for this assessment. The Committee recommended that future studies should include consideration of the clinical effectiveness of different test strategies including those employing low diagnostic thresholds, and the impact of different test strategies on both clinician behaviour and the health system, with a view to reducing uncertainty in the economic model. Future studies should also investigate the role of sex and age-specific 99th percentile thresholds in the assessment of suspected acute coronary syndrome. The Committee also considered that it would be appropriate to include adjudication with high-sensitivity troponin assays at time points earlier than 10–12 hours as the reference standard in future studies.

7.4 The Committee recommended further research to understand the underlying biological causes and the clinical implications of chronically elevated troponin levels in older people, and people with conditions known to cause troponin elevation in the absence of ischaemia.

6. New evidence

The search strategies from the original diagnostics assessment report were re-run in October 2017. References from January 2013 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist committee members for this guidance topic were also consulted and asked to submit any information regarding changes to the technologies, the evidence base and clinical practice. The results of the literature
search are discussed in the ‘Summary of evidence and implications for review’ section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies
All 3 of the technologies described in the guidance are still available and are in use in the NHS. Specialist committee members noted that the AccuTnl+3 is not used in hs-Tn algorithm pathways.

6.1.1. Elecsys Troponin T high-sensitive (Roche)
There have been no changes to the Elecsys Troponin T high-sensitive assay since the original assessment and no new versions have been introduced. The CE mark remains unchanged. The FDA MAUDE and MHRA databases listed 5 adverse events between October 2013 and September 2017. A specialist committee member noted that the Elecsys Troponin T high-sensitive assay was approved for use in the USA in April 2017.

6.1.2. ARCHITECT STAT High Sensitive Troponin-I (Abbott)
There have been no changes to the ARCHITECT STAT High Sensitive Troponin-I assay since the original assessment and no new versions have been introduced. The CE mark remains unchanged. The FDA MAUDE and MHRA databases listed 190 adverse events between October 2013 and September 2017.

6.1.3. AccuTnl+3 (Beckman Coulter)
There have been no changes to the AccuTnl+3 assay since the original assessment report. The CE mark remains unchanged. The FDA MAUDE and MHRA databases listed 806 adverse events between October 2013 and September 2017.

A new version of the assay, the Access hsTnI, has been introduced with CE mark obtained in September 2017. It is designed to be used with any of the Access immunoassay analysers. The manufacturer provided an unpublished study which evaluates

The EAC found no published studies on the Access hsTnI, however, 4 conference abstracts provide information on analytical performance in laboratory testing environments. Of the 4 abstracts, the only comparative study was by Masotti et al.
(2017) who found that Access hsTnI showed significantly improved sensitivity over Access AccuTnI+3 and its performance was comparable to ARCHITECT STAT High Sensitive Troponin-I.

### 6.1.4 Additional technologies

Three additional highly sensitive assays which have a current CE mark and are available to the NHS were identified (Westermann et al. 2017). Data were available on the 99th percentiles and their associated co-efficient of variation, although it is not clear if they are able to detect troponin in 50% of the population.

**ADVIA Centaur High-Sensitivity Troponin I (TNIH) Assay (Siemens)**

The [ADVIA Centaur hs-TnI](https://www.siemens.com) is only available on the ADVIA Centaur XP and XPT Immunoassay Systems. The company’s website lists the following characteristics:

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<tr>
<td>Limit of blank</td>
<td>0.90 pg/mL (ng/L)</td>
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<tr>
<td>Limit of detection</td>
<td>2.21 pg/mL (ng/L)</td>
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<tr>
<td>Limit of quantitation (20% CV)</td>
<td>2.50 pg/mL (ng/L)</td>
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<tr>
<td>Limit of quantitation (10% CV)</td>
<td>4.50 pg/mL (ng/L)</td>
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<tr>
<td>99th Percentile</td>
<td>47.34 ng/L (pg/mL)</td>
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Abbreviations: CV – coefficient of variation; pg/mL – picograms per millilitre; ng/mL – nanograms per millilitre

There were 2 conference abstracts which evaluated the performance of the ADVIA Centaur hs-TnI assay in a laboratory setting. Payne et al. (2016 and 2017) established that the 99th percentile was equivalent to that of the ADVIA Centaur TnI-Ultra.

**Sgx Clarity cTnI assay (Singulex)**

The [Sgx Clarity cTnI](https://www.singulex.com) is available for use with the Singulex Clarity immunodiagnostics platform. The company lists the following characteristics:

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<tbody>
<tr>
<td>Assay range</td>
<td>0.14 – 25,000 pg/mL</td>
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<tr>
<td>Limit of blank</td>
<td>0.02 pg/mL</td>
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<tr>
<td>Limit of detection</td>
<td>0.08 pg/mL</td>
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<tr>
<td>Limit of quantitation (20% CV)</td>
<td>0.14 pg/mL</td>
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<tr>
<td>10% functional sensitivity</td>
<td>0.53 pg/mL</td>
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<tr>
<td>99th percentile upper reference limit</td>
<td>&lt; 8.67 pg/mL</td>
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From searches, 3 published studies and 7 conference abstracts were identified in which the Singulex Clarity cTnI assay was used. A conference abstract by Sandoval
et al. (2016) noted substantial variation in troponin values measured by the Abbott ARCHITECT hs-cTnl, Beckman Access 2 hs-cTnl, Roche Cobas e601 hs-cTnT, Siemens Dimension Vista hs-cTnl, and Singulex assays.

Schofer et al. (2017) evaluated the performance of the Singulex assay in 1560 patients with chest pain, of whom 273 had confirmed NSTEMI. Using absolute delta\(^1\) between presentation troponin measurement and 3-hour measurement, the assay had a negative predictive value of 98.2% in males (99th percentile 36 ng/L) and 98% in females (99th percentile 30 ng/L). The other 2 published studies (Bonaca et al, 2015. and Twerenbold et al. 2016) evaluated highly sensitive troponin assays and do not comment specifically on the performance of the Singulex assay.

**ST AIA-PACK cTnl 3rd-Gen (Tosoh)**

The ST AIA-PACK cTnl is available for use with Tosoh AIA immunoassay analysers. The coefficient of variation at the 99\(^{th}\) percentile is 8.5 and the limit of detection is 60 ng/L (Westermann et al. 2017). One published study was identified (Storti et al. 2015) which showed that AIA-PACK cTnl was closely correlated with STAT Architect high Sensitive TnI (Abbott Diagnostics), ADVIA Centaur Troponin I Ultra (Siemens Healthcare Diagnostics) and Access AccuTnI+3 (Beckman Coulter Diagnostics).

6.2 Clinical practice

Since diagnostics guidance 15 was published, the updated NICE guideline on chest pain of recent onset: assessment and diagnosis was published in 2016. It incorporates the recommendations from DG15 and makes an additional recommendation to use a single high sensitivity troponin test to rule out low-risk patients presenting with suspected acute coronary syndrome symptoms (Section 1.2.5.3: “consider performing a single high-sensitivity troponin test only at presentation to rule out NSTEMI if the first troponin test is below the lower limit of detection (negative)\(^1\). In common with DG15, the guideline highlights that there are sex-specific differences in 99\(^{th}\) percentile thresholds for troponin I and T.

NICE has also published a quality standard on acute coronary syndromes in adults which includes a universal definition of myocardial infarction comprising clinical signs and a rise in cardiac biomarkers. The use of high sensitivity troponin tests, as recommended in DG15, is not included.

\(^{1}\) Difference between two measurements

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In 2015 the European Society of Cardiology published guidelines for managing patients presenting with NSTEMI symptoms. According to the guidelines, biomarker testing “is mandatory in all patients with suspected non-ST-elevation acute coronary syndromes” and high sensitivity troponin tests are the most accurate. The guideline recommends a 0/3-hour rule in/rule out algorithm, which must be used alongside the Global Registry of Acute Coronary Events (GRACE) score. As an alternative, the guideline recommends 0/1-hour assessments when high-sensitivity cardiac troponin assays with a validated algorithm are available. In the 0/1 algorithm, very low troponin levels or low baseline troponin levels combined with lack of relevant increase within 1 hour can be used to rule out NSTEMI. The guideline notes that the cut-off levels are different for different tests.

The European Society of Cardiology guidelines state that 2 additional approaches can be considered for rapid rule-out: a 2-hour rule out algorithm, in which high sensitivity troponin at presentation is used alongside the Thrombolysis in Myocardial Infarction (TIMI) risk score with ECG; and a strategy combining measurement of troponin and copeptin. The guideline cautions that when using any algorithm, clinical information should be considered in conjunction. Further, in patients presenting within 1 hour of chest pain onset, the second cardiac troponin level should be obtained at 3 hours, and serial testing should be done if the clinical suspicion remains high or if a patient has recurrent chest pain.

Crea et al. (2016) provide a critique of the 0/1-hour rule in/rule out algorithm recommended in the ESC guidelines. The authors discuss the paucity of data they perceive support the ESC recommendation. They state that clinicians should apply the 1-hour algorithm with caution in low-risk patients only and base decisions on rising or falling patterns of troponin, rather than defined cut-off values. They contend that cut-off values are not validated for assays other than the Roche Elecsys hs-cTnT and that further evaluation is needed to determine sex-specific cut-off values.

The 2014 guidelines published by the American College of Cardiology/American Heart Association Task Force (ACC/AHC) do not make any specific recommendations regarding high sensitivity assays. However, the guideline does note that “Absolute changes in nanograms per liter of high-sensitivity cardiac troponin T levels appear to have a significantly higher diagnostic accuracy for AMI than relative changes and may distinguish AMI from other causes of high-sensitivity cardiac troponin T elevations”. The guideline cautions against early troponin testing given that some “values may not become abnormal for up to 12 hours”, however, high sensitivity tests were not available in the USA at the time of publication.

The 2017 publication “Asia-Pacific consensus statement on the optimal use of high-sensitivity troponin assays in acute coronary syndromes diagnosis: focus on hs-Tnl”
makes 9 recommendations including a 0/3-hour algorithm based on the change in troponin measured at presentation and 3 hours later. Acute myocardial infarction is ruled in if troponin I levels are greater than 99th percentile at presentation and show a change of more than 50% at 3 hours. The recommendations also include adopting the sex-specific cut-offs given by Abbott for the ARCHITECT assay (16 ng/L in women and 34 ng/L in men).

6.3 New studies

Studies published since DG15 were identified and assessed by an external assessment centre identified 91 studies and 19 conference abstracts that have been published since the original assessment was done; 76 prospective and 34 retrospective cohort studies. The findings from key studies are summarised in this section. A full list of identified studies is available in the references section. The population for all included studies comprised patients presenting to an emergency department with chest pain or symptoms of non-ST elevation acute coronary syndrome or myocardial infarction (NSTE-ACS or NSTEMI).

Throughout this section, the Elecsys Troponin T high-sensitive (Roche) is abbreviated as hs-cTnT or simply Elecsys; the ARCHITECT STAT High Sensitive Troponin-I (Abbott) is abbreviated as Abbott hs-cTnI or simply Abbott.

6.3.1 Diagnostic accuracy

Elecsys Troponin T high-sensitive assay

High sensitivity troponin compared with conventional troponin or clinical scores

Three studies reported on the accuracy of the Elecsys hs-cTnT compared with a conventional cTnT assay. All 3 studies found that the Elecsys hs-cTnT assay was more sensitive and had higher area under the curve values (AUCs) than the conventional cTnT assay. AUCs for detecting AMI (hs-cTnT versus cTnT) were: 0.95 compared with 0.84 (Body et al. 2015); 0.91 compared with 0.90 (Hamrer-Lercher et al. 2013); and 0.810 and 0.716 (Kitamura et al. 2013). Kitamura et al. (2013) also noted that sampling 3 hours after admission increased the hs-cTnT AUC to 0.972. Sensitivities and negative predictive values (NPV) for hs-cTnT were 100% (for patients admitted more than 120 minutes after symptom onset, Kitamura et al. 2013), 98.7% and 99.0% (LoD cut-off, Body et al. 2015), and 91% and 74% (99th-percentile cut off, Hammer-Lercher et al. 2013). Body et al. also noted that sensitivity and NPV can be increased to 100% by combining the assay result with ECG evidence.
One study compared the Elecsys hs-cTnT to the TIMI score and the GRACE score (Sanchis et al. 2016b). The Elecsys assay was found to have a lower negative predictive value than the TIMI scoring system: 91.9% vs 96.1%, respectively.

**High sensitivity troponin used at different cut offs**

Two studies focused on the rule out of AMI (Thelin et al. 2015, McRae et al. 2017) and 2 on the rule in of AMI (Mueller-Hennessen et al. 2017, Kitamura et al. 2013).

Thelin et al. (2015) reported that sensitivity for predicting NSTEMI was significantly higher for LoD compared with the 99th percentile (100% vs. 87%, p=0.004). McRae et al. (2017) reported that sensitivities and NPVs for 7-day AMI were both 100% (LoB 3 ng/L), 99.8% and 99.95% (LoD 5 ng/L), and 99.8% and 99.95% (limit of quantification 6 ng/L). For 7-day major adverse cardiac events (MACE) the sensitivities were 99.6% (3 ng/L), 97.4% (5 ng/L), and 96.6% (6 ng/L). The NPVs for 7-day MACE were 99.8% (3 ng/L), 99.5% (5 ng/L), and 99.4% (6 ng/L).

Mueller-Hennessen et al. (2017) evaluated the rule in performance of hs-cTnT. They found that for prediction of AMI, positive predictive value (PPV) was significantly increased by changing the cut off from 14ng/L (PPV 48.8%) to 60ng/L (PPV 87.2%). Cut offs higher than 60 ng/L did not give further increases in PPV. The highest PPV (91%) was generated by combining a baseline cut off of 30ng/L with a 20% relative delta at 2-hours. Kitamura et al. (2013) reported specificity of hs-cTnT increased to 92% when using a 22 ng/L cut off, and increased to 100% with a 105 ng/L cut off.

**High sensitivity troponin used in different algorithms**

Four studies looked at the accuracy of different test algorithms using hs-cTnT; 2 looking at a 0/2 hour algorithm (Reichlin et al. 2015, McRae et al. 2017b), and 2 looking at a 0/1-hour algorithm (Reichlin et al. 2015b, Su et al. (2015). Both algorithms were found to perform well.

Reichlin et al. (2015) evaluated a rule out algorithm which used a <14ng/L cut off within the first 2-hours combined with a 0/2-hour absolute delta of <4ng/L. The rule in algorithm was ≥53 ng/L within the first 2-hours, or a 0/2-hour absolute delta of ≥10ng/L. In the derivation cohort, the rule out algorithm gave an NPV of 99.9% and the rule in algorithm gave a PPV of 78%. Thirty day survival was 100% in the rule out group. The validation cohort had similar outcomes (NPV of 99.5%, PPV of 85% and 100% 30-day survival in the rule out group). McRae et al. (2017b) also evaluated a 0/2-hour algorithm alongside the 99th percentile algorithm proposed in DG15. The 0/2-hour algorithm ruled out AMI in 59.4% of patients, and had 98.7% sensitivity and
99.8% NPV. The algorithm proposed by DG15 ruled out AMI in 50.3% of patients, and had a similar sensitivity and NPV.

Reichlin et al. (2015b) assessed a rapid 0/1-hour algorithm with a rule out baseline of <12ng/L combined with a 0/1-hour absolute delta with <3ng/L and a rule in baseline of ≥52ng/L or a 0/1-hour delta with ≥5ng/L. This gave an NPV of 99.9% and a PPV of 78.2% and the 30-day mortality in the rule out group was 0%. Su et al. (2015) found that the AUC for hs-TnT was highest when baseline measurements were combined with 0/1-hour absolute delta. This algorithm had a significantly higher AUC than baseline measurement alone (0.93 vs. 0.88, p<0.001).

ARCHITECT STAT High Sensitive Troponin-I assay

High sensitivity troponin compared with conventional troponin

There were 3 studies that compared the accuracy of the Abbott hs-cTnI assay to a conventional cTnI assay. Sandoval et al. (2016) reported that sensitivity of the hs-cTnI assay was significantly higher than the conventional cTnI assay (95% for both males and females vs. 80% and 65%, p<0.01). Specificities were similar (82.8% vs. 81.7% respectively), but specificity of hs-cTnI was significantly lower in females.

Croce et al. (2017) reported that troponin was detected in significantly more patients with hs-cTnI than cTnI (89.9% vs. 68.6%; p<0.001), but that NPVs were similar (95.0% for hs-cTnI and 95.8% for cTnI using 50% delta variation between 0 and 3 hours). AUC was not significantly higher for hs-cTnI (0.92 vs. 0.72 for cTnI, p=0.08). Similarly, Sandoval et al. (2017c) reported that NPVs were similar (99.5% for cTnI and 100% for hs-cTnI using a ≤99th percentile cut off) and so were PPVs were also very similar (89.2% for cTnI vs. 89.3% for hs-cTnI using 0/3-hr absolute delta >5ng/L as a cut off).

High sensitivity troponin used at different cut-offs

There were 5 studies that reported on the accuracy of the Abbott hs-cTnI assay at different cut offs and/or combined with an ECG test. Studies reported that if LoD or less than 5ng/ml were used as cut-offs, the NPV was generally greater than 99%, but if the 99th percentile was used, NPV was reduced. Two studies reported that NPV could be increased to 100% if hs-cTnI (using cut-offs of <1.9 ng/L or 3 ng/L) was combined with ECG findings (Sandoval et al. 2017b, Neumann et al. 2017b). Two studies reported that NPV was reduced in patients who presented within 2 hours of pain onset (Sandoval et al. 2017b, Shah et al. 2015). Specific results were:

- Sandoval et al. (2017b) used a cut-off of LoD (<1.9 ng/L). In the derivation cohort NPV was 99.1% and in the validation cohort NPV was 98.8%.
Neumann et al. (2017b) used LoD (<1.9 ng/L) cut off at baseline, which gave an NPV of 99.5%. A 99th percentile cut off (27 ng/L) gave an NPV of 91.3%.

Shah et al. (2015) used a cut off of < 5ng/L at baseline, which gave an NPV of 99.6% in the derivation cohort, and an NPV of 99.4% in the validation cohort. When the 99th percentile cut off was used, patients who were ruled out had a significantly increased risk of 12-month mortality.

Ferencik et al. (2017) used a cut off of <4 ng/L, which gave an NPV of 100% in the derivation cohort. In the validation cohort an additional 5% of patients were ruled-out by adding a delta (no change or fall in troponin) at 0/2 hours.

Badciong et al. (2013) studied absolute and relative changes in hs-cTnI levels at 2-4 hours and at 4-9 hours. AUC was highest in the 4-9 hours group when using absolute delta (+/-12pg/mL) and lowest in the 2-4 hours group when using a relative delta (+/-50%). Specificity was highest in the 2-4 hours group when using absolute delta and lowest in the 4-9 hours group when using a relative delta.

High sensitivity troponin used in different algorithms

There were 4 studies that reported on the accuracy of the Abbott hs-cTnI assay using different algorithms.

Boeddinghaus et al. (2016) evaluated a 0/2-hour algorithm and determined a baseline measure (<6ng/L rule out, ≥64ng/L rule in) combined with absolute delta at 2-hours (<2ng/L rule out, ≥15ng/L rule in). Sensitivity and NPV were 99.2% and 99.8%. Specificity and PPV were 95.2% and 75.8%. Results were similar in a validation cohort (sensitivity 98.7%, NPV 99.7%, specificity 97.4% and PPV 82.2%).

Boeddinghaus et al. (2017) compared 4 ‘rule out’ diagnostic algorithms: limit of detection (LoD) cut off at baseline <2ng/L, single cut off <5ng/L, single cut off <5ng/L and 1-hour delta of <2ng/L (0-AND-1-hr), and LoD or 0-AND-1-hr (0-OR-1-hr). NPV was similar between the groups (LoD 100%, single cut-off 99.1%, 0-AND-1-hr 99.5%, 0-OR-1-hr 99.5%). A subgroup also had a 0/3-hour algorithm, which gave an NPV of 97.8%.

Boeddinghaus et al. (2017b) measured hs-cTnI at baseline and at 1 hour, and copeptin at baseline. The AUC for hs-cTnI alone was significantly lower than for 0/1-hr absolute delta (0.51 vs. 0.78, p<0.001). The AUC for copeptin alone was also significantly lower than for 0/1-hr absolute delta (0.58 vs. 0.78, p=0.02). Combined baseline hs-cTnI and 0/1-hr absolute delta gave an AUC of 0.80.

Neumann et al (2016b) evaluated the 2015 ESC guidelines algorithm. In the derivation cohort the ≤6 ng/L cut off to rule-out gave an NPV of 99.5% when
measured at baseline and 3-hours. A rule in algorithm of >6 ng/L at baseline combined with a ≥12 ng/L 0/1-hour absolute delta gave a PPV of 87.1%. A validation cohort used a similar 0/2-hour algorithm and gave an NPV of 99.7% and PPV of 81.5%. A second validation cohort, using the same 0/1-hour algorithm gave an NPV of 99.2% and PPV of 80.4%. The authors found the 0/1-hour cut off to be significantly better than cut offs using the 99th percentiles. No significant differences were seen between the 0/1-hour and 0/3-hour algorithms.

AccuTnl+3 assay

There were 4 studies that reported on the accuracy of the AccuTnl+3 assay. Storrow et al. (2015) evaluated the AccuTnl+3 and reported that the highest sensitivity and NPV were 96.9% and 99.5%, using a ≥0.02ng/mL cut off at 1-3-hours. The authors reported no significant differences when analysed by race or gender.

Storrow et al. (2015b) reported that AccuTnl+3 had good diagnostic accuracy when measurements were taken at both <8 hours and ≥8 hours after symptom onset using a 0.03ng/L cut off (AUC 0.96, sensitivity 94.3%, specificity 86.8%). The best rule out performance was with an absolute delta of <0.01ng/L and baseline of <0.03ng/L (NPV 99.6%).

Wildi et al. (2013) reported that diagnostic performance of the AccuTnl+3 was better when using absolute deltas compared with relative deltas (AUC 0.90 vs. 0.69, p<0.001).

Cullen et al. (2013) found that using the 99th percentile cut off (>0.04μg/L) gave a sensitivity of 82.9% at 0-hours and 94.3% at 2-hours. The highest specificity (95.8%) was achieved using absolute delta of ≥0.03μg/L. The best rule out algorithm was based on 0-hour or 2-hour values of ≤0.04μg/L combined with absolute delta of <0.03μg/L (NPV 99.7%). The best rule in algorithm was based on 0-hour or 2-hour >0.04μg/L combined with absolute delta ≥0.03μg/L (PPV 68.8%).

6.3.2 Clinical outcomes and resource use

Elecsys Troponin T high-sensitive assay

Seven studies compared the Elecsys hs-cTnT with a conventional cTnT assay and reported resource use and/or clinical outcomes. The main findings were:

- Elevated troponin levels were found in significantly more patients tested with the hs-cTnT assay than those tested with a conventional cTnT assay (Sanchis et al. 2014, Corsini et al. 2015).
- Two studies reported that there were fewer hospital admissions when hs-cTnT was used (Nejatian et al. 2017, Bandstein et al. 2017), but 1 study reported that admission rates were not significantly different between groups (Chew et al. 2016).

- One study reported that hs-cTnT led to significantly more coronary angiograms and subsequent revascularisations (Sanchis 2014), but a second study reported no different in angiography rates between groups (Chew et al. 2016).

- One study reported that length of stay was significantly increased in the hs-cTnT group (Sanchis et al. 2014), but another study found that mean length of stay decreased after implementation of hs-cTnT (Crowder et al. 2015).

- One study reported that both hs-cTnT and conventional cTnT were significant predictors of readmissions (Hammerer-Lercher et al. (2013), and another study reported significantly fewer 30-day readmissions in the hs-cTnT group (Crowder et al. 2015).

- Three studies reported that MACE incidence was not significantly different between groups tested with hs-cTnT and those tested with cTnT (Bandstein et al. 2017, Chew et al. 2016, Sanchis et al. 2014). However one study reported that total MACE incidence was significantly lower in the hs-cTnT tested group (Nejatian et al. 2017).

- One study reported that neither hs-cTnT nor cTnT were significantly predictive of mortality (Hammerer-Lercher et al. 2013). Most studies found that mortality was not significantly different between groups (6-month mortality, Sanchis et al. 2014; 12-month mortality, Chew et al. 2016; in-hospital and 12-month mortality, Corsini et al. 2015; Crowder et al. 2015). One study reported that the risk of death within 1 year of the visit increased by 51%, but this was not statistically significant (Bandstein et al. 2017).

**ARCHITECT STAT High Sensitive Troponin-I assay**

There were 2 studies that compared Abbott hs-cTnl with a conventional cTnI and reported clinical outcomes or resource use data. In addition there was 1 study that compared a 99th percentile algorithm (<27ng/L at 0 or 3-hours) with a rapid rule out algorithm (<6ng/L at 0 and 1-hour) using the Abbott hs-cTnl. Key results were:

- Cardiovascular death or MI was significantly more likely for patients in whom troponin was above the 99th percentile (26ng/L, Bohula May et al. 2014).

- Patients with positive hs-cTnl and negative cTnI using a 99th percentile algorithm had significantly higher rates of cardiovascular death or MI (Bohula May et al. 2014).
• The median length of stay fell significantly in a group tested with Abbott hs-cTnI compared with the group tested with conventional cTnI. However, AMI diagnoses were not significantly different between groups (Peck et al. 2016).

• At 12-month follow-up, mortality was significantly higher in patients ruled out using a 99th percentile at 0 and 3 hours than those ruled out using a cut off of <6ng/L at 0 and 1-hour. However, incidence of cardiac related adverse events, including AMI, were similar between groups. Therefore, the rapid algorithm lead to lower mortality but not for cardiac reasons (Sorensen et al. 2017).

**AccuTnI+3 assay**

There were no studies on the AccuTnI+3 assay that reported clinical outcomes or resource use.

6.3.3 *Age and sex specific cut offs*

There were 4 studies that looked at sex specific cut-offs and 2 studies that looked at age-specific cut offs. A seventh study looked at both age and sex specific cut-offs.

Cullen et al. (2016) compared sex-specific cut offs with overall cut off values using hs-cTnI. The sex-specific cut offs were 16ng/L for females and 34ng/L for males. The overall cut off was 26ng/L. The sex-specific cut offs identified an extra 25 females as high risk (7 had 1-year MACE) and an extra 29 males as low risk (12 had 1-year MACE). Eggers et al. (2014) evaluated sex-specific cut offs using hs-cTnI. Median cTnI levels were 947 and 175 ng/L in men and women, respectively (p<0.001). However, when sex-specific cut-offs were used they did not significantly improve prognostic risk prediction for AMI.

Borna et al. (2014) reported that in patients 75 years and older, 63% had a positive hs-TnT on admission, but only 39% of those with elevated hs-TnT had an ACS during hospital stay. Authors note that this indicates troponin T is elevated in elderly patients without ACS.

Bohula May et al. (2014) reported that sex-specific cut offs did not significantly affect outcomes. Similarly, Jarolim et al. (2013) reported that gender specific cut offs did not significantly improve prognostic performance.

Ichise et al. (2017) evaluated the performance of hs-cTnT in different age groups. They found the best overall cut-off value was 38ng/L, with sensitivity and specificity of 85% and 89%, respectively, and AUC of 0.945. The 99th percentile cut off had an NPV of 100%, but gave low specificity (53%), particularly in the elderly (26%) or
those with renal dysfunction (23%). In patients 75 years and older the optimal cut off was 7ng/L (AUC 0.94, sensitivity 84% and specificity 88%). Authors note that this indicates age specific cut offs do not give acceptable levels of sensitivity.

Mueller-Hennessen et al. (2016) evaluated the performance of hs-cTnT in different age groups and using sex-specific cut offs. For patients over 65-yrs, age-specified cut-offs (28ng/L rather than 14ng/L) reduced classification as risk of AMI from 29.8% to 18.3% in the entire cohort (non-ACS and ACS) and 54.7% to 40.9% in the ACS sub-cohort. Using gender-specific cut-offs, AMI classification-rate increased from 16.6% to 22.6% (entire cohort) and 62.6% to 71.7% (ACS sub-cohort) in women. In men, rates decreased from 23.1% to 21.1% (entire cohort) and 48.8% to 45.9% (ACS), respectively. There were no significant differences in outcomes when using gender-specific cut-offs.

6.3.4 Comparisons between different high sensitivity assays

Abbott hs-cTnI, Elecsys hs-cTnT and AccuTnI+3

Four studies prospectively compared the rule out performance of Abbott hs-cTnI, AccuTnI+3 and Elecsys hs-cTnT. Key results were:

- Using the limit of detection as a rule out cut off, Elecsys hs-cTnT (<5ng/L) had an NPV of 98.6%, AccuTnI+3 (<2ng/L) had an NPV of 99.2%, and Abbott (<1.9ng/L) had an NPV of 100% (Rubini Gimenez et al. 2013).

- Diagnostic performance was similar between the tests but significantly worse in patients with renal dysfunction. AUCs for non-renal dysfunction were 0.94 (Abbott and Elecsys) and 0.93 (AccuTnI+3). AUCs for renal dysfunction were 0.87 (Abbott and Elecsys) and 0.89 (AccuTnI+3 for). Optimal cut offs for renal dysfunction were 1.9-3.4 times higher than for non-renal dysfunction (Twerenbold et al. 2015).

- NPV was very high for all assays (99.6-100%) when using a 0/3-hr rule out algorithm (≤99th percentiles). During the 3 month follow-up there were 0 mortalities in patients ruled out by the 0/3-hr algorithm (Wildi et al. 2016).

- Hs-cTn combined with blood glucose testing gave 100% sensitivity and NPV in a verification cohort (all 3 assays). In a second verification cohort, Abbott hs-cTnI and AccuTnI+3 had a sensitivity of 100% but Elecsys hs-cTnT had a sensitivity of 82.4% (Shortt et al. 2015).
Abbott hs-cTnl and Elecsys hs-cTnT

Key results from studies that compared the Abbott hs-cTnl and the Elecsys hs-cTnT assays were:

- AUCs were not significantly different between groups tested with Abbott hs-cTnl and those tested with Elecsys hs-cTnT. The correlation coefficient between the 2 assays was 0.747 in the whole study population (0.732 in AMI patients). The optimal cut off for rule out was 14ng/L for Elecsys hs-cTnT (NPV 100%) and 10ng/L for Abbott hs-cTnl (NPV 99.8%) (Goorden et al. 2016).

- A rule out algorithm using Abbott hs-cTnl with a scoring system of 0 for <4ng/L, 1 for 4–14ng/L and 2 for ≥15ng/L (<2 points ruled patients out), gave an NPV of 99.4%. The Elecsys hs-cTnT with a scoring system of 0 for <5ng/L, 1 for 5–15ng/L, and 3 for ≥16ng/L gave an NPV of 98.3%. The Elecsys hs-cTnT identified fewer low risk patients than the Abbott hs-cTnl (11% vs. 15% respectively) (Kavsak et al. 2017).

- Using the pathways recommended in DG15, the overall sensitivity for Abbott hs-cTnl was 89.3% and the overall sensitivity for Elecsys hs-cTnT was 98.6%. The authors concluded that the DG15 recommendations could be improved by using stricter cut-offs (Parsonage et al. 2016).

- Using the 2015 ESC guidelines 0/1-hr algorithm, Elecsys hs-cTnT gave an NPV of 99.5% and a PPV of 63.4%. Abbott hs-cTnl gave an NPV of 99.8% and a PPV of 68.1%. Neither test achieved 99% sensitivity, which the authors suggested was unacceptable (Pickering et al. 2016).

- Using the 2011 ESC 0/3-hr algorithm (99th percentile cut-off), Elecsys hs-cTnT gave a sensitivity of 94.8% and Abbott hs-cTnl gave a sensitivity of 93.2% (Pickering et al. 2016b).

- AUCs for predicting AMI were similar between assays (Elecsys hs-cTnT 0.94 vs. Abbott hs-cTnl 0.93, p=0.619). In patients presenting within 3 hours of pain onset, Abbott hs-cTnl was significantly more accurate (AUC 0.92 vs 0.89 for Elecsys hs-cTnT, p=0.019). Elecsys hs-cTnT was more accurate when serial troponin testing was used (AUC 0.96 vs. 0.95 for Abbott hs-cTnl, p=0.004). The assays were not significantly different in predicting 24-month AMIs (p=0.07) (Rubini Gimenez et al. 2014).
Wildi et al (2017) compared 2 algorithms in both Elecsys hs-cTnT and Abbott hs-cTnI: the 2 hour-ADP algorithm (<99th percentile, ECG and TIMI risk score ≤1); and the 0/2-hour algorithm (<99th percentile and 0/2-hr absolute delta <4ng/L [Elecsys] or <6ng/L [Abbott]). Both assays had NPVs of 100% for the 2 hour-ADP and 99.9% for the 0/2-hour. 30-day MACE outcomes were not significantly different between the assays or algorithms. However, the 0/2-hour algorithm ruled out significantly more patients than the 2 hour-ADP.

Using the 2015 ESC guideline 0/1-hour algorithm, 24% of patients were in the observe zone, that is, not ruled out or ruled in. Compared with rule out and rule in patients, the observe cohort was significantly older, had a higher prevalence of pre-existing heart disease and there were more male patients. 15% of these patients had a final diagnosis of AMI. In the 24-month follow-up, deaths and AMIs in the observe cohort were similar to those in the rule in cohort. The observe group’s characteristics were not significantly different between Elecsys hs-cTnT and Abbott hs-cTnI, but the highest AUC for predicting AMI was achieved using Abbott hs-cTnI absolute delta at 0/3-hours (AUC 0.85) Nestelberger et al. (2016).

In the derivation cohort the rule out algorithm was determined to be either a 0-hour with cut off <2ng/L or a 0/2-hour with cut off <6ng/L; NPV was 99.2%. Rule in was 0-hour cut off ≥100ng/L or 0/2-hour delta ≥10ng/L; PPV was 87%. 25.5% of patients were not ruled in or out, and remained under observation. In the validation cohort, NPV for rule out was 99.4%, PPV for rule in was 74.5%, and 29.6% remained under observation. Overall, 30-day mortality was 0 in the rule out groups in both cohorts Lindahl et al (2017).

Abbott hs-cTnI and AccuTnI+3

There were no studies that compared Abbott hs-cTnI and AccuTnI+3.

Elecsys hs-cTnT and AccuTnI+3

Haaf et al. (2014) found that AUCs were not significantly different between groups tested with Elecsys hs-cTnT and those tested with AccuTnI+3. Mortality at 730 days was significantly predicted by Elecsys hs-cTnT (AUC 0.64, p=0.006) but not by AccuTnI+3 (AUC 0.57, p=0.189).

6.3.5 Cost-effectiveness

Three new economic evaluations related to high-sensitivity troponin assays were identified. Westwood et al. (2015) reported the original diagnostics assessment report.
Vaidya et al (2014) did a cost-utility analysis to assess the cost effectiveness of Elecsys hs-TnT compared with the conventional cTnT for the diagnosis of acute myocardial infarction, in patients presenting with chest pain in the Netherlands. The incremental cost-effectiveness ratio (ICER) estimated by comparing hs-TnT with cTnT was €4945 (£4389) per life year gained and €7370 (£6542) per QALY. The hs-TnT strategy had the highest probability of being cost effective at maximum acceptable ICERs between €8000 and €20,000 per QALY.

Kaambwa et al. (2017) reported a trial-based economic evaluation comparing Elecsys hs-TnT with conventional c-TnT in the management of suspected ACS in Australia. The participants treated under an hs-TnT report had higher total costs; cost difference of AUS$1285 (£629), mainly from increased inpatient stay costs. The ICER estimates were AUS$108,552 (£53,128) per adverse clinical outcome avoided (deaths, unstable angina or myocardial infarctions) and AUS$196,270 (£96,059) per QALY gained.

6.4 NICE’s research facilitation activities

NICE commissioned 2 pieces of work to explore the feasibility of further research to address the evidence gaps identified in the assessment for diagnostics guidance 15 and described in the research recommendations.

The objective of the first piece of work was to provide an overview of on-going research investigating the use of high-sensitivity troponin tests for the early rule out of NSTEMI in patients with suspected ACS and the feasibility of using existing audits to collect clinical outcome data. In May 2016 it concluded that:

- As noted in research recommendation 7.1, the AccuTnI+3 assay requires more primary research due to a lack of sufficient evidence. Because it is not novel, the manufacturers may be expected to provide such research.

- Collection of further outcome data through clinical audit, as proposed in research recommendation 7.2, will not generate the new evidence required. Prospective diagnostic cohort studies would be more suitable to explore possible variation in the performance of high sensitivity troponin assays and the optimal testing strategies for these assays in relevant subgroups.

- A moderate (Architect STAT) or large (Elecsys hs-cTnT) evidence base is available for answering recommendation 7.3 on early rule-out protocols. A systematic review and meta-analysis is advised.
Following completion of the first piece of work, a second piece of work was commissioned with an objective to assess the feasibility of further primary research on the diagnostic accuracy of the AccuTnI+3 assay. The conclusions were that:

- Information from Storrow et al. (2015) could be used to compare the assay with the other commercially available assays in DG15, as well as the use of standard troponin assays.

- A large study which was due for completion in October 2017 (NCT02789904) may provide diagnostic accuracy data to inform an update.

- Further research is likely to be expensive and would involve heavy investment of research resources. Funding would probably have to come directly from the company because as a “me too” technology it is unlikely that further research on the AccuTnI+3 assay would receive support from a grant funding body.

7. Summary of new evidence and implications for review

The clinical evidence base has expanded substantially since the original diagnostics assessment report was published in 2014. A large number of the included studies were focused on evaluating different diagnostic pathways such as early rule out algorithms and a few studies directly compared the performance of the assays. There were some studies which reported resource use data and end clinical outcomes data – evidence that was not available when the original assessment report was done. In addition, some studies suggested specific cut-offs for subgroups. In summary:

Recommendation 1.1 for the Abbott hs-cTnI and Elecsys hs-cTnT assays remains supported by the evidence.

Recommendation 7.1 called for further evidence on the AccuTnI+3 assay, because in the original DAR no published studies for the AccuTnI+3 assay were identified. In this review, 3 studies reported that that AccuTnI+3 could deliver NPVs of >99% (when using algorithms that involved absolute delta troponin; Storrow et al. 2015 and 2015b, and Cullen et al. 2013). Further, several studies reported that the AccuTnI+3 assay performs as well as the Elecsys hs-cTnT and Abbott hs-cTnI assays (Rubini Gimenez et al. 2013, Shortt et al. 2015, Twerenbold et al. 2015 and Wildi et al. 2016). However, Haaf et al. (2014) found that Elecsys hs-cTnT was better than AccuTnI+3 at predicting long-term mortality. Specialist committee members noted that the AccuTnI+3 is not used in hs-Tn algorithm pathways, and Beckman Coulter stated that a new version of the assay, the Access hsTnI, has been introduced.
Recommendation 1.2 stated that 'early rule-out protocols' should be used, which typically include a blood sample for cardiac troponin I or T taken at initial assessment and a second blood sample taken after 3 hours. It also recommended that absolute values should be reported and the cut-off should be set at the 99th percentile. Several studies found that absolute values alone did not deliver optimal diagnostic accuracy and the addition of absolute (but not relative) delta troponin significantly improved rule out accuracy (Badciong et al. 2013, Rubini Gimenez et al. 2014 and 2015, Shortt et al. 2014, Kavsak et al. 2013b, 2017 and 2017b, Boeddinghaus et al. 2016, 2017 and 2017b, Wildi et al. 2013 and 2017, Cullen et al. 2013, Goorden et al. 2016, Lindahl et al. 2017, Morawiec et al. 2017, Nestelberger et al. 2016, Parsonage et al. 2016, Pickering et al. 2016, Reichlin et al. 2015 and 2015b, Sandoval et al. 2017c, Su et al. 2015, Yokoyama et al. 2017, Mueller et al. 2014).


NICE’s guideline on chest pain of recent onset: assessment and diagnosis recommends that for people at low risk of MI, a single high-sensitivity troponin test can be done at presentation, and NSTEMI ruled out if the troponin test result is below the lower limit of detection.

Recommendation 7.2 called for further research into early rule-out protocols, and there is some evidence to suggest that these may be clinically viable. The 2015 ESC guideline proposed 0/1-hour and 0/2-hour algorithms and NICE’s guideline on chest pain of recent onset: assessment and diagnosis recommends that for people at low risk of MI, a single high-sensitivity troponin test can be done at presentation to rule out NSTEMI. Several studies have reported that these algorithms can deliver NPVs of >99% (Rubini Gimenez et al. 2015, Neumann et al. 2016b, Pickering et al. 2016, Reichlin et al. 2015, Cullen et al. 2013, Munro et al. 2015 and Wildi et al. 2017).

Recommendation 7.3 called for further research into clinical effectiveness of different test strategies and the impact on clinician behaviour. No randomised controlled trials were identified, however cohort studies were identified that reported clinical effectiveness. Some studies found significantly lower rates of mortality, subsequent AMI or MACE in patients ruled out as low risk by hs-cTn testing (Body et al. 2015,
Recommendation 7.4 called for further research into the underlying causes of troponin elevation in older people and people with conditions known to cause troponin elevation in the absence of ischaemia. The evidence confirms that troponin can be elevated in elderly patients who do not have ACS/AMI, but none of the included evidence addresses the underlying biological causes.

8. Implementation

All 3 of the technologies described in the guidance are still available and are in use in the NHS. Specialist committee members noted that the AccuTnI+3 is not used in hs-Tn algorithm pathways.

9. Equality issues

No new equality issues have been identified since the publication of the guidance.

Paper sign off: Mark Campbell

Contributors to this paper:

Technical Lead: Frances Nixon
Technical Adviser: Rebecca Albrow
Project Manager: Donna Barnes
## Appendix 1 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

<table>
<thead>
<tr>
<th>Options</th>
<th>Consequence</th>
<th>Selected – ‘Yes/No’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard update of the guidance</strong></td>
<td>A standard update of the Diagnostics Guidance will be planned into NICE’s work programme.</td>
<td>No</td>
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</tbody>
</table>
| **Accelerated update of the guidance**       | An accelerated update of the Diagnostics Guidance will be planned into NICE’s work programme.  
Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment. | No                 |
| **Update of the guidance within another piece of NICE guidance** | The guidance is updated according to the processes and timetable of that programme. | No                 |

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:

<table>
<thead>
<tr>
<th>Options</th>
<th>Consequences</th>
<th>Selected – ‘Yes/No’</th>
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<tbody>
<tr>
<td><strong>Transfer the guidance to the ‘static guidance list’</strong></td>
<td>The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.</td>
<td>Yes</td>
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<tr>
<td><strong>Produce a technical supplement</strong></td>
<td>A technical supplement describing newer versions of the technologies is planned into NICE’s work programme.</td>
<td>No</td>
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<tr>
<td><strong>Defer the decision to review the guidance to [specify date or trial]</strong></td>
<td>NICE will reconsider whether a review is necessary at the specified date.</td>
<td>No</td>
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</table>
Appendix 2 – supporting information

Relevant Institute work

Published

Chest pain of recent onset: assessment and diagnosis (2010; updated 2016) NICE guideline CG95

Acute coronary syndromes in adults (2014) NICE quality standard 68

In progress

Acute coronary syndromes NICE guideline. Publication expected May 2020

Emergency and acute medical care in over 16s: service delivery and organisation NICE guideline. Publication expected December 2017

Referred - QSs and CGs

None identified

Suspended/terminated

None identified

Details of new technologies

<table>
<thead>
<tr>
<th>Device (manufacturer)</th>
<th>Details (phase of development, expected launch date)</th>
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<tbody>
<tr>
<td>ADVIA Centaur High-Sensitivity Troponin I Assay (Siemens)</td>
<td>Available to the NHS</td>
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<td>Sgx Clarity cTnI assay (Singulex)</td>
<td>Available to the NHS</td>
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<tr>
<td>ST AIA-PACK cTnI 3rd-Gen (Tosoh)</td>
<td>Available to the NHS</td>
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### Registered and unpublished trials

<table>
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<tr>
<th>Trial name and registration number</th>
<th>Details</th>
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<tbody>
<tr>
<td>High-Sensitivity Cardiac Troponin On Presentation to Rule Out Myocardial Infarction. ClinicalTrials.gov Identifier: NCT03005158 Sponsor: University of Edinburgh</td>
<td>Assay: Abbott Architect hs-cTnl Design: A stepped wedge cluster randomized controlled trial. The primary efficacy end-point is length of stay from time of presentation until final hospital discharge and the primary safety end-point is survival free from type 1 or 4b myocardial infarction or cardiac death from discharge to 30 days. Status: Ongoing, but not recruiting</td>
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<tr>
<td>High-Sensitivity Cardiac Troponin T to OPTimize Chest Pain Risk Stratification. ClinicalTrials.gov Identifier: NCT02984436 Sponsor: University of Florida (Collaborator: Roche Diagnostics)</td>
<td>Assay: Roche Elecsys hs-cTnT Design: Prospective observational cohort study of ED patients with symptoms suggestive of ACS. Results from hs-cTnT will be used for research purposes only. Providers will be blinded to results and patients will be treated as per standard of care. Follow-up phone calls at 30 and 90 days. Status: Recruiting</td>
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<td>Aiming Towards Evidence Based Interpretation of Cardiac Biomarkers in Patients Presenting With Chest Pain. ClinicalTrials.gov Identifier: NCT02620202 Sponsor: Haukeland University Hospital</td>
<td>Assay: hs-cTnT and hs-cTnl (Abbott) Design: A cross-sectional observational cohort study to: investigate the ability of 2 hs-cTn assays to diagnose ACS and predict prognosis in different patient populations; to validate the suggested 1 hour protocol for rule in and rule out of ACS; to investigate different biomarkers ability to predict long term prognosis Status: Recruiting</td>
</tr>
<tr>
<td>Evaluation of hsTnl in the Management of Patients With Chest Pain in the Emergency Department. ClinicalTrials.gov Identifier: NCT02789904 Sponsor: National Heart Centre Singapore (Collaborators: Beckman Coulter GmbH, Abbott)</td>
<td>Assays: Beckman Coulter AccuTnI+3 and Abbott Architect Design: A chest pain registry will be set up to compare high sensitivity troponin I (hsTnI) versus high sensitivity troponin T (hsTnT) for all patients who present to the emergency department and require a blood draw. Status: Recruiting</td>
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<tr>
<td>High-sensitivity cardiac Troponin I and risk stratification in patients with suspected acute coronary syndrome: a collaborative meta-analysis. PROSPERO 2017 CRD42017059128</td>
<td>Assay: Abbott Architect Design: A systematic review and individual patient level meta-analysis to evaluate the use of high sensitivity cardiac Troponin I thresholds in the risk stratification of patients with suspected acute coronary syndrome. Status: Completed</td>
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Clinical evidence


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Confidential information is redacted.


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